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EDITORIAL

Let us take pride in caring: organ donation

Rohini Jagtap

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It's good to be blessed. It's better to be a blessing!

Anonymous

Recently in 2015, Pune city witnessed a coordinated action which resulted in reaching the heart at a moment's notice to Mumbai from Pune in record time. This was the first successful heart transplant in Maharashtra. Clockwork precision and concept of green corridors made it possible.Organ transplantation is one of the miracles of modern medicine and it has become a reality in tertiary care centers. It is gaining momentum in India. Transplants, as an option, have successful outcomes, and the number of people needing a transplant is expected to rise steeply due to an ageing population and an increase in organ failure.

In the last half century transplant surgery has transformed from research to life-saving surgery. Advancement in medical technology and immunosuppressive drugs have made the success rate encouraging. Transplantation is currently considered an accepted treatment modality for patients with end stage organ failure where therapy with drugs or restorative surgery is not feasible[1]. Transplant surgery is the platform that can give the jump to our healthcare and take it to a higher level of capability.

Organ donation is the process of giving an organ or a part of an organ for the purpose of transplantation into another person.

In nearly 40–50% of all fatal road accidents in the world, the cause of death is head injury leaving potential organ donors in India from road traffic accidents alone. Many of these deaths could be averted by timely organ transplants But still, unfortunately there is a deficit of organs available for transplants. Other causes of brain death such as subarachnoid hemorrhage and brain tumors would potentially add more numbers. Promoting the deceased donation program would not only help kidney transplants, but also liver, heart, pancreas, and lung transplants to thrive in the country.

Most of the organ donation in the country is performed annually between the relatives, means the person donate the organs only to his relative s. It is reported that annually around 4000 kidney and 500 liver live donations are being carried out by relatives to their patients in the various hospitals. Statistics are distressingly poor in case of heart or lung transplants. Around 20 heart and lungs are transplanted annually at the centres in Chennai whereas the demand is high. 2 lakhs cornea transplantation are required per year whereas only 50000 are being donated[3]. In India, Chennai leads in organ donation.

There is a need to increase the potential donor pool so that organs can be retrieved from the unrelated people also. The current organ donation for cadaver in India is around 0.34 PMP (per million population)[2]. This is an incredibly small and insignificant number compared to the statistic around the world. Spain is widely acknowledged as a world leader in organ donation.[3] It has the highest number of organ donation rate from brain dead patients at 33 per one million population. We, Indians, need to catch up and that too fast.

For every successful transplant there are many who are on the waiting list and probably die waiting to receive the graft. There are many challenges in organ donation and transplantation such as scarcity of organ donors, lack of public awareness, religious beliefs, family pressures the myths and confusions all contribute to bringing down the number of potential cadaver donors.

Currently, organ shortage is the main obstacle to the full development of the transplant programme. It should be tackled by increasing the cadaveric and promoting the living organ donation.

Worldwide thousands of lives are transformed by organ donation. The organs which can be donated are kidney, lungs, heart, liver, pancreas, small intestine. Tissue transplants e.g. skin, cornea, bone-marrow,vessels are also invaluable. Anybody, irrespective of age, caste, religion or race current or postmedical illness *except* HIV, autoimmune diseases and actively spreading cancer can donate the organs.

There are two ways to donate organs: -

1. By pledging for organ donation when a person is alive
2. By consent of family after death- cadaver donation

Two voluntary consent systems include :– 1.Opt In - where the donor gives consent 2.Opt Out - where anyone who has not refused is considered as a donor. In India we have the opt in system, while many western countries practice the opt out system.

Patients who have been declared dead using neurologic criteria are the single largest source of transplantable organs[4]

Brain death is defined as absence of brain stem reflexes, motor responses and respiratory drive in a nonthermic, non drugged, comatose patient with a known irreversible brain lesion and no contributing metabolic derangement[5].

To curb organ commerce and promote donation after brain death the government enacted a law called "The Transplantation of Human Organs Act (THOA)" in 1994 that brought about a significant change in the organ donation and transplantation scene in India[6]. It makes mandatory for transplants to register with an authority appointed by the state government. Many safeguards against misuse have been built in the rules. Cadaver organ donation surgeries can only be conducted at recognised centres. Maharashtra government accepted the amendments made to the Human Organ Transplant Act 1994 by the Centre in 2011 by consenting for including grandparents and grandchildren in organ donation and widened the definition of relatives to maternal and paternal uncle and aunts. The Act will now allow inter-State organ transplant. Another key change will be the formation of a state and regional registry of people waiting for organs. The Act also makes it mandatory for all hospitals with ICUs to report brain deaths. This is a welcome step taken by the government.

NOTTO- National organ and tissue transplant organization which works under the aegis of Directorate General of Health Services, Government of India situated at New Delhi. It lays down policy guidelines and protocol for organ transplantation. NOTTO has been commissioned and has two divisions: (1) National Human Organ and Tissue Removal and Storage Network (2) National Biomaterial Centre (National Tissue Bank).

The NOTTO website has become functional and operational guideline of NOTP has been released in 2015.

According to NOTTO, there were 14038 living organ transplants - Out of these 7476 were the near relatives who donated the organs and 6563 were given by others. It received 3947 donor pledges in 2014.[7]

Maharashtra government has established ZTCC to create awareness about organ donation among the people and to ensure fair distribution of organs in the concerned city. Zonal Transplantation Coordination Committee (ZTCC) is located in Mumbai.

There are 102 registered transplant centres in Maharashtra, which have the facility for retrieval of organs from brain-dead patients.

In Pune zone, Sassoon General Hospital functions as regional authorisation committee.

There is a wide gap between demand and supply of organs though potential organ donors are not less in number. We need to find a solution on how we can utilize the potentially large pool of trauma related brain deaths for organ donation.[8] This is possible with greater awareness about organ donation.

Various agencies such as the Mohan Foundation (Chennai, Hyderabad), Organ retrieval banking organization -ORBO (Delhi) and Zonal Transplant Co-ordinating centre (Mumbai). Other NGO's and organizations involved in organ donation are: Gift Your Organ Foundation, Shatayu ,Gift A Life and Dadhichi Mission.

There is a facility of online organ registry for the people all over India who are willing to donate organs on their own will. Organ registry ensures the proper organ donation as well as the fair use of donated organs in the future according to the priority of need and requirements of the organs to the recipients. Indian Society of Organ Transplantation initiated the Transplant Registry in India in 2005[9]. and Cadaver Transplant Programme was initiated by the Government of Tamil Nadu in 2009. It helps in saving crucial time in the process of organ donation.

Organ donor card provides access to donate organs after death. This facility is provided by the MOHAN Foundation to spread awareness all over the country and get organ pledges[10]. It is important to know that one always has the option to change one's mind by withdrawing the registration by informing the registry and letting the family know that you have changed your mind. We should encourage the people to join the organ donation registry and speak to their next of kin about their wishes.

Organ Donation Day is celebrated on 13th of August every year in order to motivate normal human beings to donate the organs as well as to understand the value of organ donation in the life of an individual. It provides a great opportunity in everyone's life to come ahead and pledge to donate their precious organs.

What can be done to increase the organ donation?

Since one cadaveric donor can provide multiple organs, this is a natural source to increase the number of available organs.

1. There is a need to change the mindset. Public education is important to modify attitudes and to create awareness among the people about the need of organ donation prior to a donation opportunity. Educational efforts focus on increasing the number of people who consent to be an organ donor before they die as well as educating families when they are considering giving consent for their deceased loved one's organs.
2. Medical students and nurses can also be motivated at entry level.
3. Social media engagement and national community awareness campaigns can make positive impact by spreading the messages of organ donation all over the country. A dynamic and motivated organ retrieval apparatus should be established at the national level[11].

It is observed that increased public engagement and strengthening of a shared view among professionals and the public in living donation practice and policy is important[12].

Organ donation is founded on the premise of altruism[13].

Receiving an organ donated from a living or deceased donor is a life changing event. Organ donation makes it possible for the person to get involved in selfless act of saving human life and even after death, a person can be remembered for his noble gesture.

DONATE ORGAN, SAVE LIFE!

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Ethics of Research in Children

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Research involving children is important, but among present unique challenges. Children represent vulnerable sub group. It is therefore incumbent on parents, researchers & institutions to ensure that their rights are protected & they are shielded from undue risk. In conducting child research, social researchers have paid growing attention to research ethics but whether those same researchers have focused correspondingly upon the rights of children and their inherent relationship with research ethics is questionable.[1] Surprisingly, the rights of children and ethical practice related to children have been ignored in the social sciences, professional practice, and research literature.[2]

The usual problems faced when any research has to be undertaken in children are

- Fear among parents that their children are used in clinical experiment as guinea pigs.
- The overpowering pressure of the pharmaceutical industry to pushthrough research at any cost.
- The pressure on the academicians to conduct research for professional advancement.

Medical literature is replete with opinions, explanations, advice & guidelines regarding various ethical aspects of conducting & publishing research. Morrow and Richards contend that `the biggest ethical challenge for researchers working with children is the disparities in power and status between adults and children.[3] Part of the task is to redress the power imbalance between child participant and adult researcher, in order to enable children to participate on their own terms. Ethics is today a subject of lively public interest. Research is important for the benefit of all the children & should be supported & encouraged. Research should be undertaken in children only if -

- Same question cannot be answered by research in adults.
- There is an identifiable prospect of benefit.
- Research must never be done for financial gains.
- The study should be well designed & there should not be any duplication.
- Poorly designed study & scientifically invalid research is unethical.
- The investigator should be qualified & ensure that the physical, emotional & psychological safety of a child &its family is safeguarded.

Key issues regarding research in children.

Risk vs. benefits:

While considering any research proposal the risk must be balanced against the likely benefit to the child. The risk includes -

- Physical discomfort.
- Inconvenience.
- Fright.
- Separation from the parents.
- Unfamiliar surroundings.
- Effect on growth & development.

There has to be clear cut distinction between therapeutic (with direct benefit) & non therapeutic (with no direct benefit), It is currently accepted that non therapeutic / research may be permitted if it presents no greater than minimal risk.

The National Children's Bureau's Guidelines for Research (1993) emphasize the duty of researchers to pass information `to a professional who can take the steps necessary to protect the child or other children'. However, others take the view that such a position can reduce the researcher's credibility.

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Consent:

While children are potentially compromised in each of the elements of informed consent, it is important to acknowledge that they live in an evolving context that may assist or hinder capacity by virtue of their illness and experience. Factors that may influence the adequacy of consent include information that is too complex or overwhelming in volume, parental or familial pressures that may curb voluntariness; and capacity, in part, related to neurocognitive development[4,5,6]

Child is legally unable to provide consent & so proxy consent of parents/guardians is a must informed consent must explain the purpose of research, the difference between treatment & research, the potential risk & benefits the care of adverse events if any. Consent must be voluntary without any financial inducement. Refusal to give consent by the parents should not jeopardize the child's treatment in any way. Most current guidelines require that child's assent should also be taken if he is old enough to comprehend usually six to seven years of age. A determined refusal of an older child to participate in a study must be respected despite parental consent.

Drug trials:

Pharmacy & physician are among the integral components of health care delivery system. Drugs are the basic tools available to a physician in treatment of illness. Virtually, daily a pharmaceutical weapon is added to the physician's therapeutics armamentarium. However there is a relative paucity of good medical research in children. Many medications that are widely used in children are rarely first tested on children.70% of the current medications lack sufficient data in children.[7] The US federal drug administration mandates that the pharmaceutical firms must recruit children in all their drug trial. If children are to be excluded from the clinical trial acceptable justification has to be provided.

We are currently in the midst of an onslaught of pharmaceutical company sponsored drug trial. Children who take part in the research trial must benefit by getting the best available treatment when the trial ends. Data through these clinical trials must be available freely even if it is unfavorable or insignificant.

ICMR (Indian Council Of Medical Research) special ethical guidelines:

Before undertaking trial in children the investigator must ensure that –

a. children will not be involved in research that could be carried out equally well with adults;

b. the purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children;

c. a parent or legal guardian of each child has given proxy consent;

d. the assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of seven years up to the age of 18 years.;

e. research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support;

f. interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society;

g. the child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/ tested, provided the consent has been obtained from parents / guardian;

h. interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions;

i. the risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.[8]

Recommendations:

National bodies must identify primary areas for research & direct funds to these areas.

There is urgent need to educate medical fraternity in India in basic research methodology& ethical principles if research has to improve.

Ethic should be part of medical curriculum. MUHS (Maharashtra University Of Health Science) has already proposed it to be implemented by 2006, the infrastructure & support for quality research needs to be strengthened.[9]

Negative media coverage must be proactively balanced with positive feedback about the social benefits of good clinical research. Public education & awareness campaigns would help to achieve this goal.

Research ethics may exist that fall outside the parameters imposed by such committees, making it necessary for researchers to think about 'researcher ethics' alongside 'research ethics' and for the guidelines themselves to reflect their co-dependency.[10]

Adherence to ICMR guidelines must be mandatory by law for conducting Research. Currently revised schedule Y of the drug & cosmetics rules governs trial in / India.

For critical surveillance the institutional ethical committee must play a role ofprotecting the rights of research subjects as envisaged in the declaration of Helsinki.

The committee must ensure that consistent ethical standards are followed so that participants from developing world are safe from exploitation.

Multicentric trials should be encouraged as it helps in recruiting large patient load in as shorter span of time & also enhances the cooperation between various institutions.

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REVIEW ARTICLE

Awareness Under Anaesthesia

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General anaesthesia is defined as reversible loss of consciousness & it is expected that an anaesthetised patient is oblivious of his surroundings & of the surgical intervention. Unfortunately sometimes there is failure to achieve sufficient depth of anaesthesia & the patient is aware of whatever is happening intra operatively.The term awareness under anaesthesia implies that during a period of intended general anaesthesia the brain is aroused by stimuli that are stored in memory for further explicit recall.[1]

In 2006 American society of anaesthesiology task force was established to study this problem which defined awareness as " consciousness under general anaesthesia with subsequent recall of the experienced event "[2]. Insufficient anaesthesia allows a state of consciousness that permits memory formation resulting in awareness [3]

This definition describes awareness as Awareness With Recall (AWR) but awareness can occur even without explicit recall. There are three types of awareness.

1) Amnesic wakefulness - Patient is aware intra operatively but postoperatively there is amnesia about this wakefulness. This awareness can be detected by Isolated Forearm Technique in which one arm is isolated from the effect of the neuromuscular blocker with the help of a tourniquet . The patient is instructed to indicate his awareness by moving the finger of that arm intra operatively. That movement is a proof of his / her awareness but it has been observed that in spite of the positive response, sometimes postoperatively the patient has amnesia about this wakefulness.[4] This is called amnesic wakefulness. A cochrane review of 51 year's data revealed that wakefulness was significantly more common than awareness [2]

2) Implicit awareness - There is awareness but there is no explicit recall. The events are stored in implicit memory & only indirect tests like word recognition test can diagnose this type of awareness. [4]

3) Awareness with explicit recall - AWR Here the patient may voluntarily speak about awareness in the postoperative period or it can be elicited by using a structured questionnaire (Brice questionnaire) in the postoperative period.

There are two types of memory in human brain [5]

a) Explicit memory - This is conscious recollection of previous experience. This is also called as semantic memory or factual memory. This develops at the age of three years, hence below that age AWR does not occur.[3,4]

b) Implicit memory - This is also called as procedural memory. This is an unconscious memory aiding in the performance of a task without any recollection of prior experience facilitating the task.

The implicit awareness phenomenon is more complex which needs neuro psychologic testing to discover traces of perceived sensory stimuli that remain concealed in the subconscious. The implicit memory can result in dreaming. [6]

The basic reason in the causation of awareness is the fact that in spite of remarkable advances in science, even today it is not yet completely understood how anaesthetics really act on the brain & there is no direct unit of measurement for unconsciousness. There are four components which are expected to be achieved during general anaesthesia.

1) Mental block - That is a state of hypnosis where perception is blocked along with consciousness & memory.

2) Sensory block - Analgesia is produced by blocking of pain perception

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3) Motor block - Blocking of muscle tension & stimulus triggered patient response

4) Reflex block - Blocking of autonomic, nervous & cardiovascular reactivity, prevention of blood pressure spikes &/or cardiac arrythmias

Exactly how the four components work together & determine overall level of anaesthesia is not understood.[6] In history, there was an era when all the components were achieved by using a single agent e.g. Diethyl ether which achieved Anaesthesia, Analgesia & Muscle relaxation - the three components constituting the triad of anaesthesia. Then the balanced anaesthesia technique came into existence. where combination of different drugs was used to produce the state of anaesthesia - inhalational / intravenous anaesthetic agents for mental block, narcotic analgesics for sensory block, neuromuscular blockers (NMB) for motor block & drugs like beta blockers to control the reflex response. With the use of balanced anaesthesia technique, anaesthesia became safer, more easily titratable, more patient friendly & allowed rapid reversal without many side effects as dose of each agent was reduced, but the flip side of this technique is, it can block the patient's response to light anaesthesia making it difficult to diagnose awareness intra operatively. The concomitant use of NMB has been implicated in many studies on awareness. In one study, in 11785 patients who had received GA, the incidence of awareness was 0.18% in cases with NMB & 0.10 % in cases where NMB were not used[7,8]. In the cases of awareness with the use of NMBs there was higher incidence of negative perception ranging from nightmares, agony to feeling of helplessness & powerlessness since these patients could not draw attention of the treating staff to the fact that they were aware as they were paralysed with NMBs

INCIDENCE -

A) In the absence of risk factors the incidence of this occasionally occuring critical event has been generally estimated to be 0.1 - 0.2 % (1 - 2 per 1000 cases) [6,9] but many new studies have shown lesser incidence. (Pollard et al 1 in 42000[10] in a 3 yr study of 80,000 patients & 5th national audit project NAP5 in Uk studying over 3 million cases across 5 countries -1 in 15000 cases [11] to 1 in 19000 cases [12])

B) In presence of risk factors the incidence is much higher. cardiac surgery (1 in 100) & obstetric surgery (4 in 1000)[13] Paediatric patients also show a much higher incidence of awareness. In different studies the figures vary from 0.6 - 0.8 % to 1.4 - 5 %[4,14] The reason for the higher incidence in paediatric age group is the higher requirement of the anaesthetic agent due to more rapid distribution of the anaesthetic agent. The MAC of the inhalational agents is higher in paediatric age group. The MAC is defined as concentration of the inhalational agent to abolish motor response to painful stimulus in 50% of subjects As the required MAC is higher, there are higher chances of administration of inadequate dose.

CAUSES OF AWARENESS & RISK FACTORS -

Absolute or relative inadequacy of dose is the main cause of awareness. The reasons for that & the risk factors are as follows -

1) Equipment malfunction / errors -

a) Faulty vaporizer delivering lesser concentration than the dial setting - This can be avoided by regular servicing of the equipment

b) Failure to fill the vaporizer or turn it on

c) Improper use of vaporizer - I have witnessed awareness under anaesthesia due to attachment of Goldman halothane vaporizer at the wrong side of Medisys ventilator

d) Selection of inappropriate agent - The speed of attainment of desired MAC by the anaesthetic agent depends on it's potency, blood solubility, fat solubility & volatality (boiling point). The newer inhalational agents like isoflurane, desflurane or sevoflurane can attain it pretty fast achieving fast induction. In old times, because of cost & availability constraint we were forced to use trichloroethylene (trilene) for longer cases which takes a very long time for induction. I still remember a case of complicated oesophageal surgery on a young chap who had explicit recall during surgery & repeated our conversations during surgery postoperatively. We were shocked to know this. Fortunately trilene is a powerful analgesic so the recall was entirely painless & there was no untoward sequelae. Usually during use of such agents, the agent has to be shut off pretty much in advance before the end of surgery as it's tremendous fat solubility is responsible for a prolonged recovery The awareness usually occurs either in the beginning before attainment of MAC or at the end of surgery when the

patient is coming out of anaesthesia. With newer agents with faster induction & recovery this danger has diminished.

e) Absence of alarms on the machine to indicate empty vaporizer or lower end tidal MAC than desired

f) If IV agent is being used, unobserved blockage of IV tubing or disconnection can cause awareness

g) Mis judgement of timing of switching off the vaporizer at the end of surgery

2) Inability to deliver sufficient concentration due to patient's condition - Now a days very extensive surgeries are performed in very compromised patients. All anaesthetic agent are cardio depressants. Patients with poor cardiac function or hemodynamically compromised patients like trauma patients in shock or after blood loss during surgery or during cardiac surgery, concentration of the agent has to be reduced as the patient does not tolerate it. In obstetric patients operated under GA higher concentrations can not be used in the parturient before delivery of the baby for the fear of neonatal depression. Due to these reasons, cardiac surgery, obstetric surgery, trauma surgery & emergency surgery are associated with higher incidence of awareness.[1] In emergency surgeries done at odd hours, the anaesthesiologist's fatiguability may be one more important contributing cause.

3) Obese patients - It is difficult to estimate the pharmacokinetics of the agent in obese individuals which may result in under dosing & increased chances of awareness [1]

4) Young patients & females - These are shown to have higher MAC values & higher incidence of awareness may be seen in them [15] According to some authors, the incidence of awareness is independent of age & sex [8]

5) Masking of physiological signs of light anaesthesia due to concurrent drug therapy [15] The clinical signs of awareness are due to sympathetic stimulation like hypertension, tachycardia, sweating, tear production & movement of the patient. There are various factors under anaesthesia like beta blocker therapy, vasodilators, antimuscarinic drugs, NMBs & other causes of sympathetic stimulation like blood loss which may mask these signs making intra operative diagnosis of awareness difficult

6) Resistance to anaesthetic drugs -

a) Drug abuse - Drug addicts, alcoholics, smokers, patients of chronic pain on long term opioid treatment, chronic use of sedative hypnotic agents & repeated exposure to anaesthetic agents are the conditions in which the patient's requirement for the anaesthetic agents increases, resulting in increased chances of awareness with administration of standard doses [6, 16, 17]

b) Pharmaco genetic basis to the resistance of anaesthetic drugs[17,18]- Studies have shown that immobilising dose of anaesthetics may vary as much as 24% in the populations with different genetic backgrounds[19] Recently , in mice it has been shown that genetic deficiency in one type of receptor for the inhibitory neurotransmitter Gamma amino butyric acid GABA (receptors containing alfa - 5 subunit called as GABRA5) conferred resistance to memory blocking property to anaesthetic etomidate [20] Poly morphism for this receptor 5 gene exists in human genome & at least 3 isoforms exist[17,18] Interestingly enough, expression of this memory blocking receptor changes after long term exposure to alcohol or persistent seizures, the conditions known to have anaesthetic resistance in humans

c) H / O awareness in previous surgery – The incidence of awareness is higher in these patients in next surgery [17, 21] They might be resistant to the action of anaesthetic agents due to genetic reasons or otherwise

MONITOTING DEPTH OF ANAESTHESIA -

There are no reliable monitors to assess the depth of anaesthesia. The monitoring can be done on following lines

A) Anaesthetic agent concentration monitoring -

a) Inhalational agents -If inhalational agents are being used monitoring of concentration of the anaesthetic agents in the exhaled gases is useful because there is a reasonable correlation between recall & exhaled MAC. Patients exhaling more than 0.8 MAC are unlikely to recall intra operative events & spontaneous recall is virtually eliminated if >1 MAC is exhaled by the patient[18]

Avidan et al [22] have shown that maintenance of 0.7- 1.3 exhaled MAC is as effective as EEG monitoring to prevent awareness. The limiting factors in the MAC monitoring are

i) Availability of AGM (anaesthesia gas monitoring) on the anaesthesia machine which may not always be possible

ii) Factors increasing alveolar dead space like hypotension, bronchodilators & emphysema may erroneously give high end - tidal MAC readings.

iii) By definition MAC value denotes the concentration required to prevent the motor response which is predominantly a spinal reflex. It does not directly refer to the patient's level of arousal. Also, MAC is a median value indicating loss of motor response in 50% of the subjects, therefore 50% patients may still move in response to a stimulus.

b) Intravenous agents - An equivalent concept to MAC in case of intravenous agents is MIC i.e. minimum inhibitory concentration., but there is even greater inter patient variability for dosage requirement with these agents. We don't have any means of measuring real time blood concentration of these agents like MAC [23]

B) Monitoring signs of anaesthetic depth - as mentioned above the signs of inadequate anaesthetic depth can be masked by concurrent drug therapy. Also it is not mandatory that all patients having awareness exhibit these signs. Tachycardia & hypertension are seen only in one in 5 patients of awareness [1]

C) Monitors developed to measure electrical activity. These can be divided broadly in two groups [17]

a) EEG based monitors - These analyze electroencephalographic activity using electrodes placed on patient's forehead.

b) Those that acquire & analyze evoked responses to auditory stimulus

a) EEG based monitors [23] - Anaesthetic agents suppress the normal EEG pattern in a dose related manner. Monitors like Bispectral Index Monitor (BIS) convert a single channel of frontal EEG into an index of hypnotic level. The target range is 40 - 60. Many studies proved usefulness of BIS in decreasing awareness (5 fold reduction,[24,] 82 % reduction[25]) To conclusively prove that EEG monitoring is effective in prevention of awareness, a prospective study has to be designed & considering the incidence of awareness as 0.1 - 0.2 %, the prospective study design should include 20,000 - 50,000 patients, which is quite impractical.[26] There are certain limitations of BIS like electrical interference, head low position, use of NMBs. NMBs may affect BIS & may show an erroneously low reading. [27] Ketamine may increase the electrical activity & N2O doesn't suppress EEG [23] Mychaskir et al demonstrated failure of BIS as a reliable monitor of depth of anaesthesia. Their patient had a horrifying experience of both hearing the sternal saw as well as feeling his chest being cut open during surgery when BIS was 47 under sevoflurane anaesthesia [18] The american task force did not consider the use of BIS as mandatory & advocates its use only when risk of awareness is considered high. In our country, the availability of BIS facility & AGM facility is not very frequent. Hence its use is still restricted only to few centers.

b) Auditory evoked potential - There are electrical responses of the auditory cortex to a sound stimulus. These (Midlatency auditory evoked potentials) change in a predictable manner with increasing concentration of volatile anaesthetic agent.AEP index is scaled from 0 - 100 & when AEP < 25, there is a low probability of awareness [18]

CLINICAL PRESENTATION OF AWARENESS -

Intra operatively awareness may be detected by intense tachycardia & hypertension, tears in the eyes, sweating & grimacing. There is a report of cardiac arrest due to awareness which was luckily revived[7] Usually a standardized interview - Brice questionnaire in the postoperative period helps to know the intra operative perception.

Brice questionnaire -

- What is the last thing you remember happening before you went to sleep ?

- What is the first thing you remember after waking up ?

- Can you remember anything that happened between these two points ?

- Did you dream or have any other experience while you were asleep ?

- What was the worst thing about your operation ?

The questionnaire helps to find out the type of awareness the patient has

The prevalence of perception of patients during intra operative awareness as per Sammuelsson et al &

Ghoneim et al is as follows [28,1,6]

Perception of Noise (85 – 100%), Visual (27 – 46%), Fear (78 – 92%), Helplessness (46%), Details of operation (64 %), Paralysis (60 -89 %) & Pain (41%)

Ghoneim et al [1] also reported that -

1) Patient movement was noted in about 1 in 7 patients

2) Tachycardia & hypertension was noted in 1 in 5 patients

3) Episodes were more frequent during maintenance, less during induction & emergence

4) 37 % cases reported awareness more than one week postoperatively

Analysis of compensation claims in USA showed that rise in B.P. was seen in 15% of cases & increase in heart rate in 7% cases. Movement was seen only in 2% of cases [29]

Sometimes the patient can experience out of body experience . A young lady undergoing nose surgery had an out of body experience with absolute maintenance of cardiovascular hemodynamics [21]. I personally know two patients who had a poor hemodynamic status intra operatively probably dictating decrease in the anaesthetic drug concentration & had an out of body experience during a CABG surgery

CONSEQUENCES OF INTRAOPERATIVE AWARENESS -

Awareness can be without any consequences but may lead to acute stress reaction followed by Post Traumatic Stress Disorder (PTSD). Pain free awareness is less disturbing than painful recall. I personally know one friend who developed a PTSD after a painful recall during malignancy surgery. She required a lot of counseling before her second surgery after the recall.

Cook et al have described following findings after 5th National Audit Project [30]

1) Patient's interpretation of what is happening at the time of awareness seemed to control the later impact.

2) Patient's experiences ranged from isolated auditory / tactile sensation to full recall

3) 75 % of the experiences were < 5 minutes duration but 51% experienced distress & 47 % suffered from long term adverse effects

4) Distress & long term harm is more common when patient experienced paralysis

5) 12.11 % had taken a legal action

In Pollard's study they observed following features [10]

- Most common complaints were auditory perception & loss of motor power
- Awareness may lead to both, immediate & late psychological problems
- Inability to move & feeling such as helplessness, anxiety & panic were significantly related to persistence of late psychological symptoms

Even in surgeries done under sedation & regional anaesthesia, psychological impact of unexpected explicit recall of events can cause distress & persistent psychological sequelae like AAGA (Accidental Awareness under General Anaesthesia) [31]

In cases of awareness where there is no explicit recall & only implicit memory formation, that can bring about changes in the patient's behavior postoperatively, may result in dreaming & can cause long standing psychological distress. It must be noted that perioperative dreaming not constituting awareness as also common (3 – 6 %)

On 30th Nov. 2007, a Movie "Awake" was released which is about a young patient who experienced awareness during cardiac surgery[17]. This has increased the public awareness of this problem

The psychological sequelae of this problem includes insomnia, depression, anxiety & PTSD[18] PTSD development is the most significant sequelae. Psycho pathologically, Post Traumatic Stress Disorder involves stress reactive impaired information processing.

CLINICAL SYMPTOMS OF PTSD - [6]

1) Re- living the trauma - e.g. agonizing recall of the trauma, flashbacks, nightmares, exaggerated emotional or physical reaction on exposure to cue.

2) Avoidance symptoms - avoidance of activities, places, thoughts, feelings

3) Emotional numbness - general lack of interest, detachment, restricted affect range

4) Hyper arousal - sleep disturbances, irritability or outburst of anger, difficulty concentrating, excessive

alertness, exaggerated startle reaction

MEDICOLEGAL IMPLICATIONS -

ASA closed claims analysis revealed that 2 % of all claims are for awareness [29] & almost all are granted. One patient got a compensation of 15000 lbs in the UK [21] Cook et al have shown that in 5 NAP study 12.11% patients had taken a legal action[21] Occasionally awareness occurs in spite of apparently excellent practice in the apparent absence of equipment malfunction. Successful defense against litigation requires that the anaesthesiologist has made thorough records of timing & doses of agents with exhaled concentration of anaesthetic agents & timing of start & end of surgery

PECULIARITIES OF AWARENESS IN PAEDIATRIC AGE GROUP -

■ Incidence of awareness is about 8 - 10 times higher in paediatric age group

■ In one study, 27% paediatric anaesthesiologists claimed to have seen awareness in a patient [3]

■ The explicit memory develops after 3 years of age, so there is no AWR till that age, but implicit memory develops during the first year itself, so implicit memory formation during awareness episode can not be denied in that age group

In a dutch study, H.S. Blurie et al have reported following observations [14]

◆ Self reporting is very rare

◆ Patients did not seem disturbed due to recall

◆ None was afraid to undergo anaesthesia again

◆ The memory of awareness was short lived

◆ PTSD is not common in paediatric age group, one year follow up of cases has shown no evidence of PTSD (Osterman study) but he has described one adult PTSD who had awareness in childhood

◆ Brain maturation & synapse formation occurs till the age of 5 years & BIS is not validated in this age group, hence BIS is not reliable

◆ Practice of anaesthetic induction in the induction room & shifting to O.T. may be responsible for awareness as the patient is likely to be light during transport. In India the anaesthetic induction is still done in the O.T. Itself decreasing this risk..

TREATMENT & PREVENTION OF AWARENESS STRATEGIES -

❖ Preoperatively the risk should be explained to the patient. This is particularly true in high risk cases

Royal college of anaesthesiology patient information booklet is available on the net [32]

❖ If awareness is suspected intraoperatively, immediately a benzodiazepine should be given which will ensure anterograde amnesia, if not retrograde amnesia & anaesthesia should be immediately deepened. Benzodiazepine premedication should be a routine practice. In long duration surgeries it should be remembered that the amnesic effect of a benzodiazepine may not last for the whole surgery & a dose may have to be repeated [32]

❖ Inadvertent & excessive use of NMB should be avoided

❖ Frequent calibration & checking of anaesthesia machines is mandatory

❖ Intraoperative close hemodynamic monitoring is desirable

❖ 0.8 - 1 MAC exhaled concentration of inhalational agent should be maintained

❖ BIS should be used in high risk cases

❖ Technical errors should be avoided

❖ When consciousness is lost, it is possible that acoustic signal transmission may reach the brain, hence acoustic protection for the patient by ear plugs, quiet room & silence in the O.R. is desirable

❖ Negative comments should be avoided

❖ Music can be provided via earphones

Preservation of acoustic signal transmission has been made use of for giving positive intra operative therapeutic suggestions which are not recollected by the patient, are recorded in the implicit memory & have a favorable effect on the patient's recovery. There are equivocal results of the effectiveness of this technique on the recovery of the patient.[6] I had carried out a study regarding such positive suggestions in SGH which had very promising results decreasing the need for analgesia in the postoperative period. During that study, we had

one patient who told in the postoperative period that somebody was continuously talking to him & giving instructions intra operatively. This must have been a case of awareness as there was an explicit recall of the suggestions. The suggestions were expected to have an effect at the implicit memory level. This patient of ours probably remained at a lighter plane than expected, hence the factual recall. All the same, the patient had a very good result as far as the postoperative analgesia was concerned.

❖ Postoperative evaluation of the patient by Brice questionnaire should be a routine practice The interview should be conducted 24 hours after surgery, on the third postoperative day & should be repeated one week postoperatively

❖ Good analgesia should always be ensured as, if at all awareness occurs, pain free awareness is less disturbing than a painful recall

❖ If the patient complains of awareness, it should be taken seriously. This is important medico legally also.

❖ A psychologist's help should be sought early

❖ Earlier intervention decreases chances of chronic sequelae, so patient should be counseled for that

RECENT ADVANCES ON THE HORIZON -

1) A new drug Penehyclidine HCL has been studied by a group of chinese workers for its effect on intra operative awareness in patients undergoing breast cancer surgery under GA. 0.01 mg/kg of P. HCL was given 30 minutes before surgery in the study group. Pre op anxiety score & post op Brice questionnaire was used (2-6 hrs & 24 - 48 hrs post op.) It was a double blind study on 920 patients . The incidence of awareness was 0 % in the study group as against 1.1 % in saline group. [33]

2) A research is published by MIT recently on slow waves on the EEG & unconsciousness. EEG monitoring & MRI imaging scan was done simultaneously It was shown that when slow brain waves on the EEG reach a plateau (state of slow wave saturation on the FMRI) - sensory signals no longer reached the thalamo cortical region which is linked with conscious awareness. So may be in future, we might get an individualized marker for unconsciousness which may help the anaesthesiologists to convert the rare critical event of awareness to a never event[34] & this dreadful complication can be successfully avoided .

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REVIEW ARTICLE

Pre-implantation Genetic Diagnosis

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Introduction

Preimplantation Genetic diagnosis (PGD) is an option for couples who are at risk of transmitting serious genetic diseases that enables them to have unaffected progeny without facing the risk of pregnancy termination after prenatal diagnosis. It is also used in assisted reproduction techniques to improve chance of conception for infertility cases with a poor prognosis[1].

Before PGD, couples at a high risk of conceiving a child with particular disorders would have to initiate the pregnancy and then undergo chorionic villous sampling in the first trimester or amniocentesis in second trimester to test the fetus for the presence of disease.

PREIMPLANTATION GENETIC SCREENING (PGS) & Preimplantation Genetic Diagnosis (PGD)

The term PGS is used to denote procedures that do not look for a specific disease but use PGD techniques to identify embryo at risk.

Preimplantation Genetic Diagnosis (PGD) Is Helpful for those patients with unexplained infertility, recurrent miscarriages, unsuccessful IVF cycles, advanced maternal age, or male factor infertility. In these cases the most likely cause is a chromosome abnormality.

Chromosomal abnormalities include aneuploidy and structural abnormalities. Aneuploidy is the most common. Structural abnormalities include Translocations, inversions and Deletions. The transmission of a chromosomal abnormality to an embryo can result in low implantation rate, miscarriage or the birth of a baby with genetic disorder. PGD can identify these specific genetic disorders in each normally developing embryo and only those embryos free of genetic disease will be transferred to the patients uterus so as to increase the chance of conception and ultimately healthy baby.

PGD is a poorly chosen phrase and both PGD and PGS should be referred as a type of embryo screening[2].

INDICATIONS AND CONDITIONS FOR PGD

Couples are at risk of transmitting a known genetic abnormality to their children. Only healthy and normal embryos are transferred in to the mother's uterus thus diminishing the risk of inheriting a genetic abnormality and late pregnancy termination (after prenatal diagnosis)

1. *Couples who are at a risk are those with the following disorder-*

- Monogenic disorders
- Autosomal recessive disorders (cystic fibrosis, beta thalassemia, sickle cell disease, spinal muscular atrophy type-1, Tay-Sachs disease)
- Autosomal dominant or X-linked disorders (myotonic dystrophy, huntingtons disease, Charcot-Marie-Tooth disease)
- X-linked disease (Fragile X syndrome, Haemophilia A, Duchennes muscular dystrophy)[2].

2. *Advanced maternal age(>37 years)* –

Advanced maternal age has higher risk of producing Anuploid embryos, resulting in implantation failure, higher risk of miscarriage or a birth of a child with chromosomal abnormality (e.g. Downs Syndrome). The following table shows the incidence of chromosomal abnormalities with advanced age[3].

Table1.1: Chromosomal abnormalities in advanced age[3]

Age (years)	Normal Embryos(%)	Aneuploid Embryos(%)	Other Abnormality(%)
25-35	61	8	31
36-37	60	10	30
38-39	47	18	35
40-41	43	26	31
42-44	39	30	31

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3. Recurrent pregnancy loss –

PGD can be performed for couples with a balanced translocation, allowing them to implant only chromosomally balanced embryos, thus reducing their risk of miscarriage.

4. Unsuccessful IVF cycles and Unexplained infertility–

PGD dramatically improves the chances of successful IVF pregnancy in couples where prior IVF failures have remained unexplained.

5. Male Factor Infertility-

Various genetic defects have been found to be associated with male factor infertility. This includes aneuploidy, most commonly Klinefelter's Syndrome, Robertsonian translocation, Y chromosome microdeletions, androgen receptor mutations (e. g. Cystic fibrosis trans-membrane conductance regulator gene and sex hormone binding globulin gene mutations). In patients with severe male factor infertility, PGD/PGS may not increase pregnancy rate but also limit the prevalence of chromosomal abnormalities.

6. Mitochondrial disorders –

Mitochondrial DNA associated (mtDNA-assosiated) Leigh syndrome and Neurogenic ataxia retinitis pigmentosa (NARP) are transmitted by maternal inheritance. For couples increased risk of these Mitochondrial disorders PGD is possible by analysis of mtDNA extracted from single blastomerses[4].

7. Human Leukocyte Antigen Matching –

among the new indications of PGD is preimplantation human leukocyte antigen (HLA) matching. It provide potential donor for stem cell or bone marrow transplantation to an affected child with recessive diseases, including thalassemias or acquired malagnacis such as leukemia[5].

COUNSELLING

GENETIC COUNSELING

It is sharing of information and advice about inherited conditions. Counseling depends on an accurate diagnosis and is mandatory for PGD. It provides appropriate and sufficient information to allow patients to give informed consent to PGD.

It includes the following issues[6];

- Explanation of nature and severity of inherited genetic disorder
- Mode of inheritance of disorder and recurrence risk
- Number of embryos expected to be affected according to Mendelian ratios
- Testing only for genetic disorders previously characterized for that couple and for which testing is available
- Information on specific laboratory tests to be used and their limitations
- Reliability of PGD, chance of misdiagnosis or adverse outcomes, and possibility of allele dropout
- Decision-making about transfer of carrier embryos and disposition of affected embryos or undiagnosed embryos.

TREATMENT RELATED COUNSELING

- Description and details regarding IVF/ICSI procedures
- Number of embryos to be transferred and the possibility that all embryos are affected
- Risk of multiple pregnancy and miscarriage
- Cost of treatment and the risk of medical complications during ovarian stimulation or oocyte retrieval.

PATIENT SELECTION

For appropriate patient selection for PGD, a team approach involving the geneticist and gynecologist is before starting treatment. A complete evaluation of IVF and PGD is required and relevant documentation to be maintained. This includes following:

- Written informed consent.
- Genetic counseling report including detailed pedigree and family history data.
- Documents of DNA tests or other specific tests of affected child and appropriate family members.
- Other preliminary tests in conjugation with IVF/ICSI with respect to both male and female reproductive history.

TECHNICAL ASPECTS OF PGD

INTRACYTOPASMIC SPERM INJECTION (ICSI) –

In majority of reported cycles, ICSI used instead of IVF. The main reasons are to prevent contamination with residual sperm adhered to the zona pellucida and avoid unexpected fertilization failure.

EVALUATION OF EMBRYO

The two main steps of implantation genetic studies are

- Obtaining nuclear material for genetic analysis
- Analyzing methodologies

Obtaining nuclear material for genetic analysis

There are three methods for obtaining nuclear material for genetic studies from the oocytes/embryo

1. POLAR BODY BIOPSY-

for aneuploidy screening and single gene defects involving maternal mutations both first and second polar bodies are biopsied from zygotes following IVF/ICSI procedures for either chromosomal or single gene defect analysis[7].

Polar bodies do not contribute structurally to the developing embryo. The embryo integrity is maintained in polar body biopsy and therefore it is a safe technique. However the main drawback is that the polar body analysis can detect only maternally transmitted genetic or chromosomal abnormalities. Paternally derived defects and those originating after fertilization post zygotic cannot be diagnosed by this technique[8]. Low quality of polar body chromosomal spreading can limit the accuracy and reliability of FISH analysis

2. CLEAVAGE STAGE BIOPSY-

Cleavage stage biopsy or blostomere biopsy is the most commonly used biopsy technique. Non contact infrared lasers are now used for zona drilling and embryo biopsy. One or two blastomeres are biopsied for analysis on the third day when the embryos reach the 8 cell stage. Cleavage stage biopsy is performed before compaction, the process of intracellular adhesion and junction formation. Embryo transfer is performed on day 4/5, allowing time for analysis. Disorders of both maternal and paternal origin, as well as those originating after fertilization, can be checked from blastomeres obtained on the third day. The implantation rates for the biopsied embryo are lower. There is evidence for significant chromosomal mosacism in cleavage stage embryos. Therefore biopsied cell may not be representative of the whole embryo[9].

3. BLASTOCYST BIOPSY-

on day 5/6, the embryo becomes a blastocyst containing approx 150 cells. Cells are differentiated into an inner call mass and trophoectoderm cells. The trophoectoderm cells may be biopsied safely. More number of cells can be obtained for examination at this stage without compromising the embryo. However the time left for diagnosis is very small as the embryo should be transferred before day 5 or 6. The clinical application of this technology is recent and only limited data has been reported.

ANALYZING METHODOLOGIES

1. Polymerase chain reaction (PCR)

PCR is used for the diagnosis of single gene defects, including dominant and recessive disorders.

This technique enriches DNA for a specific oligonucleotide fragment. After 30 to 40 cycles an initial minute quantity of DNA is amplified several times. This then, is subjected to analytical technique to determine the presence of point mutations deletions, insertions and other genetic markers. Direct sequencing of DNA can also be performed. Studies on DNA are performed using ethidium bromide staining of separated DNA fragments on agarose gels. Currently, fluorescent PCR has been used when fragments are separated and identified using color fluorochromes. This method is more sensitive and accurate[10].

Whole genome amplification

The PCR technique amplifies only the genetic area of interest, where as the whole genome amplification (WGA) amplifies the whole genome, producing many times more DNA for analysis. This can then be applied for diagnosing a huge range of genetic disorders

PCR has 3 pitfalls

I. *Amplification failure* – It occurs in about 10% of isolated blastomers. The main causes being the biopsy technique, premature cell lysis and PCR conditions.

II. *Allele Drop-out (ADO)* – It occurs when one of the two alleles present in a cell is amplified to detectable level. ADO may affect either of the allele in a heterozygous cell. The absence of mutated allele

may be due to drop-out, and this may result in misdiagnosis of affected fetus as normal.

III. *Contamination* – Contamination may arise from the fact that many spermatozoa are still lying in subzonal space after IVF. This may be mistakenly sampled with blastomere, second polar body or even trophoectoderm cells during embryo biopsy. This pitfall can be eliminated by ICSI instead of IVF.

2. *Fluorescent in situ hybridization (FISH)*

The FISH technique is most commonly used for determination of sex for sex linked diseases, chromosomal abnormality and aneuploidy screening.

FISH applies chromosomal specific probes for up to 9 chromosomes on a single blastromere. FISH probes are labeled with different colored fluorochromes that bind to specific gene sequences on specific chromosomes. Although it allows the evaluation of only limited number of chromosomes (between 5 to 9), FISH can still detect over 80% of all chromosomal abnormalities. The common probes used are those most likely to be anueploid in spontaneous abortions such as 13, 16, 18, 21, 22, X and Y. because probes hybridize to a specific locus, FISH provides information only about very small segment of the chromosome. This allows for selecting out abnormal embryos and choosing normal embryos for transfer. The primary use of FISH is to determine sex chromosomal content for couples at risk of various sex linked disorders such as hemophilia and for chromosomal abnormalities. The FISH technique is limited because only a few chromosomes can be identified at a time. A complete karyotype that will provide maximum information cannot be obtained by FISH technique[11].

3. *Comparative genomic hybridization (CGH)*

Comparative genomic hybridization (CGH) is relatively new and still experimental technique. It is a molecular cytogenetic technique based on the analysis of genomic DNA and does not require metaphase chromosome. CGH analyzes the entire chromosomal complement. However plyploidy and balanced translocations can not be detected by CGH. It also takes long time, abut 72 hours which limits its use.

DIAGNOSTIC METHOD FOR SINGLE GENE DISORDERS

I. *Gender Determination and Diagnosis of Chromosomal Aneuploides*

Sex detection was done in early days of PGD to avoid the transfer of embryos affected with X linked disease such as Hemophilia[12]. PGD for sex selection, in order to prevent the birth of healthy female carriers of X linked recessive disorders, thereby avoiding reproductive dilemmas for future children related to serious health risks for grandchildren has also come up.

At present, FISH is used for sexing of embryos and to detect most common chromosomal Aneuploidies associated with birth defects and early pregnancy loss. FISH has also been used for PGD for chromosomal abnormalities such as translocation.

II. *PCR-based Diagnosis*

Polymerase Chain Reaction (PCR) allows the amplification of well defined DNA sequences enzymatically in an exponential way.

III. *Nested PCR*

Here first PCR reaction of typically 20-30 cycles is followed by second PCR round, with a few micro liters of first PCR product used as template. The primes in second PCR amplify a sequence smaller than in first PCR product[13].

IV. *Fluorescent PCR*

In this technique a fluorescent oligonucleotides, labeled at the 5' end with a fluorochrome, can be substituted for one of the primers used for the gene amplification by PCR. This will produce fluorescent DNA fragments that can be separated by electrophoresis. It is very sensitive and accurate method. Fluorescent PCR product detection is over thousand times greater than the conventional PCR product analysis and moreover the time required is also lesser and screen[14].

V. *Multiplex PCR*

With multiplex genomic analysis (multiplex PCR) it is possible to amplify and screen multiple segments of a gene for mutation analysis. This rapid and single technique permits the detection of many single gene disorders from one cell within 6 to 8 hours, allowing embryo transfer the same working day, which is great advantage for patients undergoing PGD.

VI. Primed in situ Labeling

The Primed in situ Labeling (PRINS) technique represents a relatively new approach to the detection of specific DNA or RNA sequences in situ, and therefore, can be used for single blastomers spread on microscope slide. This method consists of annealing of chromosome-specific primers, followed by Taq polymerase driven extension and thus resembles PCR. However, in this case, replication occurs in the glass slide rather than in a tube and in the presence of labeled nucleotides. This leads to generation of a fluorescent signal on chromosomal nuclei[15].

EMBRYO TRANSFER

Embryo transfer is usually performed on day 3 or 5 post fertilization, the timing depending on the techniques used for PGD and standard procedures of IVF center where it is performed. It is recommended that selection criteria for embryo transfer are based primarily on unaffected diagnosis and secondarily favorable embryo morphology. Transfer of carrier embryo (autosomal recessive or X-linked disorder) is acceptable if healthy embryo is not available, since adverse health consequences to the resulting child are unlikely. In Europe single embryo transfer policy is implemented now. If more than one embryos are suitable for transfer rest of the embryos can be cryopreserved for use in another cycle.

FOLLOW UP

An important aspect of PGD is confirmation of diagnosis by follow up of pregnancies (including multiple pregnancy rate and outcome), prenatal testing, deliveries, the health of children at birth and beyond, which should be carried out along with appropriate data.

TECHNICAL PROBLEMS AND LIMITATIONS

- An older women produces less number of embryos, making it inappropriate to apply the technique in this situation .
- PGD/PGS does not detect mosacism.
- Increasing embryonic mosacism with increasing maternal age makes PGD less accurate in older women.
- The FISH probe binds to very small area of chromosome and does not provide information on rest of chromosome.
- FISH does not detect chromosomal structural abnormalities.
- Other technical problems that may be encountered are
  - Contamination of PCR sample
  - Failure of DNA amplification
  - Loss of nuclear material during fixation
  - Overlapping of signals
  - Background staining
  - Split spots
  - Non-diagnosis due to allele droup-out
  - Misdiagnosis

RECENT ADVANCES IN PGD

Late Onset Disease- PGD for Alzheimers disease

Verlinsky et al.[16] have reported the use of PGD by a women who carried a gene for early onset Alzheimers disease (AD) and who is wish to have a child that would be free of that condition. PGD was carried out and she gave birth to a child free of that condition.

Cancer Predisposition Syndrome

PGD can be used to avoid the birth of children who are healthy at birth but face a higher than average risk of having cancer or some other serious disease. The procedure was performed for patients with predisposition to familial adenomatous polyposis coli, Von Hipple-Lindau syndrome (VHL) and Retinoblastoma with successful outcome of healthy children.

PGD for Sex Selection

Many couples request PGS for sex selection, which can be motivated by cultural, social, psychological, and other reasons, such as the desire for family balancing, which is possible because of PGD. The use of PGS for sex selection unrelated to disease is controversial with the danger of Sex discrimination.

PGD for Non-Medical Traits – Inherited deafness

Tests for GJB2 mutations - the largest known contributor to inherited deafness, if available, will lead to people with a family history of deafness to possibly request PGD to screen out embryos with mutation, in order to

increase their chances of having a child without hearing disability.

Conclusion

PGD/PGS is a very good option for couples who are at risk of transmitting genetic diseases in In Vitro Fertilization set-up. It benefits the couple by providing unaffected healthy child. It also improves the success rate of IVF and decreases the chances of recurrent abortions due to chromosomal anomalies. PGD/PGS Should be still considered experimental and offered in trial setting and more research needed for its wide application.

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ORIGINAL ARTICLE

Sensitivity and specificity of ADA levels in Broncho Alveolar Lavage Fluid (BALF) with solid culture as gold standard in diagnosis of sputum smear negative Pulmonary Tuberculosis.

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ABSTRACT

Background : ADA has been proposed as useful marker of TB pleuritis, pericarditis, and peritonitis. Its diagnostic value in BALF in pulmonary TB remains ambiguous. **Aim:** To find diagnostic value of ADA in the BALF of TB patients in western Maharashtra. **Materials & methods :** This cross sectional observational study done for 1 year in B.J. G.M.C., Pune included adult patients with symptoms suggestive of tuberculosis with AFB negative sputum smears subjected to bronchoscopy. BALF samples were submitted for cytology, ZN stain, solid culture & ADA levels. **Results & Conclusion:** Sensitivity, specificity, PPV, & NPV of ADA in BALF were 50%, 52.78%, 19.05%, & 82.61%, respectively. ADA activity in the bronchoalveolar lavage was not clearly diagnostic of smear-negative pulmonary TB.

Key words: ADA, BALF, TB.

Introduction

Tuberculosis (TB) is a major global health problem. The clinical manifestations of TB are highly variable, depending on the affected organ, which are usually the lungs. Symptoms range from asymptomatic, to non-specific complaints, to mild respiratory symptoms, to respiratory failure. Radiographically, TB can present with varied patterns of abnormality on chest radiographs, mimicking other pulmonary diseases. The gold standard TB diagnosis requires the growth of Mycobacterium in specimen cultures and confirmation with biochemical tests or DNA probes. However, sensitivity is low.[1, 2] Other diagnostic methods have been developed and investigated in order to improve the diagnostic rate of TB.

Adenosine deaminase (ADA) has been proposed as a useful surrogate marker of TB pleuritis, pericarditis, and peritonitis. However, its diagnostic value in bronchoalveolar lavage fluid (BALF) in the diagnosis of pulmonary TB remains ambiguous.[3,4,5,6,7] Therefore, the aim of this study was to determine diagnostic value of ADA activity in the BALF of patients with TB in western Maharashtra.

Material & Methods

This was a cross sectional observational study done for a period of one year in department of pathology, B.J. Government Medical College, Pune. It included adult patients with symptoms suggestive of tuberculosis fulfilling the WHO criteria for clinical diagnosis but with acid-fast bacillus (AFB) negative sputum smears who were subjected to bronchoscopy for diagnostic evaluations of pulmonary diseases at BJGMC, Pune. Written informed consent was obtained from all patients before starting the bronchoscopy procedure. This study protocol was approved by the Institutional Ethics Committee of B.J.G.M.C. and S.G.H., Pune.

Sputum samples were collected & submitted for solid culture. BALF samples were obtained & submitted for cytology, ZN stain, solid culture & ADA levels. BALF was collected according to standard guidelines using fixed quantity (100ml) of normal saline. BALF was centrifuged & smears were prepared, air dried & stained with Leishman stain. ZN stain was done using 20% acid

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alcohol. Solid culture was done on sputum samples with L J medium. Standard data collection tools as recommended by WHO & CDC were used for collecting data.

BALF was centrifuged at 6000 rpm for 10 min and the ADA activity of the supernatant was measured using the ADA assay kit (Tulip Diagnostics).

Sensitivity and Specificity of ADA levels were estimated with solid culture (sputum/BALF) as a gold standard. We also estimated a 95% Confidence interval for sensitivity and specificity. A ROC curve was estimated for several levels of ADA. The level of ADA was selected as a cut-off for TB diagnosis for which the area under the ROC curve was maximum. We also estimated the positive and negative predictive values of the selected ADA levels for TB diagnosis among sputum negative patients with clinically suspected TB. Those patients who had positive sputum or BALF cultures for AFB were selected as the pulmonary TB group; those who had other forms of pulmonary diseases and were negative for TB were included in the non-TB lung disease group. Mean ADA levels in BALF were measured and compared.

Results

Eighty eight patients were enrolled in this study. Sixteen patients (10 males, 6 females; mean age: 39.87±23.54 years) had pulmonary TB, 72 (54 males, 18 females; mean age: 47.03±14.47 years) had non-TB lung disease. Sputum culture and BAL culture were positive in 6 and 10 patients, respectively, in pulmonary TB group. As a whole, all TB patients had positive sputum culture or positive-BAL culture. In the non-TB lung disease group, sputum smear and culture and BAL culture were negative for TB.

ADA levels in BAL fluids of pulmonary TB group and non-TB lung disease group were 5.38 ± 6.71 IU/L, and 6.38 ± 8.22 IU/L, respectively.

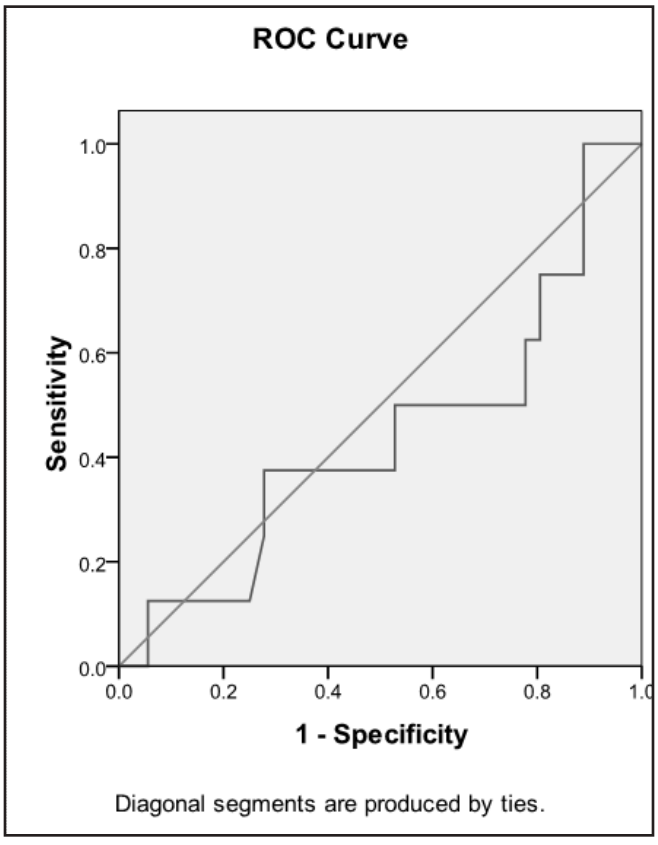
To determine the best predictive value of ADA levels in diagnosis of pulmonary TB, a ROC curve was used. (Figure1) Area under curve was 0.439 with 95% confidence interval of 0.207 to 0.672. It did not show a significant difference (P = 0.594). Using cut-off point in ADA = 2.19 IU/L, the sensitivity, specificity, positive-predictive, and negative-predictive values were 50%, 52.78%, 19.05%, and 82.61%, respectively.(Table1)

Table 1: Association between ADA level and culture

ADA (IU/L)	Culture		Total
	Positive	Negative	
<2.26	8	34	42
≥2.26	8	38	46
Total	16	72	88

Sensitivity = 50% Specificity = 52.78% PPV = 19.05% NPV = 82.61%

Figure1: ROC curve.



Discussion

Our findings showed no significant difference in ADA levels among two groups. ADA is an enzyme that increases in TB because of the stimulation of T-cell lymphocytes by mycobacterial antigens. Since 1978, when ADA activity was found to be high in tuberculous exudates[8], ADA has been used in the diagnosis of tuberculosis.[9, 10] The laboratory method for measuring ADA is inexpensive and relatively simple to perform. Thus, it may be useful in laboratories with limited resources, particularly in developing countries such as India. Orphanidou et al. [11] compared ADA activity and lysozyme levels in BAL fluid of smear-negative pulmonary TB patients and non-TB lung disease patients and found that there was no significant difference in lysozyme level of BAL fluids between the two groups, but ADA level in BAL fluids of pulmonary TB patients was significantly higher than that of non-TB lung disease patients ($P < 0.001$). In a study conducted by Kubota et al.[12] mean ADA level in BAL fluid of miliary TB patients, sarcoidosis patients, idiopathic interstitial pneumonia patients, and control group was 5.02 ± 3.75 IU/L, 1.06 ± 0.99 IU/L, 0.21 ± 0.43 IU/L, and 0.3 ± 0.51 IU/L, respectively, and ADA level in BAL fluid of miliary TB patients was higher than that of other groups ($P < 0.01$). In a study by Kayacan et al.[3], ADA level in BAL fluids of pulmonary TB patients, non-TB lung disease patients (like interstitial lung disease, lung cancer, pneumonia, and COPD) and controls was 3.1 ± 2 IU/L, 0.4 ± 0.5 IU/L, and 0.2 ± 0.4 IU/L, respectively, ($P < 0.001$). However, Reechaipichitkul et al.[7] compared ADA levels in BAL fluid of pulmonary TB patients, lung cancer patients, and those with other forms of pulmonary diseases and found no significant difference among these three groups ($P = 0.56$).

Orphanidou et al.[5] showed that ADA level in BAL fluid of patients with pulmonary TB is significantly higher than that of other pulmonary diseases. On the other hand, Boonsarngsuk et al.[13] revealed that BALF ADA had limited value in differentiating pulmonary TB from some other pulmonary diseases. In our study, the mean ADA activity in the bronchoalveolar lavage for the pulmonary TB and non TB lung disease groups was 5.38 ± 6.71 IU/L, and 6.38 ± 8.22 IU/L respectively. No difference was detected in the ADA level in the pulmonary tuberculosis vs nonTB groups ($p=0.594$). We found that ADA activity in the BALF was not clearly diagnostic of smear-negative pulmonary tuberculosis. Our findings correlated with those of Reechaipichitkul et al. and Boonsarngsuk et al.[7,13] To explain these discrepancies, differences between reported ADA levels and their sensitivity and specificity in different studies, it must be considered that it may be due to different methods of ADA measurement, presence of other diseases, and differences in the technique of bronchoalveolar lavage. In addition, BAL fluid ADA activity may differ from one human race to another. [14] It seems, therefore, that the cut-off value should be ideally based on the results of local studies or studies performed in similar populations and with the same methodology. TB epidemiology is also important. It should be noted that the value of any diagnostic test has been related to its disease prediction ability. Positive predictive value (PPV) in diagnostic studies is related to disease prevalence and thus in population with lower prevalence we suspected to have low PPV. On the other hand it should be remembered that the predictive value of ADA depends not only on its sensitivity and specificity but also on the local prevalence of the disease. When the prevalence rose, the PPV increased.[15] The opposite relation refers to negative predictive value (NPV). Furthermore, most studies are on the total ADA level, but ADA isoenzymes may be more accurate. We were unable to determine ADA isoenzymes.

Conclusion

We concluded that ADA activity in the bronchoalveolar lavage was not clearly diagnostic of smear-negative pulmonary tuberculosis.

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ORIGINAL ARTICLE

Role of PMMC (Pectoralis Major MyoCutaneous) flap in the era of free flap for reconstruction in oral cavity malignancies.

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ABSTRACT

MATERIAL AND METHODS : Prospective Study of 30 cases ages ranging from 30-60 years with F:M ratio 2:28 of oral cavity malignancies managed by composite resection that comprised of wide excision of lesion with 1 cm tumour free margin along with modified radical neck dissection & reconstruction by PMMC flap at Sanjeevan Medical Foundation in 2013-14.

AIM & OBJECTIVES :

1. To study efficacy of PMMC flap reconstruction in oral cavity malignancies.

2. To study complications of PMMC flap reconstruction in oral cavity malignancies.

RESULTS : In a study of 30 cases, 8(26.6%) patients underwent only surgery, 20(66.6%) patients underwent surgery and received radiotherapy, 2(6.6%) patients were treated as surgery f/b chemoradiotherapy.

Out of 30 patients in 22(73.3%) patients PMMC flap is survived without any complications, In 03(10%) patients partial flap necrosis is seen, In 02(6.6%) patients wound infection is seen, In another 02 (6.6%) patients wound dehiscence is noted, single patient (3.3%) found with orocutaneus fistula.

CONCLUSION : The results from the present study emphasize that PMMCs are a reliable, versatile and feasible type of pedicled flap for head and neck reconstruction.

Though microsurgical free flaps are superior to PMMC flap, it has certain shortcomings especially in developing countries like need of a well developed plastic and reconstructive department, trained personnel, long learning curve, relatively high incidence of failure, need for specific infrastructure, cost factor and time limitations. For these reasons, pedicled flaps continue to play an important role in many institutions worldwide, with special regard to cancer treatment centres in developing and emerging countries. Among these flaps, pectoralis major myocutaneous flaps (PMMCs) are undoubtedly the most reliable and versatile type of flap and are still considered to be the "workhorse" in head and neck reconstruction...

KEYWORDS : Pectoralis major myocutaneus flap, PMMC, Head and neck surgery.

Introduction

Oral malignancy is one of the commonest malignancy seen in our country. Annually, almost 7% of all cancer deaths in males and 4% in females have been reported due to oral cancers.[1] This is basically because of the widespread habit of chewing various irritants. Consumption of alcohol acts synergistically as a risk factor.

Agency for Research on Cancer[2]. Different therapeutic options for oral cancer include surgery, radiation therapy, or chemotherapy or a combination of treatments Surgical excision of the primary and the cervical lymph nodes remains the mainstay of the treatment followed by adjuvant radiotherapy and/or chemotherapy. After extensive resections there are functional, cosmetic and psychological effects on the patients. A variety of functions like speech, deglutition, and mastication may be affected which needs to be managed with proper reconstructive options and rehabilitation.

The Pectoralis major myocutaneous (PMMC) flap is quick, easy to harvest and reliable. This flap is used in most head and neck reconstruction sites. Its rich blood supply by thoraco-acromial artery makes the flap extremely safe, as regards its viability and resistance to the infections.[3] It neither involves any complicated measurements nor requires special instruments. PMMC and its modifications were used in resectional surgery for malignancy of the oral cavity with minimal morbidity and no mortality.

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PMMC flap in head and neck cancers has earned the synonym "WORK HORSE" of head and neck reconstructive surgery replacing the deltopectoral and forehead flap as a flap of choice[4]

Material & Methods

30 patients were included in this study with ages ranging from 30 to 60 years. 20 patients were in 3rd & 5th decade of life. Female to male ratio was 2:28. Follow up period ranged from 1 month to 1 year. Site of malignancy were as shown in Table 1.

Table 1 : Site of malignancy

Site of malignancy	No. Of patients
Ca Tongue	01 (3.3%)
Ca Buccal mucosa	16 (53.3%)
Ca Gingivobuccal sulcus	09 (30%)
Ca Alveolus	04 (13.3%)

(3.3%) Ca tongue, (53.3%) Ca buccal mucosa, (30%) Ca gingivobuccal sulcus & (13.3%) Ca alveolus. All these were biopsy proven cases of squamous cell carcinoma of oral cavity.

First an oncosurgeon performed complete Levels 1a to V lymph node dissection. Segmental mandibulectomy is preferred, so it was done before resecting the Floor of mouth tumour as it improves surgical exposure. With ***segmental mandibulectomy*** the bone is cut at least 2cm from visible tumour. Composite Resection of the tumour was done with 1cm tumour free margin. Frozen section was obtained for confirmation of margins.

Surface marking of vascular pedicle of PMMC flap was determined & PMMC flap was harvested. Defect of oral cavity after composite resection of tumour was repaired by PMMC flap. Primary closure was done at donor site. The neck & chest were drained by suction drains. Antibiotic dressing was done. Patients routinely requires a temporary tracheostomy for possible airway compromise related to bleeding, soft tissue swelling. Average operating time is 3-4 hours & average amount of blood transfusion is 0-2 units.

Immediate postoperative care of the patient is best performed in a dedicated intensive care unit (ICU) for 24 to 48 hours. Routinely extubation is done after 24 hours of surgery. Daily dressing was done under all aseptic precaution.

External radiotherapy was given at department of radiation oncology of Sanjeevan Medical Foundation Institute Miraj. Data was collected with repect to the site of malignancy, extend, any previous treatment modality (surgery, radiotherapy), and the complications encountered in post operative period.

In 08(26.6%) patients only surgery (composite resection that comprised of wide excision of lesion with 1 cm tumour free margin along with modified radical neck dissection type 2 & reconstruction done by PMMC flap) was done, In 20(66.6%) patients surgery+ Radiotherapy (60-65 grey)[5] was given, In 02(6.6%) patients surgery+ Radiotherapy+ chemotherapy (Cisplatin 40-50mg/m2 IV weekly for 5-6wk[6] along with RT) was done.

Results

PMMC flap survival was excellent in 22 patients (73.3%) (Figure 1)

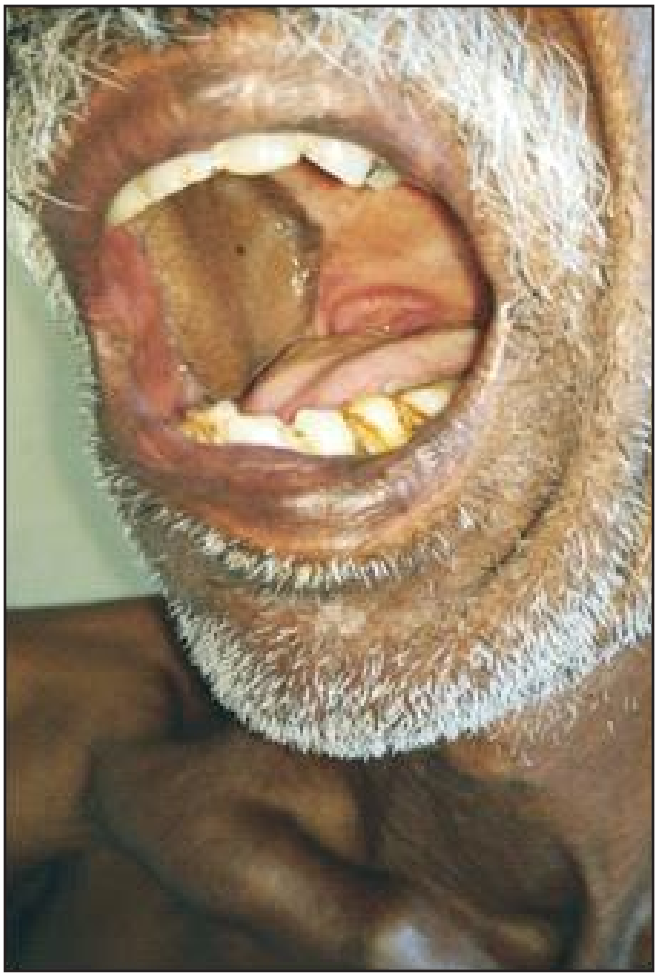

Fig 1 - Excellent Flap Survival.

Table 2 : Complications

Complications	No. Of patients
Partial flap necrosis	03(10%)
Wound infection	02(6.6%)
Wound dehiscence	02(6.6%)
Orocutaneus fistula	01(3.3%)

Table 3 : Risk factors in cases with complications.

Complications	No. Of patients	Risk factors
Partial flap necrosis	03	(02) Large tumour resection+ (01) Morbid obesity
Wound infection	02	(01)Obesity + (01) poor GC
Wound dehiscence	02	(01) Diabetes mellitus + (01)Received prior RT
Orocutaneus fistula	01	HTN with obesity

Above complications were managed as follows:

Wound infections were managed by longer courses of appropriate antibiotics & daily wound dressing.

wound dehiscence managed by local wound dressing with providone iodine & resuturing .

Partial flap necrosis (Figure 2) & Orocutaneus fistula (Figure 3) were managed conservatively by proper antibiotics and Glycopyrolate.

Fig. 2 - Partial flap necrosis

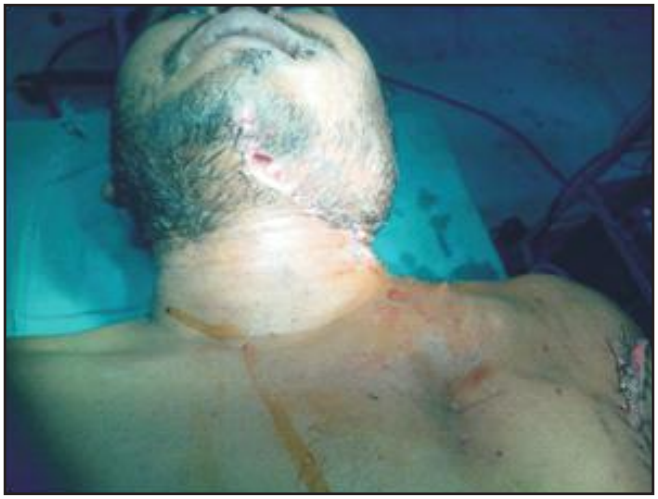

Fig 3 - Orocutaneus Fistula

Discussion

The pectoralis major myocutaneous flap was first described by Stephen Ariyan[3] in 1979.

It is now largely replacing the forehead and the deltopectoral (Bakamjiaan) flap as the flap of choice.

Reconstruction of complex head and neck defects resulting from cancer resection remains a challenge for head and neck and plastic surgeons. Free flaps, which are considered to be the "gold standard" for this kind of reparative procedure, are not available in many centres that treat head and neck tumours, because of the high costs and the highly specialized technology involved in microsurgical techniques[7].

The PMMC flap can be used for a very wide range of defects in the head and neck area including the oral cavity, neck, maxilla as well as temporo-orbital area. Cosmetically, the donor site scar is totally hidden by clothing; the functional loss is negligible.

The muscle pedicle in the neck effectively covers the exposed carotid vessels after a radical neck dissection as well as recreates the sternomastoid prominence giving symmetry. Elevation of the flap does not require any change of position during surgery and can be done quickly adding acceptable extra time to the surgery. Its use does not preclude the use of other flaps later; effective combinations with other flaps like the deltopectoral, forehead and, the Estlander flap can be used for large defects. Like other myocutaneous flaps, it involves a single stage reconstructive procedure and

does not require flap delay or release. The flap may be employed before or subsequent to the use of chemotherapy or radiotherapy[8].

There can be some problems in harvesting flap due to presence of bulky breast tissue as well as scarring of the breast[9]. Other disadvantages of the flap include excessive bulk in obese or muscular individuals and troublesome hair growth in the oral cavity.

Mayank Tripathi et al.[9] Studied 100 cases of PMMC and observed following complications as:

Table 4 : Comparison of complications with Mayank Tripathi

Complications	Mayank Tripathi et al (n=100)	Our study (n=30)
Total flap loss	0%	0%
Partial flap necrosis	16%	10%
Fistula	12%	3.3%
Wound dehiscence	26%	6.6%
Hematoma	7%	0%

Total flap necrosis has been reported by **Baek et al** [10]1982, **Mehrof et al**[11] 1983, **Brusati et al**[12] 1988, **Conley and Parke**[8] 1981 in 1.5%, 4%, 2.0% & 15% of their cases respectively. In contrast to other authors' and the present study where no total flap necrosis was noted. But partial flap necrosis was noted by various authors ranging from 6.6% to 32%. In contrast to our study where it was seen in 10% cases. Various authors have experienced wound dehiscence rates in 0% to 19% in their cases in contrast to present study where wound dehiscence was noted in 6.6% cases.this may be because of poor oro-dental hygiene, poor nutritional status of our patients and presence of diabetes mellitus and preoperative radiotherapy who developed complications. One case of DM and HTN with Ca gingivobuccal sulcus underwent hemimandibulectomy with wide excision of growth and PMMC flap reconstruction and later developed wound dehiscence followed by orocutaneus fistula. This healed by conservative management.

In this study we have got unique results of 73.3% flap survival and few patients with minimum complications due to underlying co-morbidities (DM, HTN) which could be managed easily so total flap survival was excellent. Considering patients with below poverty level whom do not afford cost factor of free flap, for such patients PMMC flap is gold standard.

Conclusion

To conclude the PMMC flap is most Versatile, Excellent and most suitable flap for oral cavity reconstruction following radical excision of tumour. With no special expertise (microanastomosis) is necessary. It is more commonly used for head and neck reconstruction with acceptable complications which can be managed with minimal intervention. However proper selection of cases & treating underlying co-morbidities (DM,HTN) is an important pre-requisite for excellent outcome. Though microsurgical free flaps are superior to PMMC flap, it has certain shortcomings especially in developing countries like need of a well developed plastic and reconstructive department, trained personnel, long learning curve, relatively high incidence of failure, need for specific infrastructure, cost factor and time limitations.

For these reasons, pedicled flaps continue to play an important role in many institutions worldwide, with special regard to cancer treatment centres in developing and emerging countries. Among these flaps, pectoralis major myocutaneous flaps (PMMCs) are ndoubtedly still considered to be the “workhorse” in head and neck reconstruction.

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ORIGINAL ARTICLE

Comparative study of health seeking behaviour of animal bite patients in urban and rural areas of Nagpur

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ABSTRACT

Introduction : The present study explores the variation in epidemiology and treatment seeking behaviour of animal bite patients in rural and urban areas.

Objective : To assess the health seeking behaviour of animal bite patients in rural and urban areas.

Methods : This Hospital based cross-sectional study was carried out in 100 patients. 50 urban patients were interviewed from anti-rabies vaccination clinic of Indira Gandhi Government Medical College, Nagpur and 50 rural patients selected from rural health centre Hingna from January to June 2013. All patients were subjected to sociodemographic profile, history of animal bites, wound toileting and treatment including both active and passive immunization.

Results : Overall, 66% were males and 34% were females. Majority of patients from rural areas were illiterate (60%) and involved in farming (36%). Most of the people in rural area were bitten by stray dog (54%) followed by wild animals like pig, monkey (16%) as compared with 38% of stray dog bite cases in urban areas. The commonest site of animal bites was found to be lower limb in both areas. Maximum cases belonged to category III (84%) in rural areas followed by category I (10%). Also, most of the rural patients (46%) preferred home remedies of treatment i.e. application of oil, salt, red chilies, and turmeric paste applications as compared with 10% urban patients who preferred visiting government hospitals. Moreover, rural patients took longer time (>48 hours) from exposure to reporting at anti-rabies vaccination clinic as they were following home remedies.

Conclusion : The rural urban differences found in present study would be imperative in effective policy making, planning and implementation of preventive and control measures.

Key words : animal bite, anti- rabies vaccine, rural- urban

Introduction

Mammals that live in close vicinity of man can inflict injury on adults and children through bites and can cause highly fatal rabies infection[1]. It is estimated that annually about 20,000 person's die of this disease and 17 million animals (mostly dog) bites occur in India. The figure is alarming and immediate action is required to stop this scourge [2-4]. The reason for this high number of mortality due to rabies is attributable to lack of awareness among people regarding management of animal bites which prevents them from obtaining medical care including post exposure prophylaxis (PEP) and most importantly the health seeking behaviour of people regarding animal bite [5].

Moreover, there are many myths, superstitions and false beliefs prevalent regarding wound care among layman. These include home remedies like application of oils, salt, lime, herbs, red chilies and turmeric paste on the wound inflicted by animal bites. It is noteworthy that people have more faith in indigenous and traditional medicines having unproven efficacy[6]. Surprisingly, people also have tendency of not washing the wound properly with soap and water because of unknown fears that the entry of water into the wound might cause infection. With this background, the present study has been undertaken to explore the variation in epidemiology and to assess the health seeking behaviour of animal bite patients in rural and urban areas.

Material and Methods

A Hospital based cross-sectional descriptive study was carried out in rural areas [Rural health training centre (RHTC) of Hingna] which is under the administrative control of department of community medicine, Indira Gandhi Government Medical College (IGGMC) and urban area [anti-rabies vaccination (ARV) clinic of IGGMC] of Nagpur city from January to May 2013. The study was approved by Institutional Ethics Committee (IEC).

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50 animal bite patients belonging to Category I, II and III were drawn by random selection from the rural and 50 from urban areas after obtaining written informed consent from them. Data regarding health seeking behavior of animal bite patients was collected with the aid of preformed structured questionnaire.

Statistical analysis

Percentages and chi square test trend was used to analyze the data using Epi Info statistical package programme version 6.0 updated 2009. Statistical significance was assessed at a type I error rate of 0.05.

Result

The number of animal bite patients studied was 50 in rural and 50 in urban areas. Children up to the age of 10 years were found to be 26% in rural areas and 12% in urban areas. Maximum number of patients was found in the age group of 20-40 years in both rural and urban areas. Considering gender distribution of patients overall, 66% were males and 34% were females. Almost same pattern of sex distribution was found in rural and urban areas. More than 50% of patients from rural areas were illiterate (60%) whereas only 36% of illiterates were from urban area. Most of the people in rural areas were involved in farming (36%) as compared to 16% in urban areas. The proportion of rural patients belonging to low socioeconomic status was more (84%) as compared to urban patients (28%). Also, some or other type of addiction (smoking, chewing tobacco, alcohol) was also seen in rural (18%) and urban (11%) patients. The above socio-demographic correlates of study subjects are summarized in Table 1.

Table 1: Socio-demographic correlates of study subjects

Socio-demographic correlate	Rural (N = 50)	Urban (N = 50)
Age group (years)		
0-10	13 (26)	6 (12)
10-20	10 (20)	3 (6)
20-40	18 (36)	21 (42)
40-60	6 (12)	16 (32)
60-80	3 (6)	4 (8)
Gender		
Male	31 (62)	35 (70)
Female	19 (38)	15 (30)
Educational status		
Illiterate	30 (60)	18 (36)
Higher secondary	10 (20)	17 (34)
Graduate and above	10 (20)	15 (30)
Occupation		
Student	24 (48)	14 (28)
Farmers/ laborers	18 (36)	8 (16)
Housework	8 (16)	28 (56)
Socio-economic status		
High	8 (16)	36 (72)
Low	42 (84)	14 (28)
Addictions (smoking, chewing tobacco, alcohol)		
Present	18 (36)	11 (22)
Absent	32 (64)	39 (78)

Figures in parentheses indicate percentage.

Table 2 shows the distribution of study subjects according to type of animal bite. Most of the patients in rural area were bitten by stray dog (54%) followed by wild animals like pig (8%), monkey (8%) as compared with 38% of stray dog bite cases in urban areas. Bite by other mammals included rat, rabbit, mice and human bite.

Table 2: Distribution of study subjects according to type of animal bite

	Rural (N=50)			Urban (N=50)			Statistical test χ^2	df 1	P value
Type of animal	Pet	Stray	Wild	Pet	Stray	Wild			
Dog	21(42)	27 (54)	-	15 (30)	19 (38)	-	13.28		0.0002
Cat	2 (4)	-	-	-	-	-	2.04		0.15
Pig	-	-	4 (8)	-	-	2 (4)	0.70		0.39
Monkey	-	-	4 (8)	-	-	3 (6)	0.15		0.69
Others	2 (4)	-	-	4 (8)	-	-	0.70		0.39

Figures in parentheses indicate percentage.

Table 3 shows the characteristics of animal bites. The commonest site of animal bites was found to be lower limb followed by upper limb, trunk and head in both rural and urban areas. Maximum cases belonged to category III (84%) in rural areas followed by category I (10%); also in urban areas most patients belonged to category III (78%) followed by category II (16%). 86% of the dog bites were found to be unprovoked in urban areas and 60% in rural areas. Animal bites were mainly inflicted upon during the activity of children playing (34% in rural areas) and during walking (60% in urban areas). Moreover, rural patients took longer time (>48 hours) from exposure to reporting at anti-rabies vaccination clinic as they were following home remedies as compared with urban patients. The children mainly presented with deep tissue injuries in both the areas with predominance among rural areas (28%) as compared to 18% in urban areas. Previous history of animal bites was present in 22% of rural patients and 10% of urban patients.

Table 3: Characteristics of animal bites

Characteristic	Rural (N=50)	Urban (N=50)	Statistical test χ^2	df 1	P value
Site of bite					
Lower limb	25 (50)	20 (40)	1.01		0.31
Upper limb	17 (34)	13 (26)	0.76		0.38
Head neck face	3 (6)	2 (4)	0.21		0.64
Trunk	5 (10)	2 (4)	1.38		0.24
Category of exposure					
Category I	5 (10)	3 (6)	0.54		0.46
Category II	3 (6)	8 (16)	2.55		0.11
Categor0y III	42 (84)	39 (78)	0.58		0.44
Mode of					
Provoked	19 (38)	7 (14)	7.48		0.006
Unprovoked	30 (60)	43 (86)	8.57		0.003
Activity during bite					
Playing	17 (34)	5 (10)	8.39		0.003
Walking	14 (28)	30 (60)	10.39		0.001
Sleeping	(6)	2 (4)	0.21		0.646
Working	16 (32)	13 (26)	0.43		0.5
Reporting time					
Within 24 hours	26 (52)	33 (66)	2.02		0.15
Within 10 days	15 (30)	14 (28)	0.04		0.82
After 10 days	9 (18)	2 (4)	5.00		0.02
Type of wound					
Superficial (abrasion)	36 (72)	41(82)	1.41		0.23
Deep (lacerated)	14 (28)	9 (18)			
Previous history of animal bite					
Present	11 (22)	5 (10)	2.67		0.10
Absent	39 (78)	45 (90)			

Figures in parentheses indicate percentage.

Table 4 shows the distribution of study subjects according to treatment mode and health seeking behaviour. Out of 50 rural patients, 54% had received tetanus toxoid (TT) vaccine, whereas in urban areas 96% had received TT vaccine. Active immunization i.e. anti-rabies vaccine (ARV) was administered to 48% patients in rural areas and 58% in urban areas. Whereas passive immunization i.e. immunoglobulin (Equirab) was given to 26% in rural and 10% in urban areas. Also, most of the rural patients (46%) preferred home remedies of treatment i.e. application of oil, salt, lime, red chilies, and turmeric paste applications as compared with 10% urban patients who preferred visiting government hospitals for treatment. Local toileting i.e. washing the wound with soap and water was done in 54% of rural patients and 90% of urban patients.

Table 4: Distribution of study subjects according to treatment mode and health seeking behaviour

Treatment	Rural (N=50)	Urban (N=50)	Statistical test χ^2	df 1	P value
Injection tetanus toxoid	28 (56)	48 (96)	21.93		0.001
Active immunization (Antirabies vaccine)	24 (48)	29 (58)	1.00		0.31
Passive immunization (Immunoglobulin-equirab)	13 (26)	5 (10)	4.33		0.03
Observation for 10 days	19 (38)	21 (42)	0.16		0.68
Other (antibiotics, antacids, painkiller)	26 (52)	21 (42)	1.00		0.31
Local toileting done	27 (54)	45 (90)	16.07		0.001
Home remedies (application of oil/salt/lime/turmeric paste)	23 (46)	5 (10)	16.07		0.001

Figures in parentheses indicate percentage.

Discussion

We evaluated the health seeking behaviour of animal bite patients in urban and rural areas of Nagpur city. The present study reported more cases of animal bites from rural areas (56% bitten by stray dogs) as compared to 38% in urban areas. Our study findings are consistent with other studies done by Agrawal N et al [7] Sudarshan MK et al [8] and Shetty RA et al [9]who also demonstrated more animal bite cases in rural areas. This could be attributed to the fact that rural people, mainly farmers and laborers proceed for work in early hours of the day and continue work till late evening thereby getting more

exposed to animal bites due to poor visibility.

Moreover, it was found that majority of the patients in our study belonged to productive age (age group of 20-40 years) in both rural and urban settings. Because of frequent migration from one place to another for job or other purpose, people in this age group are more vulnerable to animal bites. This result correlates well with the findings of the study done by other authors [10-15].

Apart from dogs, bite by other animals like cat, pig, monkey, rat, rabbit, mice and even human bites were also observed in present study with 86% being unprovoked in urban areas and 60% in rural areas. The commonest site was found to be lower limb followed by upper limb. Similar findings were noted by other researchers [9-10, 12].

It is noteworthy that more proportion of rural patients reported after 48 hours of bite with predominance of deep tissue injuries than urban patients. This is particularly of great clinical significance in the management of animal bite patients wherein treatment should be instituted at the earliest. In our study, significantly more proportion of urban patients had received tetanus toxoid injection, anti-rabies vaccine and performed local toileting of wound as compared to rural patients. Rather than seeking treatment from health care center rural patients preferred indigenous methods and home remedies (46%). However contradictory results have been obtained by Singh J et al [6] who noted late reporting to health care center in 50% of bite cases in both rural and urban areas. In rural area, it was due to initial involvement in indigenous or home remedies whereas in urban area it was due to ignorance and negligence. They found that 22 % of people preferred indigenous methods and home remedies including application of chilly/turmeric powder, jhaadphook rather than seeking medical help.

Thus our study findings suggest that the health seeking approach as well as the behaviour of the patients is defective or not up to the mark which is not only among people in rural areas, but also among urban population. Surprisingly, majority of people still today believe in indigenous methods or home remedies for treating animal bite wounds and still others will do nothing and will keep it untreated. So a thorough workout is needed to organize awareness programme regarding management of animal bites in both rural and urban areas. In absence of a National Rabies Control Programme, local health authorities and Medical Institutions should take the lead to increase awareness amongst the community regarding primary prevention of animal bites as well as health problems associated with it.

Conclusion

Our study revealed that majority of the patients from rural areas were inflicted upon by stray dogs (54%) and relied more upon home remedies thereby reporting late to government hospitals. Thus it is evident from the present study that majority of the patients in both rural and urban areas had little knowledge about rabies, its transmission, management and prophylaxis. It is, therefore, of utmost importance that adults and children should be properly educated about rabies so that they can avoid dogs, recognize potential exposures, report to health center and pass on the knowledge to their peers.

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SHORT COMMUNICATION

Wiseness lies in losing the wisdom teeth early

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Third molars are commonly called as "teeth of wisdom" or "wisdom teeth" as they generally erupt between the ages of 17 and 25 when a person reaches adulthood. According to the linguists, wisdom teeth appear late, at an age when a person matures into adulthood and is "wiser" than when other teeth have erupted. There are four wisdom teeth; two each in the maxillary and mandibular dental arches. This article is focused on the management of mandibular third molars.

A lot of things have changed for us in the evolutionary phase, some of which include but are not limited to, the acquisition of an erect posture, increase in the human intelligence, changing dietary habits from a raw diet to a more refined, cooked one and many more. These changes are important to enable us to adapt to the continuously changing environmental conditions. [1]

Human facial skeleton has undergone lot of changes in the course of evolution. There has been an increase in the size of the cranial cavity owing to an increase in the human intelligence and proportionately, the jaw size has reduced. With reference to the Functional Matrix Hypothesis (Moss' Hypothesis)as the human diet has changed from a raw one to a more refined, cooked one; the efforts required to chew the bolus of the food have reduced considerably. Thus, the activity of the muscles of mastication has reduced proportionately and this has resulted in reduction in the jaw size.

Jaw bones have specialized function to perform and so are provided with teeth. Every developing tooth is covered by a soft tissue sac called the dental follicle. This dental follicle serves many important functions in the developing stages of a tooth like providing nourishment, providing a pathway for eruption of the tooth. However, "A weapon is an enemy to its owner itself". Many pathological conditions are known to arise from the dental follicle, if retained for a prolonged period. Pathologies developing from the dental follicle and seen in the mandibular third molar region include but are not limited to ameloblastoma, dentigerous cyst, odontogenic keratocyst, odontomes, Pindborg's tumor[2,3,4]. These pathologies are known to spread through the marrow spaces and thus, assume huge proportions before they produce obvious facial disfigurement or pain due to neurological involvement or secondary infection. Anatomical structures that may interfere in the path of eruption of the mandibular third molars include fibrotic mucosa, adjacent molar tooth, and the anterior border of the ramus or any developing pathology in the dental follicle.

Figure 1 PA Mandible view showing a multilocular osteolytic lesion involving the left half of mandible.

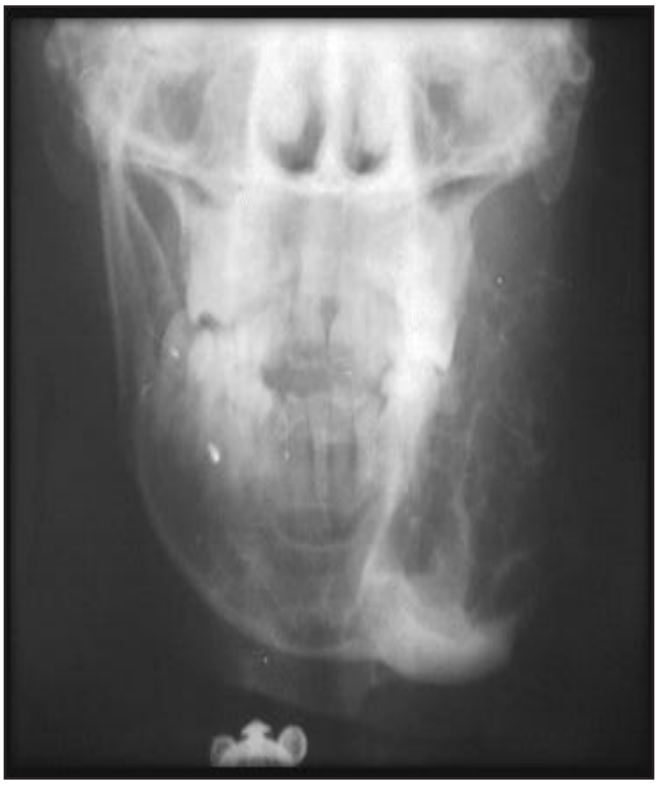

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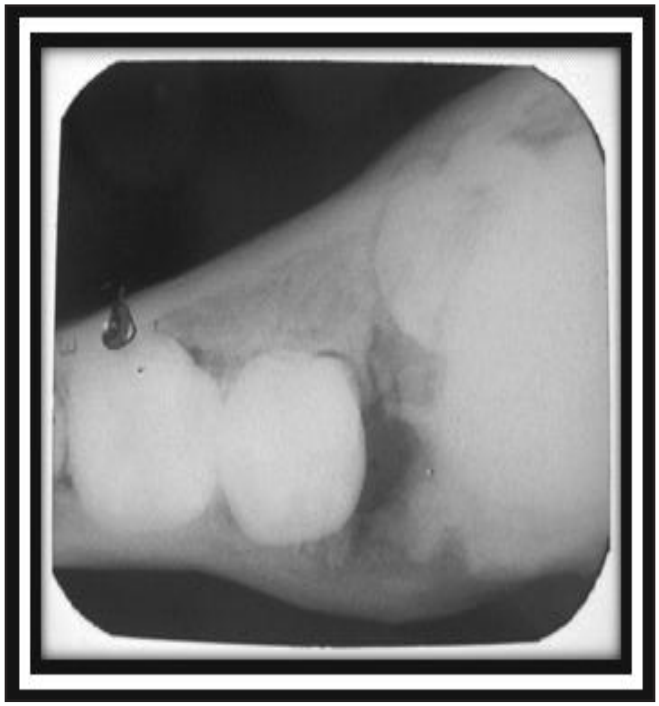
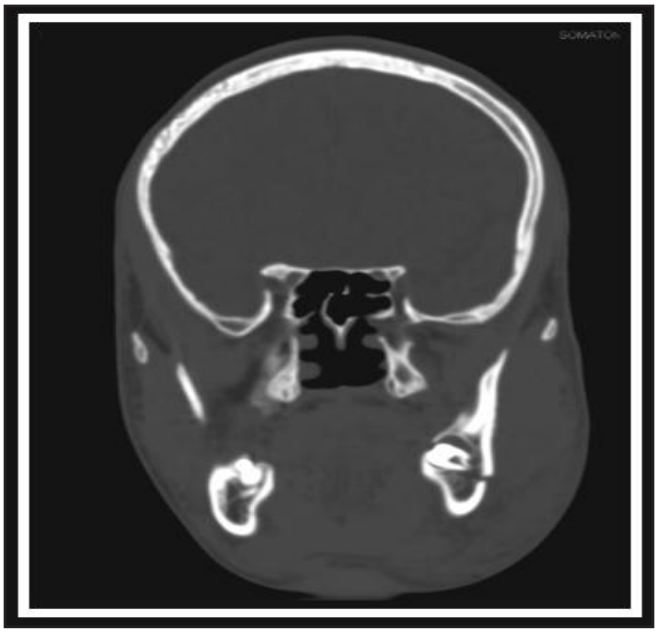
Figure 2 Mandibular true occlusal view showing a radiopaque mass associated with the mandibular third molar probably suggestive of complex composite odontome.



The mandibular third molars are located in the region of the angle of mandible which marks the junction of the body with the ramus of mandible. This is the region where the third molars are more commonly located. Mandible is a dense cortical bone. It has an outer and inner cortical bone plate and interspersed in between is the cancellous bone. It has got many inherent anatomical weaknesses such as a narrow condylar neck, the presence of a hollow inferior alveolar canal and the presence of teeth. The teeth are lodged in the alveolar processes and are held in the jaw by a fibrous type of joint called the "gomphoses". However, in the angle region a partially erupted mandibular third molar interrupts with the cortical continuity of the superior border of mandible making the jaw more susceptible to fracture following an injury, as compared to an impacted third molar which is lodged completely within the bone.

Figure 3.CT Scan image (Coronal section) showing a dilated follicular space associated with mandibular left third molar suggestive of fracture of angle of mandible.

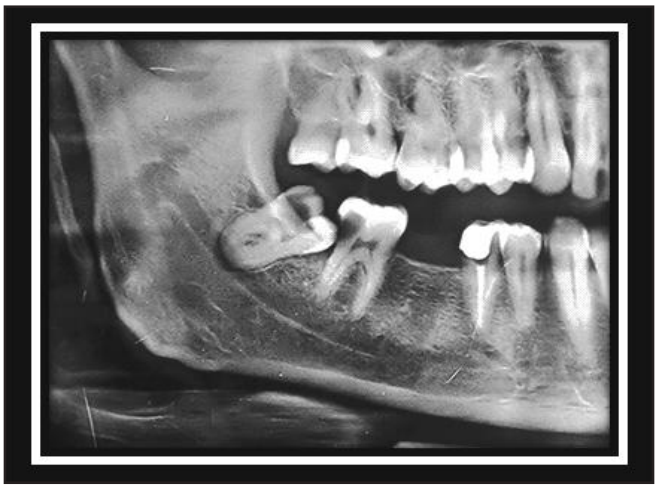


EXAMINATION OF THIRD MOLARS

Patients frequently consult a maxillofacial surgeon with a complaint of pain and/or swelling in the region of the angle of mandible. At times, patient may suffer from trismus or there may be neurological signs like mental nerve paraesthesia.

It is imperative to have a thorough case history of the patient followed by clinical examination.

Figure 4. An OPG showing periapical rarefaction associated with mandibular right third molar in close relation to the inferior alveolar canal.



Examination should include hard and soft tissue evaluation. The position of the third molar, presence of a periodontal pocket in relation to the third molar, signs of inflammation of the pericoronal flap, caries with the adjacent molar, tenderness with the submandibular lymph nodes are few of the signs to be looked for when examining the patient. Signs of tenderness along the anterior border of ramus or in the angle region of mandible may suggest involvement of the muscles of mastication like the temporalis or the masseter secondary to odontogenic infection. The classical clinical sign of involvement of the masticator spaces is "trismus".

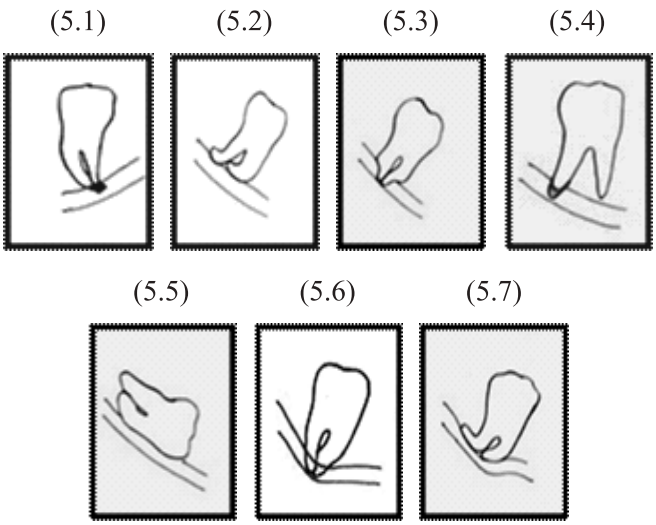
The position of the maxillary third molar should also be checked. At times the maxillary third molars are buccally placed and the cusps of such teeth cause repeated mechanical trauma to the pericoronal flap associated with the mandibular third molar resulting in pericoronitis.

The radiological prediction of inferior alveolar nerve injury during third molar surgery

Radiological assessment of the third molars on plain radiographs includes studying the position of the third molar, it's root configuration and relation to the inferior alveolar canal.[5] An important anatomical structure seen close to the roots of the mandibular third molars is the inferior alveolar nerve. The following radiological signs can predict close proximity of the roots of the third molar to the inferior alveolar canal.

1) Darkening of the root.(Figure 5.1)
2) Deflected roots (Figure 5.2)
3) Narrowing of the roots (Figure 5.3)
4) Dark and bifid roots (Figure 5.4)
5) Interruption of the white line(s) (Figure 5.5)
6) Diversion of the inferior alveolar canal (Figure 5.6)
7) Narrowing of the inferior alveolar canal (Figure 5.7)

Figures 5.1 to 5.7. Schematic diagrams showing the radiological signs predicting injury to the inferior alveolar nerve following a third molar surgery. The red outline shows the inferior alveolar canal and it's association with the third molar.



Risks Involved In The Surgical Management Of Mandibular Third Molars [6,7,8,9,10]

1) Inflammation of the alveolar bone (Alveolitis sicca dolorosa).
2) Neuropraxia of the inferior alveolar nerve.
3) Fracture of mandible.
4) Displacement of a root portion of the third molar into the sublingual space or the submandibular space.
5) Excessive bleeding.
6) Damage to the adjacent tooth.
7) Trismus
8) Neuropraxia of the lingual nerve.

Advantages of treating the impacted third molars early include: less morbidity, better healing, bone in young patients is elastic, less risk of inferior alveolar nerve injury. Teeth which remain impacted for a long time may migrate close to the inferior alveolar nerve and surgical removal of such a tooth in future may predispose the inferior alveolar nerve to injury.

Conclusion

Patients presenting to a maxillofacial surgeon with complaints related to the third molars need a comprehensive evaluation. It is important to take into consideration the physical condition of the patient and understand the status of any medical ailments the patient may be suffering from. Third molars which are not in a favourable position and are not likely to come in

alignment with the adjacent teeth are likely to cause problems in future. Such teeth should be diagnosed during a consultation and following a clinicoradiological assessment, appropriate management suggested. However, one factor that may prevent a patient from undergoing the surgery is "fear". In such a situation the patient should be instructed to follow up yearly for a clinico-radiological examination to diagnose any developing pathology in relation to the third molar at the earliest and thus enable the maxillofacial surgeon to keep the morbidity and mortality associated with the surgical management to a minimum.[4]

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CASE SERIES

Case series of curious dermal deposits

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ABSTRACT

Cutaneous deposition disorders, characterized by endogenous or exogenous material in dermis, may be the presenting manifestation of an undetected systemic metabolic, genetic or neoplastic disorder. We report three rarely encountered cases. The present case series includes an elderly male with cutaneous amyloidosis secondary to multiple myeloma, a child with tuberous xanthomas detected to have primary hypercholesterolemia and a middle aged male with joint pain due to chronic tophaceous gout. Diagnosis was confirmed by histopathology and special stains.

Key words : Cutaneous deposits, Amyloidosis, Tuberous xanthoma, Gout

Introduction

Case1: A 50 year male presented with multiple asymptomatic waxy, shiny, soft fleshy, pedunculated and sessile papules and hemorrhagic papulovesicles over bilateral peri-orbital areas (Figure1a) nares, angles of mouth and perineum with history of fatigue and backache since three years. General and systemic examination was unremarkable. Routine hematological examination was normal except for raised erythrocyte sedimentation rate (ESR) 60mm/ 24 hours. X-ray revealed multiple punched out lytic expansile lesions involving ribs, clavicle, skull vault and cervical vertebrae. Histopathology showed dense homogenous and globular eosinophilic deposits in dermis, which stained salmon pink with Congo red. (Figure1b) On polarized microscopy apple green birefringence was seen. Direct immunofluorescence of skin biopsy demonstrated kappa light chains. 24 hours urinary protein was raised (32 mgs/dl), urinary Bence Jones protein was negative. Serum protein electrophoresis was normal. Proliferation of plasma cells on bone biopsy confirmed the diagnosis of multiple myeloma. The diagnosis of cutaneous amyloidosis secondary to multiple myeloma was reached on clinico-pathologic correlation. Patient was started on melphalan, prednisolone, thalidomide regimen. After four months of treatment minimal improvement in skin lesions was noted along with marked alleviation in fatigue and malaise. Subsequently, patient was lost to follow-up.

Case 2: A nine year old female child presented with asymptomatic skin colored lesions since six years without contributory family history. Examination revealed multiple, skin coloured, waxy papules coalescing to form plaques over peri-orbital area, (Figure 2a) nape of neck, bilateral hands, wrists, elbows, knees, gluteals and intertriginous areas. General and systemic examination was unremarkable. Hemogram, blood sugar, liver function tests, serum amylase, serum lipase, thyroid profile was normal, but serum lipid profile was grossly deranged (cholesterol 866mg/dl, LDL-741 mg/dl, LDL/HDL ratio-18.83%, triglycerides normal). Histopathology revealed lipid laden macrophages characteristic of xanthoma. (Figure 2b) X-ray chest, electrocardiogram, glucose tolerance test and ultrasonography of abdomen were normal. A final diagnosis of primary hypercholesterolemia with tuberous xanthomas was reached. She was started on tablet rosuvastatin 10 mg once daily along with lifestyle and dietary modifications and weekly topical trichloroacetic acid application (70%) over cosmetically significant areas.

Case 3: A middle-aged male presented with joint pain (great toe, heel, ankle, knee, fingers) and multiple tender nodules over lateral aspect of feet, soles (Figure 3a) and base of left index finger. Few nodules showed ulceration. Investigation revealed elevated serum uric acid levels- 9 mg/dl. (normal 3.4 -7.2 mg/dl for men). RA factor was negative. Polarized microscopy of nodular aspirate showed intracellular, negatively bi-refringent, needle-shaped crystals (Figure 3b) that clinched the diagnosis of gout. He was started on tab. allopurinol (200 mg twice a

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day) and NSAIDs, but was lost to follow up before a detailed workup could be done.

Discussion

Cutaneous deposition disorders can be classified as follows:[1]

First group – calcium , salt, bone and cartilage.

Second group - hyaline deposits, metabolic disorders such as amyloidosis, lipoid proteinosis, gout.

Third group- various pigments, heavy metals, complex drug pigments.

Fourth group- cutaneous implants.

Fifth group -miscellaneous.

Amyloidosis is a disease caused by deposition of highly insoluble fibrous protein amyloid in tissues. Polypeptide chain gets folded to form a secondary structure of the protein molecule. Helical structure and pleated structure are two important secondary structures of protein molecule. The amyloid protein has a beta-pleated sheet structure, which makes it highly insoluble and resistant to proteolytic digestion and hence difficult to remove from tissues.

Amyloidosis can be classified clinically as systemic (generalized) forms with involvement of several organ systems, and organ- limited (localized) forms with deposits limited to a single organ like skin. Systemic amyloidosis has four sub-categories; primary systemic, secondary systemic, hemodialysis associated, genetic (inherited). Localized form is sub-classified as; cutaneous, endocrine, cerebral amyloidosis.

Our patient fits in primary systemic variant, the commonest form of systemic amyloidosis accounting for 60% cases, characterized by amyloid fibrils composed of AL protein [where L stands for light chain of immunoglobulin molecule, usually lambda (75-80%)]. In our case we found kappa restriction which is rare. Usual cutaneous manifestations of primary systemic amyloidosis are petechiae, pinch purpuras, ecchymoses, macroglossia, waxy papules and plaques, hyperkeratotic and pigmented papules and rarely scleroderma, alopecia, nerve enlargement and nail dystrophy.

Hepatomegaly occurs in 50% of patients and splenomegaly in 10%. Cardiac involvement leads to conduction defects, arrhythmias, congestive cardiac failure and may account for 40% of deaths. Renal involvement is frequent and presents as proteinuria and progressive renal impairment. In our patient, liver function tests, renal function tests, ultrasound abdomen, ECG, 2D Echo and X-ray chest were normal, ruling out organ involvement.[2]

Prognosis of myeloma associated amyloidosis is poor depending upon response to therapy and extent of involvement.3 Major causes of death are cardiac and renal failure. Median survival in myeloma associated amyloidosis is five months. Treatment of amyloidosis is aimed at reducing the supply of precursor proteins. In AL amyloidosis, the precursor is immunoglobulin light chain produced by B lymphocytes/plasma cells, hence treatment with cytotoxic agents (like melphalan and prednisolone) that reduce plasma cell proliferation is useful.[3]

Xanthomas are commonly caused by a disturbance of lipoprotein metabolism.[4] Alterations in lipoproteins may be a result of a genetic defect (e.g. primary hyperlipoproteinemia) or secondary to underlying systemic disorders like diabetes mellitus, hypothyroidism, chronic biliary cirrhosis, monoclonal gammopathy or nephrotic syndrome. These underlying diseases can cause elevated levels of certain lipids and lipoproteins presenting as cutaneous xanthomas. Various sub-types include xanthelasma palpebrum, tuberous xanthoma, eruptive xanthoma, tendinous xanthoma, plane xanthoma, etc. Xanthomas may also be seen in normolipemic conditions such as, histiocytosis, xanthoma disseminatum, diffuse plane xanthomatosis, juvenile xanthogranuloma.

Tuberous xanthomas generally present as yellow or reddish nodules located mainly on extensor surfaces of extremities and gluteal region.[5] These xanthomas are commonly seen with hypercholesterolemia and increased levels of LDL (familial hypercholesterolemia) and familial dysbetalipoproteinemia (Type III) as well as in secondary hyperlipidemias. Prompt diagnosis and treatment may help prevent serious consequences like early coronary artery disease and pancreatitis. The main aim of treatment for xanthomas is to identify underlying cause and treat the same along with dietary and lifestyle modifications. Occasionally surgical intervention may be required.

Legends

Figure 1a- Multiple discrete and confluent, waxy and shiny, soft, fleshy, pedunculated and sessile papules and hemorrhagic papulovesicles in bilateral periorbital region.

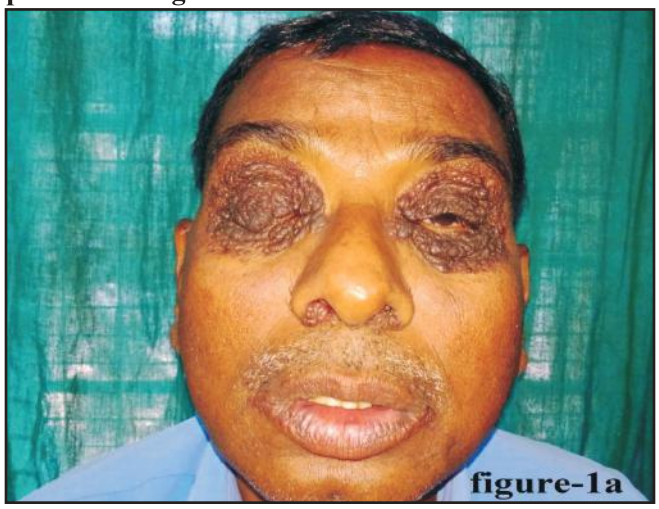


Figure 1b- Skin biopsy : Congo red (10X) stains the deposited material in the dermis salmon pink

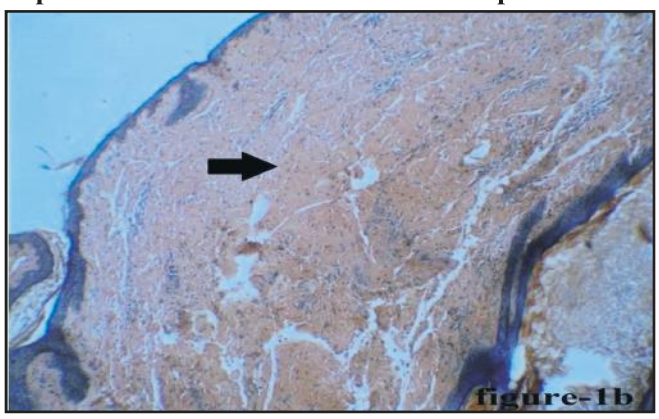


Figure. 2a- Multiple, skin coloured, soft, waxy papules coalescing to form plaques over periorbital region.

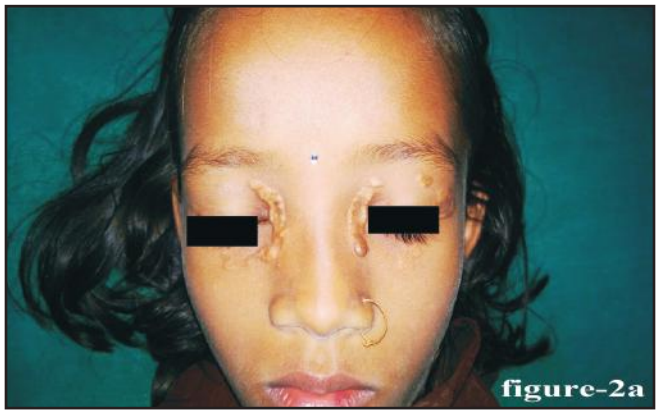


Figure. 2b- Skin biopsy (H&E, 20X) : normal epidermis along with foamy cell infiltration in papillary and reticular dermis in perivascular pattern.

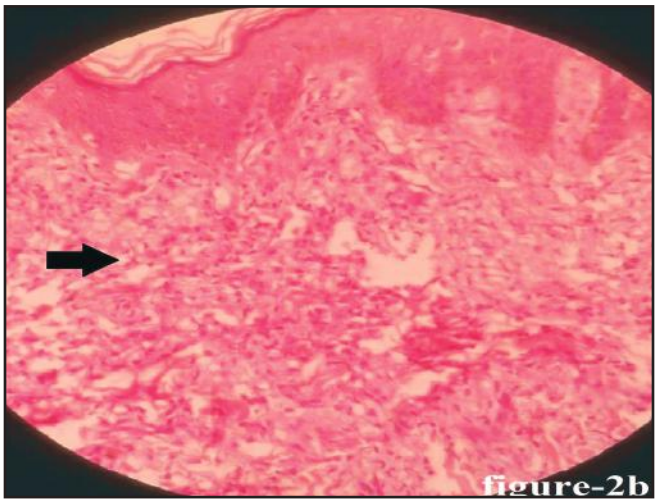


Figure. 3a- Multiple tender nodules over lateral aspect of soles and few nodules show ulceration.

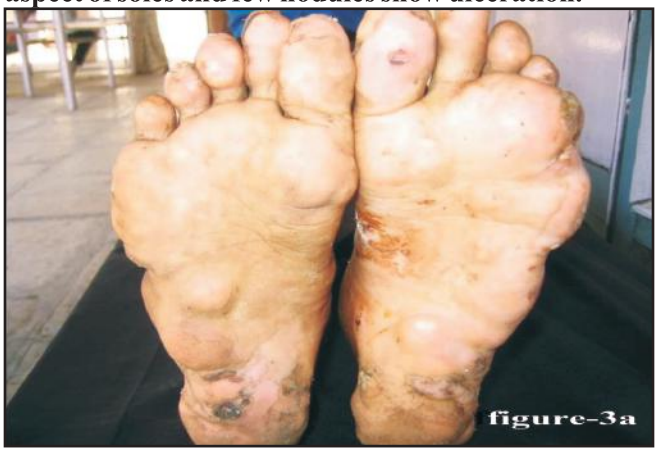
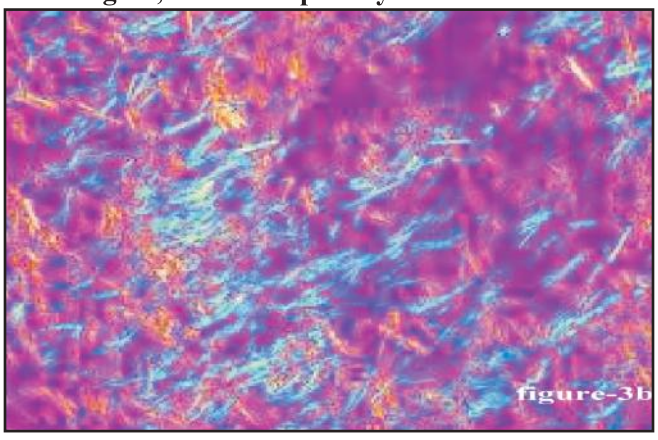


Figure. 3b- Polarized microscopy of the nodule aspirate - shows intracellular, negatively birefringent, needle-shaped crystals.



Gout, is an inflammatory arthritis caused by deposition of monosodium urate (MSU) crystals in articular or peri-articular tissues and kidney.[6] It affects 1- 2% of adults in developed countries constituting the most common form of crystal induced arthritis. Men aged 40-50 years are most commonly affected. Male to female ratio is 9:1.The formation of MSU crystals depends on local concentration of urate, which is tightly correlative with the articular hydration state, temperature, pH, concentration of cations and the presence of extracellular matrix. Peripheral joints with low temperature (i.e. the dorsal aspect of the proximal interphalangeal, metacarpophalangeal joints and dorsal toes) are the predilections of gouty tophi.[7] Etiologically two main forms are recognized. Primary gout where most patients appear to have reduced excretion of uric acid, but metabolic abnormalities are poorly understood. Fewer than 10% of patients with primary gout have an increase in the rate of purine biosynthesis. There are two very rare specific enzyme deficiencies associated with gout, which have X-linked inheritance. These are partial deficiency of hypoxanthine–guanine phosphoribosyl transferase (HGPRT) and increased activity of phosphoribosyl-pyrophosphate (PRPP) synthetase. Secondary gout may result from decreased uric acid excretion, most important cause being diuretic therapy. Other culprit drugs known to elevate uric acid levels include cyclosporine, azathioprine, aspirin, niacin, ethambutol, pyrazinamide, beta blockers and ACE inhibitors. Increased uric acid production is usually secondary to increased turnover of nucleic acid in conditions such as polycythemia rubra vera, lymphoma, myeloma and in patients with leukemia receiving active chemotherapy.

Generally there are four stages in development of gout with ill-defined boundaries: Asymptomatic hyperuricemia, acute gouty attack, intercritical period and chronic gouty arthritis. Hyperuricemia can exist for many years before the first clinical attack, and skin manifestations may appear at any stage even without a prior history of gout. This condition has several mimickers including histiocytic, rheumatological, infective, immunological and storage disorders. In our patient, clinical features supplemented by characteristic laboratory findings and pathognomonic appearance on polarized light microscopy confirmed the diagnosis. Treatment of chronic tophaceous gout depends on stage of presentation. It comprises dietary modification, medical and surgical therapy. Medical treatment includes NSAIDs, colchicine, hypouricemic drugs like allopurinol and uricosuric drugs like probenecid and sulfinpyrazone. Surgery is indicated when tophi are in a critical location, drain chronically or there is intractable joint pain, restriction of mobility and massive joint destruction.

Thus, our case series highlights how cutaneous deposits may lead to diagnosis of hitherto undetected medical disorders.

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CASE SERIES

Functional outcome of the sandwich technique for giant cell tumours of proximal tibia

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ABSTRACT

Background : Giant cell tumour (GCT) of bone is one of the most common benign bone tumours occurring around the knee in those aged 30 to 40 years. It is locally aggressive and prone to recurrence and malignant transformation. In our hospital, the treatment of GCT of bone has been intralesional curettage followed by the use of phenol and reconstruction using the sandwich technique.

Methods : Eleven women and 7 men aged 19 to 46 (mean, 29.6) years underwent intralesional curettage, use of phenol, and reconstruction using the sandwich technique for GCT of the proximal tibia . Two of the cases were recurrences. 10, 8 tumours were classified as grade I and grade II respectively Patients underwent intralesional curettage, use of phenol, and reconstruction with allograft, gel foam, and cement (the sandwich technique). Pathological fractures were fixed with plates. Functional outcome was evaluated using the Musculoskeletal Tumor Society (MSTS) score.

Results : The mean follow-up period was 2-3 years. The mean MSTS score was 27.7 out of 30 (standard deviation, 3; range, 16–30) . No patient had malignant transformation.

Conclusion : We concluded a good to excellent functional outcome without compromise of prognosis, can be achieved by using a bone graft or sandwich technique following intralesional curettage. Most patients could resume their previous work and reach the earlier level of physical activities. A longer duration of follow-up of a larger group of patients is necessary to study the recurrence rates.

Key Words : GCT, INTERLESIONAL CURRATAGE, MSTS, Sandwich Technique

Introduction

Giant cell tumour (GCT) of bone is one of the most common benign bone tumours occurring around the knee in those aged 20 to 40 years. It is locally aggressive and prone to recurrence and malignant transformation.[1] Treatment by curettage alone has a high risk of recurrence.[2,3] Use of adjuvants (phenol, cement, cryosurgery, or a combination of these) is recommended, followed by reconstruction with autograft, allograft, cement, and/or hydroxyapatite. In our hospital, the treatment of GCT of bone has been intralesional curettage followed by the use of phenol and reconstruction using the sandwich technique,[4] in which the autograft in the subchondral region is overlaid with a layer of gel foam, and the rest of the cavity is filled with cement.

Materials and Methods

Between January 2010 and December 2014, 11 women (Premenapausal) and 7 men aged 19 to 46 (mean, 29.6) years underwent intralesional curettage, use of phenol, and reconstruction using the sandwich technique for GCT of the proximal tibia. Out ot 18 patients 13 patients had left proximal tibia GCT and 5 patients had right Tibia GCT. Two of the cases were recurrences. Mean operative time was 1.20hr. and mean blood loss was 150cc. None of patient required blood transfusion. Preoperatively all patients were investigated with routine blood tests and MRI of proximal tibia, Chest radiograph and CT chest to stage Tumour. According to the Campanacci grading system,[4] 10 tumours were classified as grade I (with a well defined margin and an intact cortex), 8 were grade II (with a relatively well-defined margin but no radiopaque rim, and the thinned and moderately expanded cortex).

TECHNIQUE:

In all patients spinal-epidural anaesthesia was used. Tourniquet was used, operative limb was elevated for 5 minutes but not exanguinated. Adequate exposure was achieved by making a large cortical window to access the tumor so as to avoid having to curette under overhanging shelves or ridges of bone. A dental mirror

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was used which helped for better visualization. The part of the wall of the cavity which is composed of soft tissue or a thin bony shell was excised. Multiple angled curettes helped to identify and access small pockets of residual disease which may otherwise result in recurrence. The remaining cristae and septa in the cavity were excised. When the wall of the cavity contains many small holes caused by local invasion of the tumour, each hole should be meticulously cleared. They usually do not penetrate the periosteum, but a dead space may be found between them and the periosteum. A high power burr was used to break the bony ridges. The cavity was cleaned with pulsatile lavage of 5% phenol, and phenol soaked gauze was placed inside the cavity for 2 minutes. Care was taken not to spill the phenol to the surrounding tissues. Iliac crest autograft from ipsilateral side were harvested using seperate set of instruments and gloves to avoid cross contamination. Structural autografts of 3 to 5 mm thickness were packed adjacent to the subarticular surface as a 5 to 8 mm thick layer. A layer of gel foam was laid over the allograft, and the remaining cavity was packed with cement. Tumour material was sent for histopathological examination. Cloure was done under negative sunction drain and sterile dressing was applied. Post operatively operated limb was protected with posterior long knee brace.

Postoperatively, Satic quadriceps exercises and ankle pump exercises, non-weight-bearing crutch walking was started immediately. Knee range of movements started after 6 weeks. Follow up radiographs were taken at 6weeks,10 weeks,12 weeks, 6months, 1year.Weight bearing was allowed as tolerated after 12 weeks once radiological signs of consolidation seen(fig. 3b).

Functional evaluation of these patients was performed according to the most recent system of the Musculoskeletal Tumor Society (MSTS)[5] which involves 6 parameters (pain, function, emotional acceptance, use of walking aids, walking ability, and gait). Scores for each parameter range from 0 to 5; higher scores indicate better outcome. The Postoperative MSTS Score was determined and compared to study The mean MSTS score was 26 out of 30.

Discussion

Diagnosis of cancer severely affects the quality of life and emotional status of any individual. Assessment of functional score measures this aspect of tumor management and is a verdict by the patient about how well he has been treated. This study, along with presenting the details and reviewing the literature on GCT aims to focus on this aspect of assessment. Because of the relatively high rate of major complications and the adverse functional effects of en bloc resection, intralesional treatment of long bone GCT gained renewed interest after the widespread introduction of PMMA [12,13] packing for this clinical situation in 1969, by Vidal et al[14] , O'Donnell et al[16] reported a 25% local recurrence rate after the treatment of 60 GCT patients with curettage and packing with PMMA.

Treatment for GCTs around the knee include- curettage alone, -curettage with adjuvant therapy (liquid nitrogen, hydrogen peroxide, phenol, argon laser photocoagulation, bone cement, or bone graft), and -marginal/wide resection, followed by reconstruction, arthrodesis, or mega-prosthetic joint replacement. Intralesional curettage alone has a high recurrence rate of 60%,[6] whereas marginal/wide resection is associated with functional disability. Preservation of joint function is an advantage of intralesional curettage compared to wide resection. In our study, intralesional curettage and reconstruction with the sandwich technique achieved a low recurrence rate and good functional outcome.

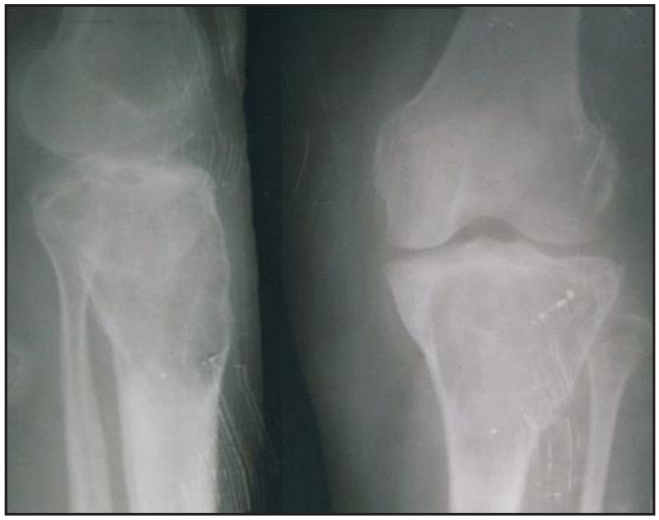
To ensure thorough curettage, adequate exposure through a wide cortical window is necessary, followed by breaking the bony ridges in the tumour using a high-power burr. The use of 5% phenol decreases recurrence,[7] as phenol causes protein coagulation and necrosis and damages DNA.[8] Structural autograft is laid in the subchondral region and overlaid with a layer of gel foam, and the rest of the cavity is filled with polymethylmethacrylate bone cement. The heating effect of cement destroys remaining tumour cells.[9] The bone graft in the subchondral region helps maintain joint function and prevents articular degeneration.[10]

Conclusion

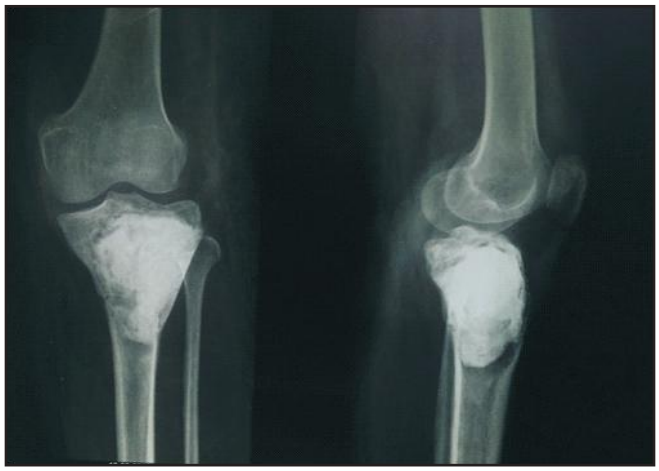
The results of this study suggest that a definite and subjectively appreciable improvement in quality of life of the patient can be achieved by using a bone graft or sandwich technique reconstruction following aggressive curettage with the use of various adjuvants. Patients of various ages and both gender equally benefitted from surgery in terms of functional improvement.

Intralesional curettage, use of phenol, and reconstruction with allograft, gel foam, and cement (the sandwich technique) for GCT of bone achieved good functional outcome and a low recurrence rate. However, a longer follow- up is required to comment if these outcomes are enduring and to assess the recurrence rates. Also a larger case series is needed to report if similar results are reproducible in majority of patients.

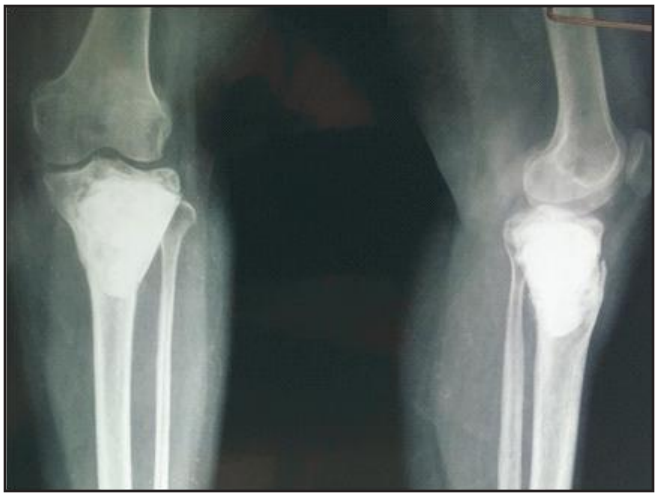
FIGURES:



1.Fig.1 Preop Xray



2.Fig 2a. Immediate postop Xray



3.Fig 2b. 3 months postop Xray

Clinical Photographs:

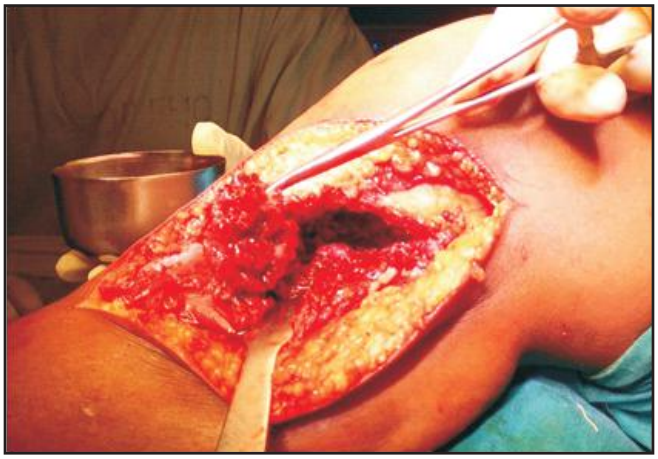


Photo1.a. Intra op GCT excision

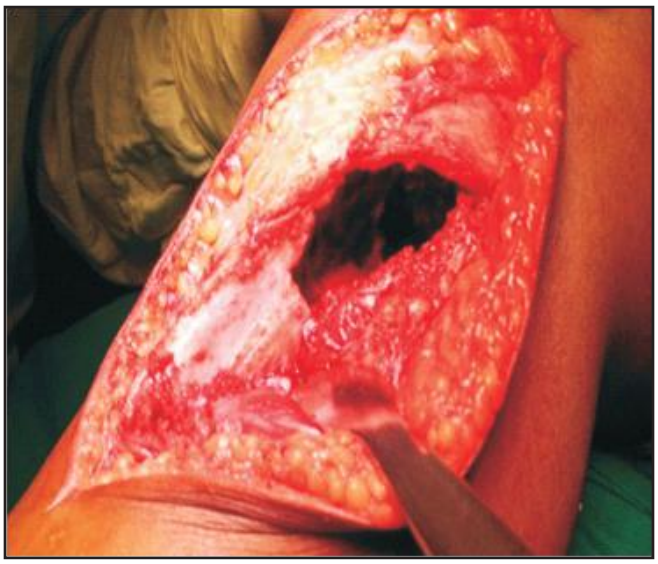


Photo1.b. Cavity after Intralesional Curettage

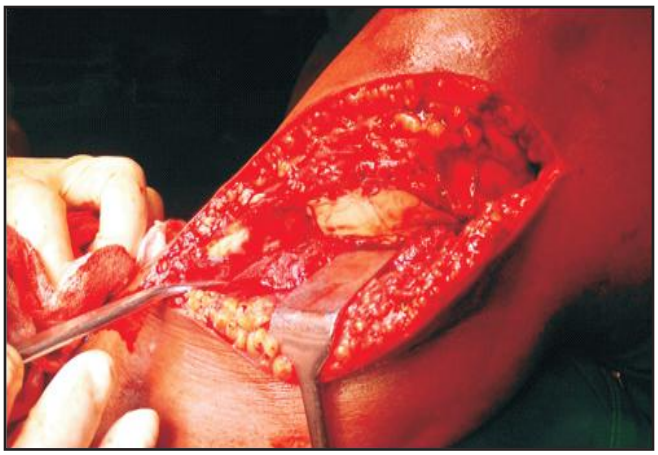


Photo2.Intraop After Sandwich Technique

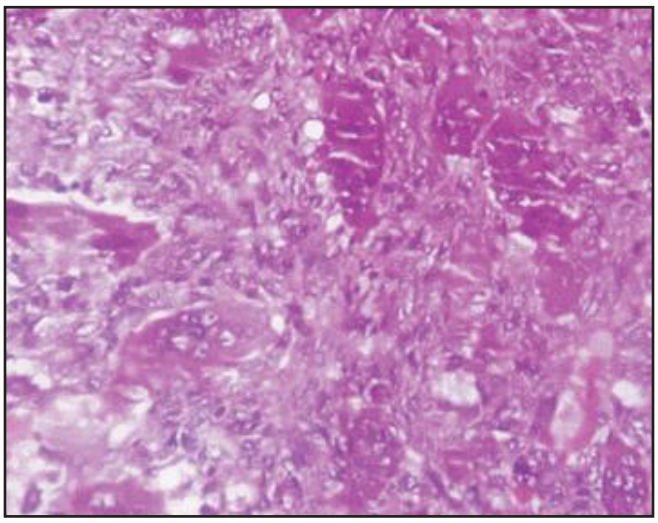


Photo 3.Histopathology slide of GCT:

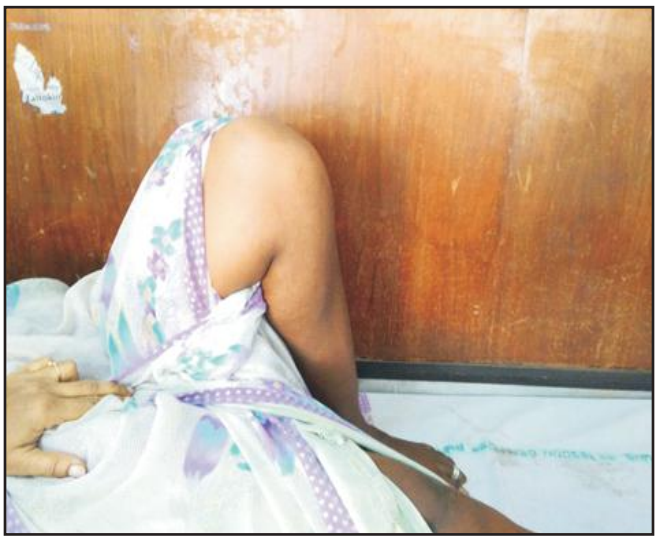


Photo 4.Postop 3 mnths F/up Knee full ROM

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CASE SERIES

Pituitary Macroadenomas - Management By Transnasal Endoscopic Approach

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ABSTRACT

Pituitary tumors constitute 10% of intracranial tumors; of these the most frequent primary tumors are pituitary adenomas. They may be micro- or macroadenomas and hormone secreting or non-functioning adenomas. Somatotroph adenomas are the second most common of the hormone secreting adenomas. We operated three patients, diagnosed by blood chemistry and radiology as having growth hormone secreting pituitary macroadenomas, by endoscopic endonasal technique (four hand technique), exclusively. On monthly follow up visits, the serum GH values were found to drop, with >50% reduction as compared to the pre-operative values at three months post-operatively. There was significant post-operative improvement of vision, with improvement in voice as well. Bony overgrowth showed changes, but to a lesser extent. In the prospective follow up of the three cases that we operated, endoscopic endonasal approach, proved to be effective for tumor removal from difficult areas with very less intra- and post-operative morbidity.

KEYWORDS : Pituitary macroadenoma, acromegaly, Endoscopic endonasal four hand technique.

Introduction

Pituitary adenomas represent 12% of primary brain tumors. They arise as a result of monoclonal pituitary cell proliferation. Somatotroph adenomas account for 15% of these adenomas.[1] These adenomas lead to what is known as **"Acromegaly",** derived from the Greek words *akros* meaning extremities and *megas* meaning big.

Untreated acromegaly causes significant morbidity, and is associated with a two- to threefold increase in mortality. When acromegaly is treated successfully and "safe" growth hormone (GH) and insulin growth factor-1 (IGF-1) values are achieved, the mortality rate normalises. Therefore, appropriate treatment of acromegaly is crucial. However, symptoms and signs of acromegaly develop insidiously, and there is often a delay in diagnosis for up to 10 years. Therefore, approximately 70% of GH-secreting adenomas are $\geqslant 1$ cm in size(macroadenomas) at the time acromegaly is diagnosed.[2]

Surgical approaches in patients with acromegaly have evolved dramatically over time; pure endoscopic endonasal transsphenoidal surgery (PEETS) is a minimally invasive technique introduced by Jho in 1993.[3] Endoscopy provides a panoramic view of surgical field with excellent lateral vision with angled endoscope. There is better tumour control for complete removal. Two surgeon (four hand technique) technique gives better control during intraoperative vascular catastrophe.

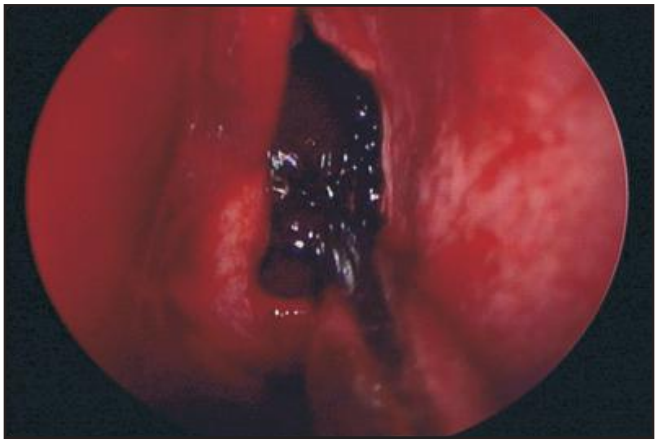

Fig.1 : Opening the sphenoid sinus after posterior septectomy

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Case Presentation

Table 1: Clinical Presentation and investigation findings of the cases

CRITERIA	CASE 1	CASE 2	CASE 3
AGE/SEX	30 yr/F	28 yr/M	32 yr/F
PATIENT'S COMPLAINTS	Giddiness – 5m Headache – 2m Blurring of vision – 2m	Swelling of hands and feet – 2y Voice change – 2y Headache – 6m	Headache – 2y Decreased vision – 1y Amenorrhoea - 6m
CLINICAL PRESENTATION	Prominent supraorbital ridges Big prominent nose Organomegaly	Macroglossia Broad and thick fingers of hands and feet Gynaecomastia	Frontal Bossing Prognathism Broad and thick fingers of hands and feet
LABORATORY PARAMETERS	BSL=590mg/dl GH=27.9ng/ml PRL=2,5ng/ml	BSL=109mg/dl GH=373ng/ml PRL=28.7ng/ml	GH=29.3ng/ml PRL=1.7ng/ml
MRI FINDINGS	Size= 4.3x3.1x2.4cm Suprasellar, sellar and left parasellar regions. Lef Internal Carotid Artery encased. Pressure on the optic chiasma and Left optic nerve.	Size=1.7x3.1x1.8cm Erosion of floor of sella into right cavernous sinus, encasing right Internal carotid artery, elevating optic chiasma.	Size= 2.8x3.5x1.3cm Suprasellar, sellar and left parasellar regions. Pressure on the optic chiasma.

We did a prospective follow up of 3 patients with acromegaly between June 2010 and March 2011, all of them were exclusively operated by PEETS.

Discussion

Surgical Technique : Endoscopic endonasal four hand technique was used - After widening the access for tumor removal with a posterior septectomy, the sphenoid ostium was identified and the sphenoid sinus opened (Fig. 1). The mucosa and bone forming the roof of the sinus was removed, extending from one carotid artery to the other. The dura was then incised and the tumor removed using a ring curette (Fig. 2).

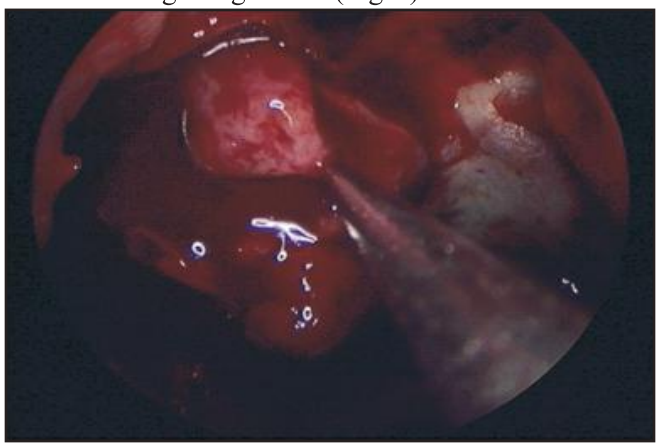

Fig. 2: Tumor removal with a ring curette

Our experience: Since all the cases we operated on were those of acromegaly we were required to do exhaustive drilling for removal of the thick bone at the sphenoid sinus roof in order to gain good exposure around the tumor. As a result we needed a little more time than would be otherwise needed for non – GH secreting pituitary adenomas.

Intra- operative blood loss was not significant with no major vascular trauma. Similar findings were observed by Gondim et.al, in their study.[4]

Improvement in visual symptoms, BSL and menstrual symptoms were observed by us. Remission rates were 71.4% for for patients with acromegaly in a study by Andreja Maric et.al.[5]

Signs of recurrence were not seen in any of the patients we operated, over a three year follow-up period; as was also seen in a study by Gondim et.al.[4]

Post- operative nasal crusting was observed in the patients and managed with nasal douching for a period of 2 months. Nasal crusting was seen in 10.4% cases in a study by Yadav et.al.[6]

Advantages: Advantages of PEETS include, panoramic view of surgical field, excellent lateral vision with angled endoscope, good tumor control for complete removal. Two surgeon (four hand) technique gives better control during intra-operative vascular catastrophes and less iatrogenic vascular injuries occur.

Limitations: There are however, certain limitations of PEETS, like sinusitis, absence of sphenoid sinus pneumatization, very close position of carotid artery, significant suprasellar extensions, firm tumor consistency, involvement or vasospasms of the circle of Willis arteries, encasement or invasion of the optic apparatus.

Complications: Complications related to the procedure, according to Gondim et.al. include post-operative CSF leaks in 2.6%, delayed nasal bleeding in 1.9%, sphenoid sinusitis in 1.6%, carotid artery injury in 0.9%, meningitis in 0.6%, endocrinological complications in 17.9%, which include anterior lobe insufficiency in 11.6% and diabetes insipidus in 6.3%. [5]

We, however, did not encounter any of the above complications. All of our patients developed nasal crusting and were given nasal douching for the same.

Conclusion

In our case series of 3 patients diagnosed as having GH secreting pituitary macroadenomas, endoscopic four hand technique proved to be effective for tumor removal from difficult areas like lateral corners of the dissection with less intra-operative and post-operative morbidity.

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CASE REPORT

Case of Pheochromocytoma

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ABSTRACT

Phaeochromocytomas are neuroendocrine tumours, derived from neural crest cells and are seen in 0.5-1% of all hypertensive patients. Paroxysmal hypertension is the dominant sign, while palpitations, headache and sweating form the classical triad of phaeochromocytoma. In this case a 37 year old female who had hypertension and diabetes mellitus was diagnosed to have phaeochromocytoma. The tumour was successfully excised surgically after the initial stabilisation of the patient medically. The patient in her 3 months of follow-up is doing well and is symptom free.

Key Words : Phaeochromocytoma, Hypertension, Adrenalectomy

Introduction

Phaeochromocytomas are catecholamine producing tumours, embryologically derived from the neural crest cells, located principally in the abdomen. These may be sporadic or inherited, adrenal or extra-adrenal, benign or malignant. This is a case report of a 37year old female with hypertension who was diagnosed to have phaeochromocytoma, which was initially managed medically and once the patient was stabilised surgical excision was carried out.

Case Report

A 37 year old female, who was a known case of hypertension and diabetes mellitus came with history of palpitation and profuse sweating. Patient was diagnosed to have hypertension 5 years back and diabetes mellitus 2 years back and was on medication for the same. On admission patient's pulse was 150/min and blood pressure was 200/130mm of Hg. Patient's blood sugar was 263mg/dl and urine sugar++. Patient was treatedinitially using prazocin (blocker, 5mg BD), metoprolol (blocker, 12.5mg BD) and insulin (mixtard 8-0-8U, insulitard 0-0-14U) along with regular blood pressure and blood sugar monitoring. Tab. Amlodipine, 5mg OD and tab. Stator 20mg HS were also added. She had paroxysms of flushing, tachycardiaand sweating in the ward, hence was suspected to have phaeochromocytoma and was investigated further.

USG abdomen and CT abdomen was done which was suggestive of a 6.477cm well defined soft tissue density mass lesion in the left suprarenal gland with multiple non-enhancing areas and no obvious adjacent invasion suggestive of neoplastic etiology. Opposite kidney and adrenal was normal. Urinary Vanilly lmandelic Acid (VMA) was 4mg/d. She was transferred to surgery for further management after stabilisation. FDG-PET scan (fig 1) was done which reported a weakly metabolic mixed density mass in the left suprarenal region with no extra-adrenal lesions. 2D echocardiography was done which showed no abnormalities.

Decision to surgically excise the tumour was taken. After explaining the risks of surgery to the patient and her relatives, patient was taken up for surgery. There was a partially solid and cystic lesion in the left suprarenal gland(fig 2a) of approximately 889cm, with no adhesions to the surrounding structures, which was approached by vertical midline laparotomy incision and was excised completely. Opposite adrenal was normal. Intra-operative fluctuations in blood pressure was managed by the anaesthetists using inj. labetalol and inj. nitroglycerine infusion and patient was kept in the ICU for observation post operatively. There was post-operative drop in blood pressure which was managed by ionotropes. Post-operative drop in blood sugar was also intensively managed. Patient was discharged on the 11th post-operative day. The histopathology report(fig 2b) was suggestive of a 876cm soft tissue mass, showing nests of tumor cells surrounded by fibrovascular stroma, with no evidence of tumor necrosis, suggestive of phaeochromocytoma. On follow-up patient is

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asymptomatic and she is off medication with blood pressure of 120/80mm of Hg and blood sugar of 110mg%.

Discussion

Pheochromocytoma is a neuroendocrine tumour, embryologically derived from the neural crest andlocated principally in the abdomen. The anatomical distribution confines to that of the sympatho-adrenalsystem with predominant origin from the adrenalmedulla in approximately 90% of cases. Phaeochromocytoma is estimated to occur in 2-8 of 1 million persons per year. The prevalence is less than 0.5% in hypertensive adults, but higher in hypertensive adolescents and children because of greater likelihood of inherited disease[1]. Pheochromocytoma is neither gender nor race specific and can occur at any age. Sporadic tumors commonly present in the third and fourth decades of life, while familial disease is manifested one decade earlier.

In 1886, Felix Fraenkel gave a pathological description of pheochromocytoma, and in 1912,Pick introduced the name to describe a tumor that stained brown when exposed to chromium salts[2]. In 1926, the first successful surgical resections by Ce´sar Roux in Switzerland and CharlesMayo were reported[2].Ulf Svante von Euler discovered that norepinephrine is the neurotransmitter of the sympathetic nervous system which earned him a share of the 1970 Nobel Prize in Physiology[2]. The isolation of two catecholamine metabolites in the urine, vanillylmandelic acid (VMA) by Armstrong in1956[3] and metanephrines by Axelrod in 1957, were landmarks in biochemical diagnosis[4].

Phaeochromocytoma can be sporadic or inherited. 10% are bilateral, 10% are extraadrenal and 10% are malignant. These percentages are higher in inherited syndromes.In von Recklinghausen neurofibromatosis Type 1 and von Hippel-Lindau disease, pheochromocytoma occursin up to 2 and 20% of such patients, respectively[5]. Close to 40% of patients with MEN 2 harbor a pheochromocytoma.

Palpitations, headache and profuse sweating are the classical triad of phaeochromocytoma. The dominant sign is hypertension which is usually episodic but can also be sustained. In children, profuse sweating is a common manifestation, often ignored due to the infrequent use of blood pressure measurements. Some unusual clinical features are transient ischemic attacks, stroke, grandmal seizures, cardiomyopathy, gastrointestinal crises[6], and diabetes mellitus orinsipidus.

In this case, the patient presented with classical symptoms of palpitation and profuse sweating. She also had paroxysms of flushing, sweating and tachycardia along with hypertension and raised blood sugar.

Initial testing is done by urinary tests for VMA, metanephrines and catecholamines. Assays of plasma catecholamines and their metabolites, especially norepinephrine and normetanephrine, are needed if the urinary test results are equivocal. The sensitivity and specificity of plasma free metanephrineshas been reported to be 99 and 89%, respectively[7]. Measurement of plasma metanephrines is the most sensitive biochemical test as it is least susceptible to false positive elevations.

Diagnostic testing can be done by CT, MRI and MIBG scans. The resolution power of CT has permitted localization of tumors as small as 5mmwith a sensitivity and specificity of 88 and 95%, respectively. Scintigraphy with meta-iodobenzylguanidine (MIBG), an analogue of nor-epinephrine, permits anatomical localization, determination of function with the highest sensitivity and specificity and detection of extra-adrenal tumors and metastases. The sensitivity and specificity of I-131 MIBG are 87 and 94%, respectively, with more recent studies reporting even higher percentages[8]. Positron emission tomography (PET) after intravenous administration of fluorine-18–labelled deoxyglucose (FDG) is the most recent scintigraphicimaging method oriented toward anatomical localization and determination of the metabolic activity of adrenal and extra-adrenal pheochromocytoma.

In this patient, initial testing was done by urinary VMA, which was 4mg/d(not elevated). Plasma metanephrines was not done as it was not affordable by the patient. USG abdomen, CT abdomen and PET –CT was done, which was suggestive of left adrenal tumor without any extra-adrenal lesions or metastases.

About 5-10% 0f the tumours are malignant. This term is restricted to tumours only with distant metastasis.

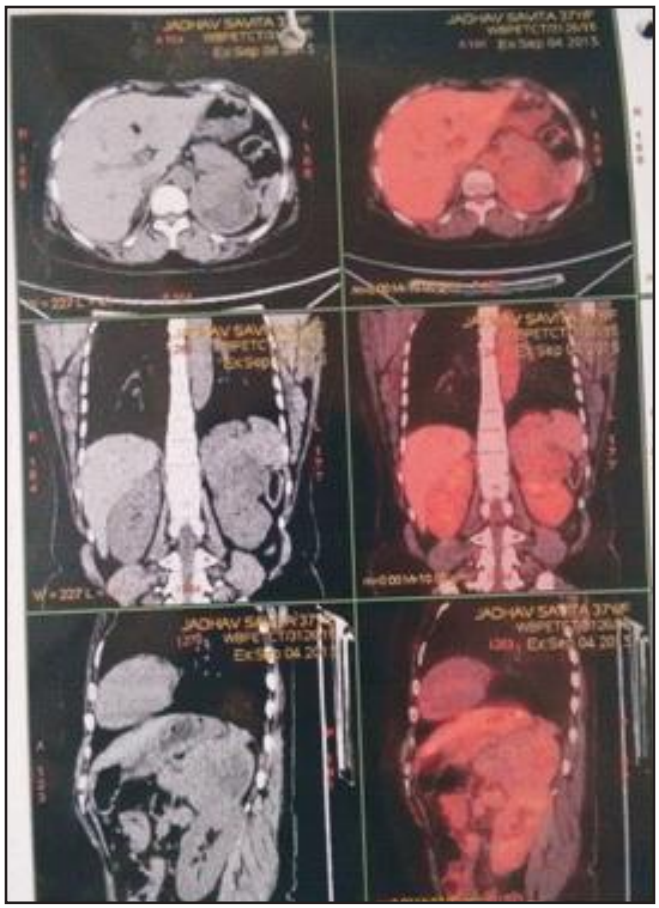

Figure1: FDG-PET images of the left adrenal tumor

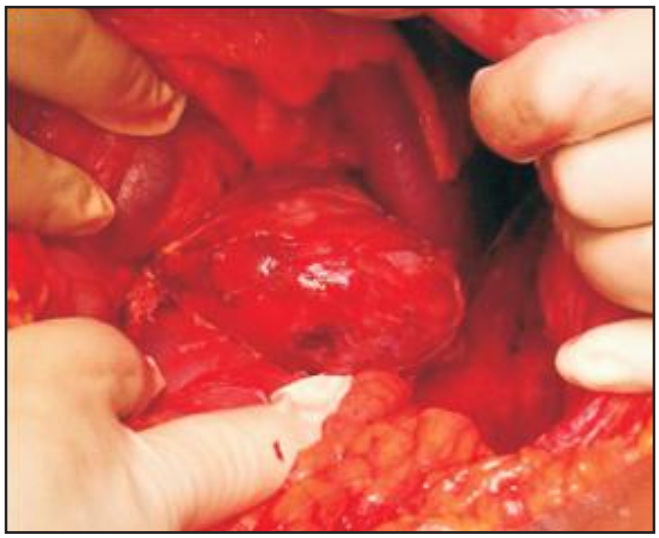

Fig 2a: intra-operative left adrenal tumour

Before the surgical management, the patients have to be stabilised by antihypertensives and other metabolic abnormalities also have to be corrected. Surgery can be done by open approach or laparoscopically. The anterior transperitoneal access remains the optimal approach to

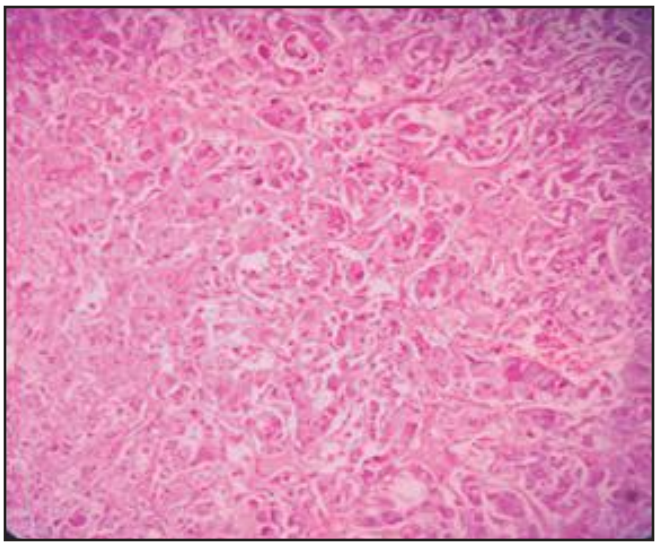

Fig 2b : Histology of the tumour - Nests of tumor cells surrounded by fibrovascular stroma

malignant and large adrenal tumors. Laparoscopic adrenalectomy is preferred for the surgical treatment of benign adrenal disease. Contraindications for laparoscopy include uncorrectable/untreated coagulopathy and unacceptable cardiopulmonary risk, previous surgery or traumain the direct vicinity of the adrenal gland, diaphragmatichernia, metastatic phaeochromocytoma, large sizeand surgeon's inexperience.

In this case, the patient was initially stabilised medically using and blockers and insulin. Patient was taken up for open adrenalectomy as the size was large. Histopathology report confirmed the diagnosis of phaeochromocytoma. Post-operative period was uneventful. In her follow-up of 3 months patient is asymptomatic.

Conclusion

In a young patient with hypertension phaeochromocytomahas to be considered as a differential diagnosis even though it is rare. Once it is diagnosed, the patient has to initially stabilised by the physician only after which the patient can be considered for surgery. Intra-operatively and post-operatively also the patient the patient has to be carefully observed as there can be complications. Therefore, treatment of phaeochromocytoma is a team effort which includes the physicians, anaesthetists and the surgeons as observed in this case.

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CASE REPORT

Case of Mycosis fungoides with ulceration

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ABSTRACT

Mycosis fungoides represents the most common type of cutaneous T cell lymphoma and accounts for approximately 50% of all primary cutaneous lymphomas, usually arising in mid to late adulthood. The incidence has been cited as 1 in 300,000 per year.It is relatively uncommon among the Asians. Large plaque parapsoriasis is now considered to be a type of mycosis fungoides. Mycosis fungoides is characterized by typical cutaneous stages of disease, consisting of patches and plaques involving less than 10% of the body surface area (stage T1/IA), more than 10% of the body surface area (stage T2/IB), tumours (stage T3/IIB) and erythrodermic variant. Herein, we present a case of 34-year-old young male diagnosed as mycosis fungoides with ulcerative skin lesions with no systemic features.

Key words: parapsoriasis, mycosis fungoides, lymphocytes

Introduction

Mycosis fungoides was first described by Alibert in 1806. It has an indolent clinical course with slow progression over years or sometimes decades, through several distinctive stages may overlap: premycotic, patch, plaque and nodule and tumour stages. The last stage is also associated with lymph node involvement and extracutaneous spread. Mycosis fungoides (MF) is a clinically and pathologically distinct form of cutaneous lymphoma characterized by an epidermotropic infiltrate of small to medium-sized T lymphocytes. Treatment options include phototherapy, oral and topical immunosuppressive agents.

Case Presentation

A 34-year-old male patient, farmer by occupation came to our out patient department with history of multiple dry patches over body since two years, multiple painful ulcers over the bilateral shins, left upper arm and right buttock since two months (Figure 1a, b). Patient was apparently all right two years back when he noticed multiple dry patches all over body (upper arm, trunk, lower limb, back). There was no history of weight loss or deformity. History of taking treatment for leprosy for the past three months was elicited.

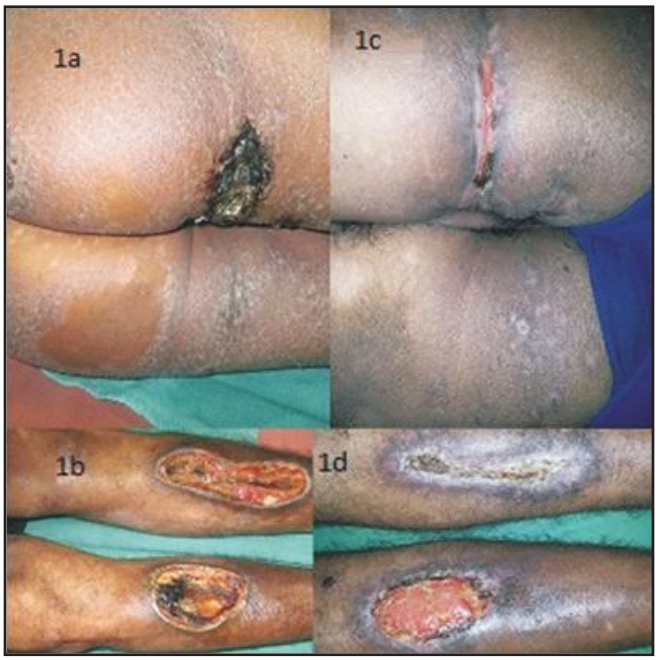

Figure 1a, b- Scaly patches over the buttock along with ulceration along with ulcerated lesions over bilateral shins

Figure 1c, d- Healing ulcers over the buttocks and shins after treatment with 11 months of cyclosporine

Cutaneous examination revealed multiple ill defined large ulcerated patches with hyperpigmentation and epidermal atrophy at a few places along with telangiectasia. All these patches were normoaesthetic and there was no evidence of nerve involvement. Multiple small ulcers in the centre of these dry patches associated with pain and pus discharge were seen. Systemic examination was unremarkable. There was no significant lymphadenopathy. Routine blood and urine investigations were normal. Nerve conduction study was normal. Ultrasonography of abdomen and pelvis was

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unremarkable. Skin biopsy from the patch showed parakeratosis, hyperkeratosis along with psoriasiform hyperplasia with vacuolar degeneration of basal cells. Papillary dermis shows band like inflammatory infiltrate of lymphomononuclear cells. Immunohistochemistry shows CD3 positivity. (Figure2a, b). Skin biopsy from the ulcerated nodule revealed ulcerated epidermis with parakeratosis and focal neutrophillic collection and mixed inflammatory infiltrate of neutrophils with lymphocytes extending upto deep reticular dermis. Majority of these cells showed CD3 positivity on immunohistochemistry.

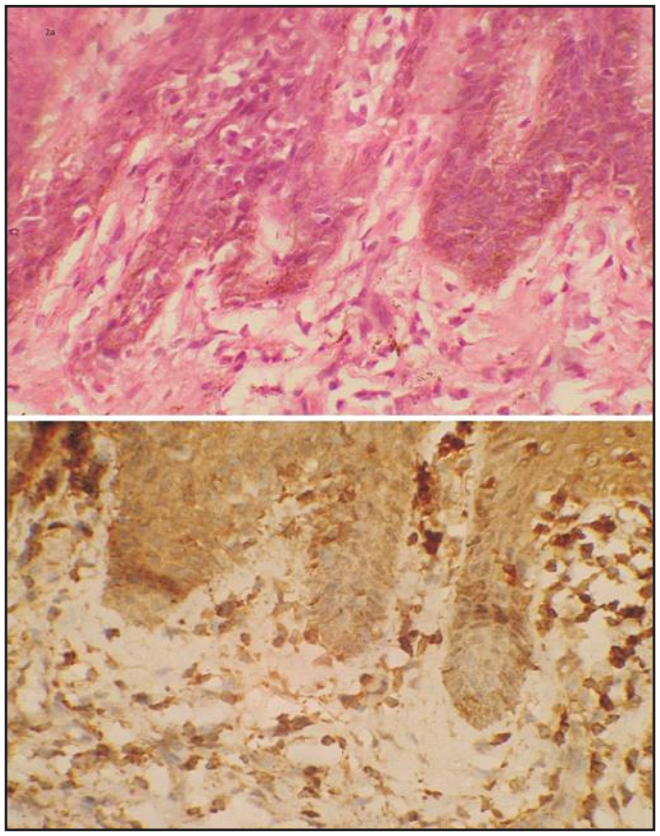

Figure 2a, b- Skin biopsy from the scaly plaque showing psoriasiform hyperplasia and epidermotropic lymphocytes on H & E stain at 40x magnification. Corresponding immunohistochemistry slide showing CD 3+vity.

Diagnosis of mycosis fungoides T3N0M0 stage was made based on clinical and histopathological findings. Patient was initially started on weekly 7.5 mg methotrexate and daily 5 mg folic acid with minimal response at the end of 6 weeks hence daily cyclosporine 50 mg was added and methotrexate was tapered off. Patient showed improvement in lesions by nearly 70% with treatment over past 11 months. (Figure.1c, d)

Discussion

Cutaneous T-cell lymphoma is generally classified as a type of non-Hodgkin's lymphoma. It consists of a heterogeneous group of lymphoproliferative disorders that primarily present in the skin and are composed of malignant clonal skin-homing helper T lymphocytes. Mycosis fungoides is the most common variant of primary Cutaneous T Cell lymphoma[1] generally associated with an indolent clinical course and characterized by well-defined clinicopathological features. Mycosis fungoides typically affects older adults (median age at diagnosis: 55-60 years)[2], but may occur in children and adolescents, with a male-to-female ratio of 1.6-2.0:1.

The aetiology of Mycosis fungoides is not yet established. Genetic, environmental and immunologic factors have all been considered. Characteristically, patients with classical mycosis fungoides progress from patch stage to plaque stage and finally to tumour stage disease and they have a protracted clinical course over years or even decades. Patients with tumour stage mycosis fungoides characteristically show a combination of patches, plaques and tumours the latter often show ulceration. Erythroderma may occur because of diffuse infiltration of the skin by neoplastic cells. In the advanced stages of MF, extracutaneous spread with involvement of various organs may occur.

Before a definite diagnosis is made, patients generally have many years of non-specific eczematous or psoriasiform skin lesions and non-diagnostic biopsies. Thus these lesions can be mistaken for those of Hansen's disease, psoriasis or eczema. In our case too, the patient was misdiagnosed for Hansen's disease initially and started on multi-drug therapy by a private practioner as the awareness about this rare entity is usually surpassed in comparison to that of Hansen's disease which is commonly encountered in our country.

Histopathologically, lesions show superficial band-like or lichenoid infiltrates, mainly composed of lymphocytes. The epidermis may show acanthosis and elongated psoriasiform rete ridges, but spongiosis is generally mild. The dermal infiltrates are more pronounced, and may contain a higher number of atypical cells with cerebriform nuclei and occasional blast cells, as well as admixed eosinophils and plasma

cells. Basal vacuolar change and epidermotropism of lymphocytes are usually present in large plaque psoriasis.[3] Immunohistochemistry shows CD3, CD4 positivity.

Therapy includes topical corticosteroids, topical coal tar products, and various forms of phototherapy[4] In resistant cases cyclosporine and methotrexate are used. The prognosis depends on the stage, and in particular the type and extent of skin lesions and the presence of extracutaneous disease. Patients usually die of systemic involvement or intercurrent infections and septicaemia.[5] Our case highlights that erythroderma and ulceration are atypical presentation of mycosis fungoides and there is a need of aggressive management using two immunosuppressants in the form of methotrexate and cyclosporine to achieve long-term remission.

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CASE REPORT

Unusual case of Rupture uterus in unscarred uterus

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ABSTRACT

Uterine rupture is an obstetric emergency which contributes to maternal as well as fetal mortality and morbidity. Uterine rupture is more common in cases of previous scarred uterus. Spontaneous rupture of uterus in unscarred uterus is very rare. Here we have a rare case of uterine rupture in primigravidae in third trimester of pregnancy in early labour, where timely operative intervention by emergency exploration saved not only the life of mother but also the baby.

Keywords- uterine rupture , bicornuate uterus, unscarred uterus

Introduction

Uterine rupture, defined as non-surgical disruption of some or all the layers of the uterus (serosa, myometrium and endometrium). It is a life-threatening condition for both the mother and the fetus. The incidence of uterine rupture accounts for 1 in 3000.[1] There has been an estimated incidence of 17.4/100,000[2] in pregnant women dying of hemorrhage secondary to rupture uterus. As per the recent center for maternal and child enquiries report, maternal mortality from uterine rupture is as high as 30% in rural India.[3]

Uterine rupture has been shown to occur in labor (whether preterm, term or spontaneous). Cases of rupture are more likely to occur in a scarred uterus, most commonly after a previous caesarean delivery or open myomectomy. The incidence of uterine rupture in scarred uterus accounts for 0.8%[4]. Unscarred uterine rupture is a rare event incidence being 1 in15000[5]. It usually occurs in late pregnancy or during labor. It is more common in less developed countries, in cases of trauma or obstructed labour with lack of access to emergency obstetric services. Other risk factors include high-parity, uterine anomaly, obstetrics maneuvers like internal podalic version, instrumental deliveries, manual removal of placenta. Incidence of congenital uterine malformation is estimated to be around 3% in general population[6]. Bicornuate uterus is a congenital anomaly that results from defective lateral fusion of the paramesonephric duct at about the 10th week of intrauterine life. It accounts for 26% of all the uterine anomalies[6].

Case Report

18 years old female married since 1 year. Primigravida with 8 months amenorrhoea registered and immunized at PHC Talegaon was referred with preterm labour with abnormal uterine shape with pain in abdomen and admitted at sassoon general hospital at 2.00 am. Patient had pain in abdomen since evening not associated with pervaginal leaking or bleeding nor decreased fetal movements. Her previous menstrual cycles were regular and she was 36+3 weeks by her last menstrual cycle date and 34+6 weeks by ultrasonography of 20+1 weeks.

On examination patient's vital parameters were stable. On per abdominal examination Uterine height was 34 weeks but deviated to left side and right side being completely empty with longitudinal lie, cephalic presentation, floating, clinically liquor adequate with estimated birth weight of 2 kg with good uterine contractions. There was fetal bradycardia 60/min with no pick up. Per Speculum examination revealed no leak or any bleeding. On Per Vaginal examination cervix was 1 cm dilated, minimally effaced, membranes were absent, liquor draining was clear , vertex as presentation, station being high at -3 and adequate pelvis. Decision for Emergency LSCS taken in view of fetal distress with unicornuate uterus. On the operation table under anaesthesia before taking incision uterine rupture was suspected as lower pole was empty and foetal head was palpable in the right flank. There was evidence of hemoperitoneum approx 150 cc and baby was found to be en-sac in peritoneal cavity. Sac was ruptured and baby

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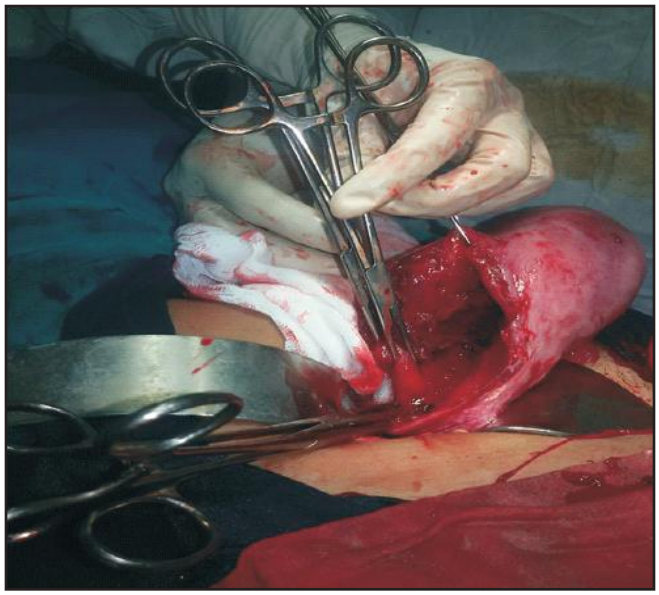
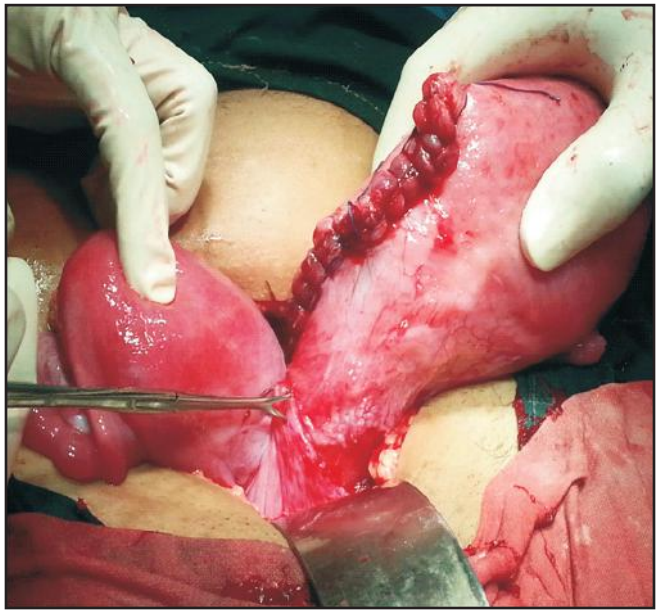
delivered out. It was a female baby weighing 1.9 kg, cried after stimulation, was shifted to HDU. Placenta was seen outside the uterine cavity and removed. Intraoperative 1 unit whole blood was transfused.



Evidence of rent of 6 to 8 cm noted in Right lateral wall of uterus from cornual end extending down posteriorly. (fig:1)



Uterine rupture site was sutured and haemostasis achieved. There was evidence of fallopian tube and ovary on left side of ruptured left horn. Also there was evidence of right horn with attached fallopian tube and ovary of right side in the pouch of Douglas with raphe was seen seperating the two horns (Fig:2).

Discussion

A scar on the uterus is a major risk factor for uterine rupture. High parity is a major risk factor in unscarred uterus. The commonest causes seen in the unscarred rupture cases are external injuries, multiparity, cephalo-pelvic disproportion with obstructed labour, adherent placenta, fundal pressure, abruption of placenta, history of intrauterine intervention causing perforation. Other risk factors for unscarred uterine rupture include, uterine anomalies, obstetric maneuvers, malpresentations, curettage, injudicious use of oxytocin, whereas some have no obvious cause. In our case, uterine anomaly may be implicated in the uterine rupture because the patient had a bicornuate uterus, and there were no other obvious risk factors.

Incidence of uterine anomalies is 3% in the general population[6]. The uterus is formed during embryogenesis by the fusion of two paramesonephric ducts (also called Mullerian ducts). This process usually fuses the two Mullerian ducts into a single uterine body. Lack of fusion of these Mullerian ducts can lead to various types of malformations.

Of all uterine anomalies, bicornuate uterus is the commonest constituting 26% of all uterine anomalies[6]. It represents a uterine malformation where the uterus is present as a paired organ resulting from the failure of the embryogenic fusion of part of Mullerian ducts. Hence, there is a double uterus with a single cervix and vagina. The bicornuate uterus often has unusually thick strong round ligaments and a thick vesicorectal fold running between them and may be associated with renal tract anomalies. Usually, the clinical classical signs of uterine rupture in pregnancy are palpable superficial fetal parts, fetal heart rate deceleration and, on pervaginal vaginal bleeding - change in station of head upwards. In a study using the Swedish Birth Registry, Kaczmarczyk and colleagues (2007) found that the risk of neonatal death following uterine rupture was 5 percent - a 60 fold increase in risk compared with pregnancies not complicated by uterine rupture.[7] Severe heart rate decelerations are seen in almost 80% of cases[8]. In our case fetal heart rate deceleration was an important sign which helped us in early intervention and was possible to save mother as well as baby.

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CASE REPORT

Laproscopic Spleen Preserving Distal Pancreatectomy

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ABSTRACT

We report the case of a 67-year-old male patient with an insulinoma of pancreas at the junction of body and tail. He underwent a laparoscopic spleen preserving distal pancreatectomy. Patient presented with episodes of giddiness and drowsiness for past 4 months. There was also history of tremor on exertion since 4 months. His symptoms improved with intake of food. During his episodes his blood sugar levels ranging from 35 mg% - to 50 mg%. Patient was thoroughly evaluated. USG abdomen and MRI abdomen showed normal study. His fasting serum insulin level raised with normal ACTH and cortisol level. DOTA PET Scan suggestive of focal octreotide receptor expressing lesion at the junction of body and tail of pancreas. There were no postoperative complications, and the patient was discharged from the hospital on day 6. The patient was ambulatory soon after the procedure. He was allowed to take orally after 12 hrs post surgery, and his hospital stay was short; therefore, the surgery was judged to have been highly useful.

Introduction

Insulinoma is the most common neuroendocrine tumor of the pancreas. Peak incidence of occurrence is between 40 to 69 years. About 40% - 90% of tumors are nonfunctional. Rest of them manifest with evident hormonal symptoms. Of the functional tumors 70% are insulinoma, of which 90% are benign. Usually present with symptoms like anxiety, confusion, dizziness, headaches, and sweating. Treatment for **insulinoma** is surgical excision, however before surgery; symptoms of excess hormones must be corrected. Patients with neuroendocrine tumor after surgery generally do well for years.

Distal pancreatectomy (DP) is the removal of the pancreatic tissue at the left side of the superior mesenteric vein and it is traditionally approached by an open or laparoscopic exposure. Preservation of the spleen is optional but appears to have a better immunological outcome.

In 1994, Soper et al first performed laparoscopic distal pancreatectomy in a pig model to document its safety and feasibility[1]. Laparoscopic partial pancreatic resection for pancreatic endocrine tumor was first reported in 1996 by Gagner and colleagues[2], and laparoscopic pancreatectomy is now considered to be indicated for that condition[3].

CASE summary

67 year male patient presented with history of episodes of giddiness, drowsiness for past 4 months. There also history of tremor on exertion since 4 months. His symptoms improved with intake of food. During his episodes his blood sugar levels ranging from 35 mg% - to 50 mg%.

INVESTIGATIONS

Patient was thoroughly evaluated. USG abdomen and MRI abdomen showed normal study. His fasting serum insulin levels were raised with normal ACTH and cortisol level. DOTA PET Scan suggestive of focal octreotide receptor expressing lesion at the junction of body and tail of pancreas. Complete hemogram was done. ECG, X-ray chest. ACTH, Sr.Cortisol, Sr.Insulin, Thyroid function test and random blood sugar done preoperatively.

OPERATIVE PROCEDURE

After taking written informed consent patient was taken for "Laparoscopic Spleen Preserving Distal Pancreatectomy". After port placement lesser sac was opened and pancreas identified Fig (1). Meticulous dissection done at the lower border of pancreas and splenic vein and splenic artery were identified Fig (2). Small branches from both vessels were clipped and cut. After complete mobilization of distal pancreas. ENDO GIA stapler blue cartridge was used for transaction of the pancreas at mid body region Fig (3). Specimen was packed in endobag and removed Fig (4), Fig (5). Total

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operative time taken was 120 min. Estimated blood loss was 50 ml. Gross examination of specimen suggested 2.2x1 cm, hard nodule in tail of pancreas. Patient tolerated the procedure well and shifted to ward.

POST OPERATIVE PERIOD

Patient's blood sugar levels normalized post operatively. Ryle's tube was removed on post operative day 2 and oral liquid started. Patient discharged on day 6.

Final histopathology examination report was Low grade neuroendocrine tumor of pancreas, surgical margin were free. Size of tumor 1.5x1x1 cm. On Immunohistochemistry Ki 67 index was 1.5.

INTRA OPERATIVE IMAGES

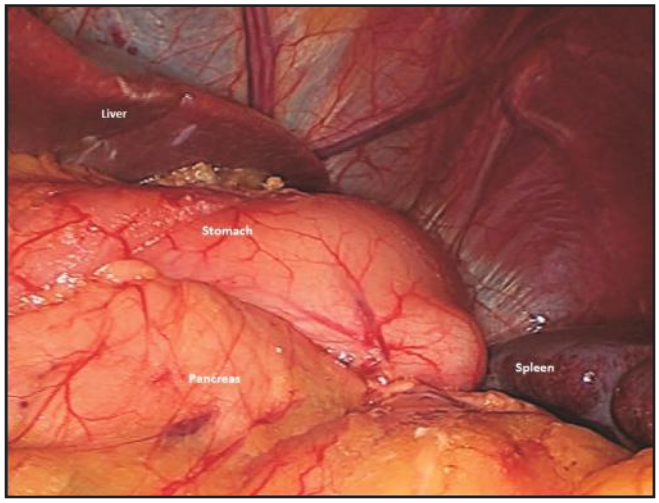

Fig (1) Laparoscopic view of pancreas, spleen, liver and stomach

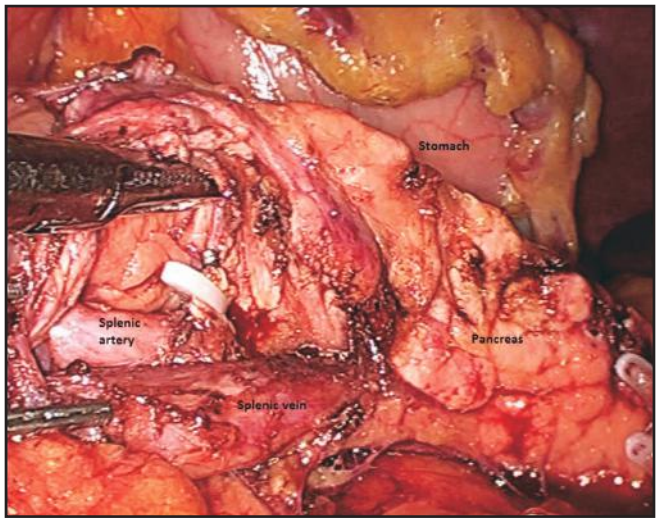

Fig (II) Laparoscopic view after dissection showing splenic artery and vein

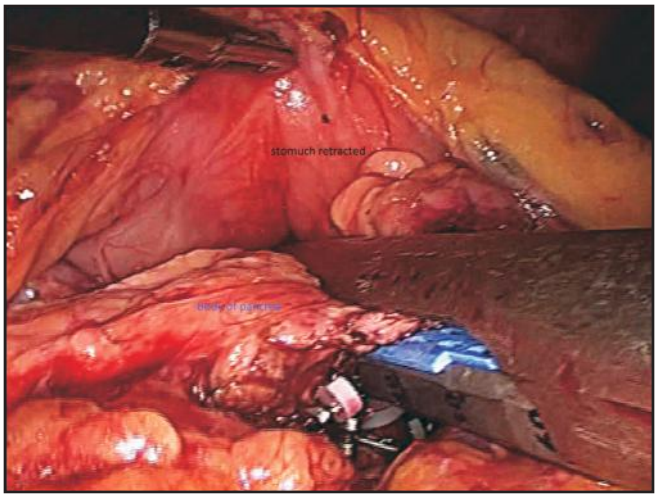

Fig (III) Illustrating view of laparoscopic distal pancreatectomy with ENDO GIA stapler

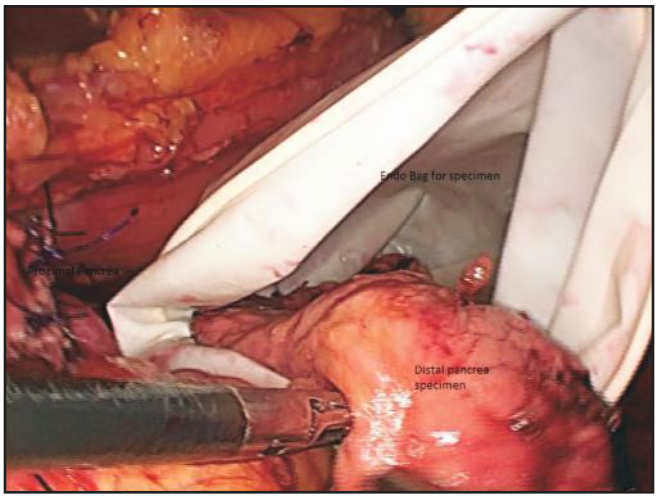

Fig (IV) Specimen extracted in endo bag

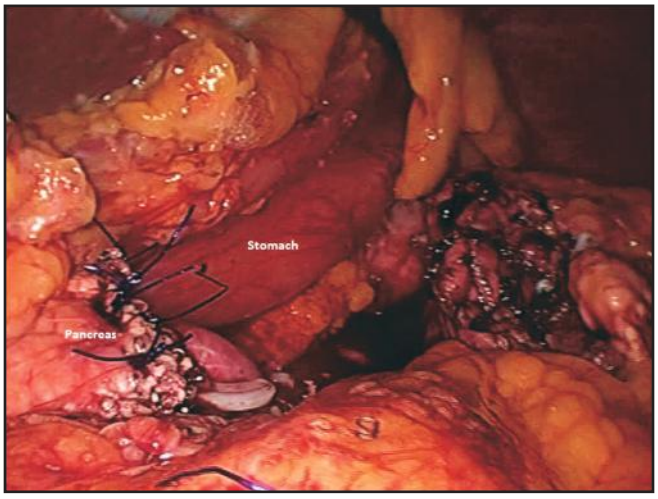

Fig (V) Post distal pancreatectomy view of Pancreas

Discussion

Neuroendocrine tumor arises from cells throughout diffuse endocrine system, mostly arising from lung, bronchi, bowel, pancreas and less commonly from parathyroid, thyroid and adrenal.[4] Most of these are sporadic in nature but sometimes can in context of inherited genetic syndrome like MEN 1 and MEN 2.[5] Neuroendocrine tumors are sub classified by the site of origin, stage, functional status and histological differentiation (mitotic count, Ki-67 index and tumor grade).[4]

Suspicion of neuroendocrine tumor of pancreas usually occurs when patient presents with symptoms of hormonal excess if it is a functional secretary tumor or is an incidental finding in a non-functional tumor.[4] Biochemical test include Serum Chromogranin - A which is positive in 60% of cases. Serum insulin level (>6mclU/ml), pro-insulin (>\= 5 pmol) and c-peptide (0.6ng/ml) and fasting blood sugar less than 55mg/dl is diagnostic for insulinoma. Radiologically EUS is the best modality to particularly localize the tumor.[4,5] MDCT or MRI is best to rule out metastasis.[4, 5] Somatostatin scintiography is less useful in insulinoma as these tumors are less sensitive for octreotide derivatives, and used only for metastatic disease follow up if octreotide derivatives are being used.[5]

Resection is the primary treatment of choice which is usually enucleation for lesions <1 cm away from MPD, for lesions 1-2 cm either enucleation or radical surgery (Pancreaticoduodenectomy / Distal pancreatectomy +/- spleenectomy) with regional lymphadenectomy is advocated and for lesions >2 cm radical surgery with lymphadenectomy.[6] Laparoscopic surgical management is the current trend especially Distal Pancreatectomy with or without spleenectomy as it is a less morbid, gives early postoperative patient recovery, but at the same times requires high level of surgical expertise.[5]

Surveillance is advocated every 3 monthly with MDCT or MRI along with serum markers for at least 10 years. Treatment for metastatic disease if operable then surgery followed by Somatostatin analogue therapy with or without chemotherapy.[5]

Conclusion

We have reported a case of laparoscopic distal pancreatectomy, with preservation of the spleen and splenic vessels is easy and safe. There was no major intraoperative bleeding. The patient was ambulatory soon after the procedure. He was allowed to take orally after 12 hrs post surgery, and his hospital stay was short; therefore, the surgery was judged to have been highly useful.

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CASE REPORT

Asynchronous Bilateral Ovarian Torsion in a Premenarchal girl

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ABSTRACT

Ovarian torsion is an infrequent diagnosis in the pediatric age group. Because of its non-specific symptoms, ovarian torsion is difficult to distinguish from other entities including acute appendicitis, ruptured ovarian cyst, renal colic and gastroenteritis etc. Hence, the diagnosis of ovarian torsion remains a great challenge to pediatric surgeons and gynecologists. Pediatric ovarian torsion is a serious condition especially in cases of asynchronous bilateral ovarian torsion. We report a case of premenarchal girl who suffered asynchronous bilateral ovarian torsion. The remaining ovary was saved by early surgical intervention.

Key words- ovarian torsion, detorsion, oophoropexy.

Introduction

Ovarian torsion is an infrequent diagnosis in the pediatric age group. Low abdominal pain, nausea, vomiting, low fever, leukocytosis are the usual presenting features. Because of its non-specific symptoms, ovarian torsion is difficult to distinguish from other entities like acute appendicitis, ruptured ovarian cyst, renal colic and gastroenteritis. Hence, the diagnosis of ovarian torsion remains a great challenge to pediatric surgeons and gynecologists. However early recognition and prompt management yield significant reduction in morbidity and an increased likelihood of ovarian salvage.

Case Report

An 11 year girl was brought to hospital with complaints of severe pain in abdomen on right side and vomiting 2 episodes since 6 hours. Examination demonstrated tenderness in right iliac fossa . This girl was admitted one month back with pain in abdomen on left side, loose motions and vomiting for 2 days before admission. She was referred from surgical unit for bulky and echogenic left ovary. Colour Doppler showed absent vascularity in left ovary lying in pouch of Douglas. Patient underwent laparotomy, three rounds of torsion of tubo-ovarian ligament with nonviable left ovary was found. Left sided salphingooopherectomy was done. Histopathological examination confirmed haemorrhagic infarction of the ovary. Her tumour markers CA 125, CEA and serum b-HCG levels were normal.

Because of this history, now torsion of right ovary was suspected. Urgent USG with Colour Doppler of pelvis was done which showed bulky right ovary with multiple prominent follicles with minimum vascularity with biphasic waveform suggesting torsion - detorsion. An emergency laparotomy was performed under general anaesthesia which revealed two rounds of torsion of right ovary. Detorsion was done. The ovary was bulky, 4*4 cm in size and haemorrhagic. We observed for 10min after detorsion. Pinkish colour was noted at some places over the surface of the ovary. Plication of ovarian ligament was done using 1-0 nonabsorbable suture mersilk. Also oophoropexy was performed by fixing the ovary to the pelvic side wall at the level of pelvic brim medial to ureter using nonabsorbable suture. Subsequent post operative recovery was uneventful. She was discharged on day 8. Follow up sonography with colour Doppler after three months showed normal size ovay with normal vascularity.

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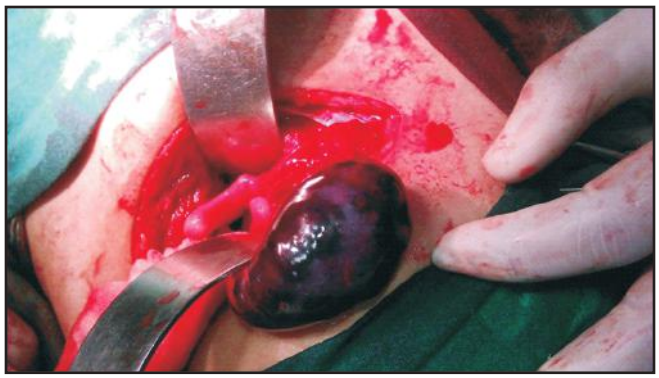

Figure: Ovary after detorsion

Discussion

Ovarian torsion as a rare entity in childhood and adolescence is an emergency event requiring prompt surgical management. Its incidence ranges from 2/10 000 to 4.9/100 000. It accounts for 2.7% of all causes of abdominal pain in children[1]. Ovarian torsion occurs due to abnormal twisting of the involved ovary with its ligamentary support which will compromise venous followed by arterial circulation of the ovary. If untreated, this will lead to ischaemia and necrosis of the ovary, resulting in loss of ovarian function or infection and peritonitis.

Ovarian torsion occurs often at the right side of the ovary in the ratio of 3:2. In pediatric patients, ovarian torsion is associated wih pathological changes of the ovary like adnexal cysts, teratomas, or other benign masses including polycystic ovaries, but it might occur even in anatomically normal ovary. The exact mechanism of this entity remains poorly understood. Excess mobility in elongated tubes and ligaments, tubal spasm, sudden changes in intra abdominal pressures, increased hormonal activity in premenarchal girls have been postulated as possible causes. Another risk for ovarian torsion is a malignant tumour; however only 1.8% malignancy rate is reported in literature[2].

Diagnosis of adnexal torsion in young girls presents a diagnostic challenge because of nonspecific symptoms and signs and may mimic constipation, appendicitis, renal colic, gastroenteritis, mesenteric adenitis. A high index of suspicion for adnexal torsion is imperative in any girl presenting with lower abdomen.

Diagnostic sonographic features are enlarged and heterogenous appearing ovary in contrast to contralateral ovary, presence of multiple small peripherally placed follicles within ovary, ovaries that cross the midline, presence of fluid collection in pouch of Douglas. Despite ovarian torsion, Doppler sonography was normal in 60% of the cases because of the presence of dual supply to the ovary. CT and MRI should be reserved for those cases where ovarian pathology is highly suspected but ultrasound is equivocal as it may delay necessary surgical intervention.

Ovarian torsion needs surgical intervention. Traditionally oophorectomy has been advocated for treatment of ovarian torsion. Currently a more conservative approach, i.e. detorsion is reported to be safe and effective in preserving fertility. The reported incidence of embolism is only 0.2% in cases of adnexal torsion[3]. But detorsion does not increase the incidence of thromboembolism. Patients with ovarian torsion of normal adnexa, treated conservatively are at increased risk of recurrent torsion of ipsilateral side and the contralateral adnexa. Thus oophoropexy is the most common procedure for the prevention of recurrence of torsion. Several techniques of oophoropexy have been reported . But there is no unified technique nor any consensus about it. The techniques include suturing of the ovary to the pelvic side wall, usually at the level of the pelvic brim or to the back of the uterus or to the uterosacral ligaments. In cases of elongated uteroovarian ligaments, plication of the ligament is suggested. Use of permanent, nonabsorbable sutures is recommended for all procedures[4].

Once the girl has lost one ovary due to torsion , she is at risk of being castrated if the contralateral ovary undergo torsion as well. This is extremely rare, but for the affected girl, it represents a catastrophic event. In our case, contralateral ovary was saved by immediate surgical intervention. However had prophylactic oophoropexy been performed at the time of initial operation, subsequent torsion and risk of castration would have been abolished. Oophoropexy, however is widely debated in literature and there are no trials evaluating its efficacy. Oophoropexy has been shown to reduce future fertility because of interference of fallopian tubal blood supply or tubo ovarian relation[5]. Fuchs et al[4] followed up six patients after oophoropexy and found that torsion recurred only in one patient. The six patients resumed normal menstruation and two of

them conceived and gave a birth. Shun[6] recommends prophylactic fixation of the contralateral ovary at the time of unilateral oophorectomy, regardless of the pathology, in order to prevent castration. Laparoscopic treatment for adnexal torsion in adults is becoming increasingly popular for diagnosis of the condition, detorsion, oophoropexy.

Although oophoropexy remains controversial in the treatment of primary ovarian torsion, it is feasible in certain clinical situations such as recurrent torsion, loss of contralateral ovary and anatomically vulnerable ovary.

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CASE REPORT

Acute cerebellar ataxia: A rare self limiting complication of severe malaria

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ABSTRACT

Cerebral malaria is common complication of Falciparum Malaria. We describe the case who presented with severe malaria with high-level parasitemia and anemia. The course was complicated by development of jaundice and altered sensorium, followed by the appearance of cerebellar ataxia during the recovery phase. This occurred after successful treatment with artisunate plus doxycycline over seven days. Peripheral blood smear was suggestive of mixed infection i.e. Plasmodium falciparum plus Plasmodium Vivax with parasite index of 3+. The patient recovered completely.

Key words : Plasmodium falciparum; malaria; cerebellar ataxia; parasite index

Introduction

Malaria is a major public health problem in the developing world owing to its high rates of morbidity and mortality. An estimated 300-500 million people contact malaria each year, resulting in 1.5-2.7 million deaths annually. Of all the malarial parasites that infect humans, Plasmodium falciparum is most commonly associated with neurological complications. The neurological complications of falciparum malaria are common and encompass a wide spectrum of clinical presentation. These complications can manifest during acute illness, or can present during convalescence. Increasing drug resistance in several parts of our country has further aggravated the problem of management. Cerebellar ataxia is an unusual complication of falciparum malaria. It was first reported by Senanayakeet al.[1]

Case Report

20 year old male presented with history of fever with rigors followed by development of jaundice in 6 days and altered sensorium in 2 days. On general examination he was Febrile, had tachycardia with pulse rate of 100/min, Respiratory rate of 24/min and Blood Pressure of 110/70 mmHg. Pallor and icterus both were present. Systemic examination was normal except for hepatomegaly (palpable 4cm below the right costal margin). His laboratory investigations were as follows: Hb-5 Gram%, WBC-7000/ cumm, Polymorphs-67% Lymphocytes-28%, Monocytes-3%, Eosinophils-2%, Platelet Count-2.4 lakh/cmm. Peripheral smear showed Trophozoite of PlasmodiumVivax and falciparum with index 3+. There were no fragmented RBCs. His Reticulocyte count was 1.5 %, Random blood sugar-97 mg/dl. Urine showed bile salts and bile pigments. His other laboratory parameters were blood urea-75 mg/dl, serum creatinine-1.8 mg/dl, serum sodium-136 mEq/L, serum potassium-3.8 mEq/L, Total billirubin -11.6mg/dl (D: 8) SGPT-59 IU/L, SGOT-99 IU/L, Serum ammonia 45 μmol/L. Viral marker were negative for HBV, HEV & HAV. Chest x ray was normal, ECG showed Sinus tachycardia.

Patient was treated with injection artisunate and oral doxycycline as per the WHO recommendations. Supportive treatment in the form of intravenous fluids and blood transfusion for severe anemia was given. Tablet primaquine was started for radical cure of p. vivax. On fifth day patient became afebrile, conscious, started accepting oral feed.

On 7th day of treatment patient had difficulty in walking in the form of swaying in both directions and slurred speech. On careful neurological examination, he had bilateral cerebellar signs including Dysdiadochokinesia, Finger nose ataxia, Knee heel ataxia. He had Scanning speech and wide based Gait with swaying on either side on tandem walk. Rest neurological examination was

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normal. There was no nystagmus. All these features suggestive of bilateral cerebellar involvement in patient recovering from severe complicated malaria. MRI Brain was normal.

Patient was treated symptomatically with proper hydration and nutritional support. He was observed for next five days. He showed gradual recovery and was able to walk with no ataxia and no dysarthria.

Discussion

Delayed cerebellar ataxia is one of the unusual complications of falciparum malaria. Cerebellar involvement in plasmodium falciparum malaria can occur in:

1) Acute stage of fever.
2) Survivors of patient with cerebral malaria during resolving stage after full control of infection.
3) The form of delayed cerebellar ataxia after afebrile latency.

   Or as a complication of anti-malarial drugs with CNS toxicity.

Delayed cerebellar ataxia is unique ataxic syndrome seen in patients recovering from falciparum malaria. There is selective impairment of the cerebellar system in otherwise conscious patient following an attack of uncomplicated or complicated malaria. The period between the fever and ataxia varies from 3 to 41 days (mean 13 days). Severe gait and truncal ataxia are striking features, which suggest that the disease has predominantly affected the midline cerebellar structures. Peripheral blood film may show gametocytes, schizonts of plasmodium falciparum. Laboratory investigations in these patients, including CBC, CSF examination, electroencephalography, and CT scan of the brain, are usually normal.[2] Cerebellar involvement appears to be the most consistent neurological manifestation of complicated, as well as of uncomplicated malaria. So far the etiology is not known but a few theories have been postulated-

1) Effect of Parasite: direct invasion, toxic effect or an immune reaction
2) An immunologic mechanism has been suggested to play a role in the pathogenesis of the condition. Marked elevation of serum and CSF cytokines including TNF, IL-6, and IL-2 in patients with cerebellar ataxia following Malaria were observed in comparison to those that did not develop[3]
3) De Silva et al suggested that the absence of cases before 1984, and the fact that most cases were reported from Sri Lanka, could be explained by the appearance of a new strain of Plasmodium falciparum in that area.[4]
4) The Purkinje cells are susceptible to damage due to hyperpyrexia causing cerebellar manifestations.[5],[6]

This condition is mostly self-limiting (3 to 6 weeks) with good prognosis requiring only antimalarials and symptomatic treatment with a few cases requiring steroids.[7]

Conclusion

Thus, the cerebellar ataxia should be included as neurological complications of P. falciparum malaria and as a differential diagnosis of acute cerebellar ataxia. Despite cases of neurological manifestations of P. falciparum malaria being reported since long[8], WHO has not included the various presentations of neurological complications of P. falciparum malaria other than cerebral malaria in the recently issued (2015) guidelines.[9] Treatment of the disease and its complications at the earliest is likely to improve the outcome of the disease. Malaria has varied clinical manifestations including neurological manifestations. Cerebellar involvement in malaria is less commonly described. Malaria should be included in differential diagnosis of acute cerebellar ataxia following acute febrile illness.

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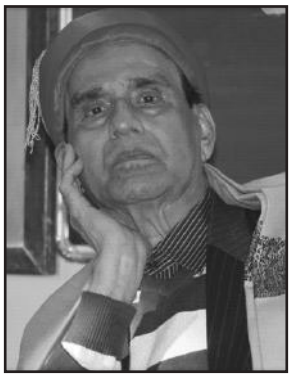
Obituary



M. G Tepan
(Birth 29th December 1931, Death 10th February 2016)

A legendary surgeon who contributed tremendously in the field of Otorhinolaryngology.

Completed Masters under Sir Harold Gillis At J.J Hospital, Mumbai.

He joined BJMC in 1972 under honourable Dr B.P Apte and Dr.W.G Atre and continued to work with this prestigious institute for 30 years.

An exemplary surgeon and dedicated teacher ,he inspired an entire generation of young ENT surgeons under his able guidance and mentorship.

He organised hundreds of surgical camps around Pune and treated thousands of patients all over India .

His pioneering works include: Use of tragal cartilage and gold prosthesis for ossiculoplasty, translabyrinthine vestibular neurectomy, middle meatus antrostomy.

He was an avid cricket fan. He believed in being fit and walked 5-6 kms daily.

He is blessed with a wonderful family of two sons, a daughter and grand children.

His message for young ENT surgeons was work hard, learn and experiment.

We all miss you sir and your work will always inspire young ENT surgeons for generations to come.

(From Dept of ENT & HN surgery, BJGMC-SGH, Pune)

Obituary

Dr. Daulatrao Sonuji Aher
(Birth 1st November 1943, Death 19th January 2016)

M.S(ENT) F.I.C.S,D.L.O DORL

Son of Shri Sonuji Aher, born on 1 Nov 1943 at Devla taluka in Nashik.

He was the former Minister of Health and Family Welfare, Government of Maharashtra who completed his M.S (ENT) from B.J. Govt. Medical College, Pune and presented a thesis on conservative laryngeal surgery in cases of carcinoma of laryngeal and laryngopharynx. He also worked as an honorary E.N.T Surgeon, Civil Hospital Nashik from 1974-85. His special interest included social work.

He organized blood donation camps, micro-ear surgery camps, deafness detection camp and other such diagnostic and surgical camps in rural areas of Nashik, Dhule and other places of Maharashtra. His favourite sports activities included playing Kabaddi, Volleyball and Body building. He also served as the President of Indian Medical Association from 1984-85 and Senate Member at Pune University from 1985-86.

The Research Society

B. J. Medical College And Sassoon General Hospitals, Pune - 411 001

ANNUAL REPORT

(April 2014 To March 2015)

Dear Life Members,

I. GOVERNING COUNCIL:

The office-bearers of the current Governing Council (2014-2015) were :

President	Dr. Shalini Thombre
Vice-President	Dr. Meenal Jadhav
Hon. Secretary	Dr. Haridas Prasad
Hon. Joint secretary	Dr. Surekha S. Shinde
Hon. Treasurer	Dr. Smita A. Tiwari

Ex-officio members

Dean : Dr. Ajay S.Chandanwale

Superintendent : Dr.Deepak G.Kulkarni

Members

Dr. Ramesh A. Bhosale

Dr. Pradnya M. Bhalerao

Dr. Bharti R. Daswani

Dr. S. P. Rao

Dr. Suvarna A. Joshi

Dr. Sunita Girish

Dr. Medha M. Khandekar

Medical Journal Of Western India:

Volume 43 issue I was released on the occasion of inauguration of annual conference of Research society of B.J.Medical College and Sassoon General Hospitals, Pune. There was an editorial on, "Dengue -Changing scenario", by Dr Sangle S.A. Besides 4 review articles,6 original articles, 2 short communications and 5 case reports were published.

Volume 43, issue 2 was released in December 2015.In this issue there was an editorial on,"Violence against doctors" by Dr.Sneha Sathe. Besides 3 review articles, 5 original articles and 9 case reports were published.

CMEs conducted :

1. Department of Ophthalmology : Oncology in ophthalmology
2. Department of Medicine : Geriatric medicine

Annual Conference :

1. The 41st annual conference of Research society B.J.Medical College and Sasoon General Hospital, Pune was held on 11th,12th & 13th Feb 2015. It was organised by Department Of Dentistry & Department of Physiotherapy under the able guidance of Dr.Vivek Pakhmode & Dr. Ganesh Pande. It was attended by 1400 delegates. The event was inaugurated by Honourable minister Mr.Girish Bapat.
2. Total number of oral presentations were 52. Besides 75 posters& 16 interesting cases were presented.
3. Dr.B.B.Dixit oration was by Dr.Shreekant Sapatnekar, Ex Director, Haffkine institute of Training, Research & Testing, Mumbai. He spoke on the topic,"Rising to the occasion- The never ending war against infectious diseases."
4. Oral & poster presentations were done on 1st day of conference. On the 2nd day besides the B.B.Dixit oration, 2 guest lectures namely, "Modern techniques in smile designing & its relationship with head, neck and shoulder pain", by Dr.Sandesh Mayekar and "Good Communication is essence of a successful medical practice", by Dr.Prafull Mokadam were presented. There was a symposium on oro-facial reconstruction. The Partcipants were Dr.Deepak Kulkarni, Dr.Satish Kale, Dr.Parag Sahastrabuddhe and Dr.Nikhil Panse. On the 3rd day there were 2 guest lectures. The first was on

"Developing Sports Medicine Facilities in India "by Dr.Ali Irani and the 2nd was on "What is new in understanding of esophageal function with relevance to understanding reflux & dyspepsia",by Dr.Sanjay Salunkhe. There was also a panel discussion on, "Overview of multidisciplinary critical care". The participants were Dr.B.D. Bande, Dr.Suhas Otiv, Dr.Shivakumar Iyer & Dr.Umesh Vaidya. Besides, a symposium on "Organ Transplantion" was held. The partcipants were Dr.Abhay Sadre, Dr.Harshal Rajekar, Dr.Vijay Ramanan & Dr.Nityanand Thakur.

5. Prizes won :

Suchintan Trophy (Rolling)- Best paper of the Conference

(Trophy) :- Ashwini Dedhwal, Dept. of Microbiology, BJGMC

Sphurti Trophy- Best paper in Anesthesia

(Trophy) Amol Pandav, Dept. of Anesthesiology, BJGMC

Harshawardhan Prize- Best paper in Undergraduate & Postgraduate category

(Rolling) (Amount – Rs. 500) Akanksha Swadi, Dept. of Radiology, BJGMC

Dr. A.R. Bhadkamkar Award- Best paper in Anatomy (Amount – Rs. 100) Smita Nomulwar, Dept. of Anatomy, BJGMC

Dr. Mrs. V.A. Bhadkamkar Award -Best paper in Pharmacology

(Amount – Rs. 100) Sagar Katare, Dept. of Pharmacology, BJGMC

Dr. Jejurikar Award -Best paper in Surgery

(Amount – Rs. 400) Unnati Prajapati, BJGMC

Dr. S.J. Kinikar Award - Best paper in Medicine by a Postgraduate student

(Amount – Rs. 2000) Ambarish Awate, Dept. of Medicine, BJGMC

Dr. Ajit Gokhale Prize- Best Poster of Conference

(Amount – Rs. 1000) Anita Basavraj, Dept. of Medicine, BJGMC

Dr. D.J. Patil Award -Best Oral paper in interesting case session

(Amount – Rs. 1000) Hamza Dalal, Dept. of Medicine, BJGMC

Dr. MB Gharpure Memorial Trust-Best Oral paper in Dermatology

(Amount – Rs. 1500) Shraddha Katkar, Dept. of Skin & VD, BJGMC

Dr. K. B. Niphadkar -Best Paper in Immunology/ Pathology/Microbiology by a Postgraduate

(Amount – Rs. 2000) Khushboo Kabra, Dept. of Pathology, BJGMC

Dr. E.P. Patil Award-Best paper in Orthopaedics

Roentgen Teachers Trophy -Best paper in Radiology

(Trophy) Akanksha Swadi, Dept. of Radiology, BJGMC

Best Oral Paper Postgraduate category - First Prize

(Pen Drive) Amol Pandav, Dept. of Anesthesiology, BJGMC

Best Oral Paper Postgraduate category - Second Prize

(Pen Drive) Priyanka Asia, Dept. of Biochemistry, BJGMC

Best Oral Paper Postgraduate category -Third Prize

(Pen Drive) Ambarish Awate, Dept. of Medicine, BJGMC

Best Oral Paper Lecturer Category (< 5 yrs)

(Pen Drive) Anupam Khare Dept. of Physiology, BJGMC

Best Oral Paper Lecturer category - Second Prize (> 5 yrs)

(Pen Drive) H. B. Prasad Dept. of Medicine, BJGMC

2nd Best paper Interesting case presentation

(Pen Drive) Neelam Singh, BJGMC

3rd Best paper Interesting case presentation

(Pen Drive) Shashank Wankhede, Dept. of Pulmonary Medicine, BJGMC

Best Poster - Postgraduate category - Second Prize

(Pen Drive) Vikram Patil, Dept. of Pharmacology, BJGMC

Best Poster - Postgraduate category - Third Prize

(Pen Drive) Aditee Yelmar ,Dept. of Anesthesiology, BJGMC

1970 Batch UG Oral Paper First Prize

(Amount – Rs. 2000) Niharika Apte, BJGMC

1970 Batch UG Oral Paper Second Prize

(Amount – Rs. 1500) Unnati Prajapati. BJGMC

1970 Batch UG Poster Prize

(Amount – Rs. 3000) 3rd element group, BJGMC

1970 Batch UG Poster Prize

(Amount – Rs. 1500) Sanket Gaikwad, BJGMC

6. List of new Life members

Dr. Kuvar Ravi Sajan

Dr. Umarji Pramod Chinmay

Dr. Agarkhedkar Sharda

Dr. Vinyanand Tanny.

Dr. Hadate Abhijit Ashok

Dr. Gosavi Prakash Anil

Dr. Naresh Dilip Munot

Dr. Zanjad Naresh Prabhakarrao

Dr. Bhitkar Harshal Narendra

Dr. Thorat Santosh Dashrat

Dr. Nalawade Niraj Manohar

7. Auditors

Deekay and Company Pune was continued as auditor for this period.

ACKNOWLEDGMENTS

The honorary secretary is thankful to the members of the governing council, past office bearers, Editor-in-chief, and the members of the organising comittee of the annual conference for their valuable help in fullfilling the objectives of the trust.

Hon. Secretary

Research Society

B.J.M.C. & S.G.Hs, Pune 411 001.

Medical Journal of Western India

Instructions To The Contributors

Medical Journal of Western India is a peer reviewed journal. It is published biannually. It accepts original articles, review articles related to the different disciplines, case reports and short communications in the field of clinical practice and medical education. Case reports of only unique and rare character are accepted. Papers are published in English. Submitted papers are accepted after peer review. To achieve wider dissemination of knowledge and information, the published articles can be accessed online at www.bjmcpune.org/medicine.htm.

Submission of manuscript : Authors should submit electronic version (Microsoft word doc) of the manuscript to the editor via e-mail on shashisangle@yahoo.com. Manuscripts should be in Times New Roman with font size of 12 points along with two hard copies. These articles should contain a covering letter, title page and abstract with key words. They should be written under appropriate sub-headings.

1. Undertaking : The manuscript must be submitted with a statement, signed by all the authors, regarding the originality and authorship.

2. Covering letter : It should include name starting with first name followed by surname, designation, address, contact details including e-mail and mobile number of the corresponding author.

3. Title page : It should include the title and the names starting with first name followed by surname (Last Name) and affiliations. Title should be informative, specific and short. The Number of authors should not exceed two for review article, four for case report and 6 for original article.

4. Main article : The main article should be drafted as a single microsoft word document elaborating following headings.

a) Abstract and key words : Abstract should not exceed 250 words for original articles and 150 words for case report.

For original article, the abstract must be in a structured form (Objectives, Methods, Results and Conclusion) and explain briefly what was intended, done, observed and concluded. Case report should have sections as: Abstract, Introduction, Case Presentation and Discussion.

b) Key words : Should not exceed 5- 6 words.

c) Manuscript : Manuscript should be typewritten, with wide margin on an A-4 size paper. It should be of 3000-4000 words for review article, 1500 to 2000 for original article and 750 to 1000 for case report.

d) Tables/Figures / Graphs.

i) The tables should appear in the text itself and should be numbered in Roman numbers (Table. I, II etc.)

ii) Should be limited to the essential (preferably not exceeding four).

iii) For figures: should be referred to as figures and numbered in Arabic numerals (E.g. Figure 1, 2)

e) Photographs:

i) The photographs should be of high definition type with legends. Maximum 4 photographs for original article,2 for case report.

ii) Coloured photographs will be charged extra as per the applicable rates (To be paid in cash to the Treasurer, Research Society, BJMC Pune).

f) Acknowledgment : Acknowledge only those who have contributed to the scientific content or provided technical support. Sources of financial support if any, should be reported.

g) References:

i) The list of references should be in the Vancouver style.

ii) References should be cited in the text in Arabic numbers. E.g Our observations are similar to those of Dowling et al.1.

iii) Maximum number of references: for review articles-40, original articles-20, case reports-06, short communications- 10

Note : 1.Accuracy of the references cited is the sole responsibility of the author/authors.

2. Views expressed by the authors do not necessarily reflect those of the Research society.