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Anaesthetic implications in paediatric patient with tuberous sclerosis: A case report

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Abstract-

Introduction: Tuberous sclerosis is an autosomal dominant rare multisystem syndrome which is now referred to as tuberous sclerosis complex, emphasizing the variance of the clinical symptoms. It is frequently associated with seizure disorder and its knowledge is thus of utmost importance to the anaesthetist keeping in mind the multiple antiepileptic drugs and their interactions involved.

Case report: An eight year old female patient, a known case of tuberous sclerosis, was scheduled for left eye lensectomy under general anaesthesia for a subluxated cataract in left eye. Patient had multiple calcified subependymal nodules and calcified cortical tubers on computerized axial tomography (CT). Her antiepileptic drug, carbamazepine was continued till the day of surgery. Premedication was done with injection midazolam, glycopyrrolate and fentanyl. Induction was done with injection thiopentone sodium following preoxygenation. Injection rocuronium bromide was given to facilitate endotracheal intubation. Anaesthesia was maintained with intermittent positive pressure ventilation under sevoflurane in gas oxygen mixture. The course and conduct of anaesthesia was uneventful and the patient could be discharged following uneventful recovery.

Conclusion: A general awareness is essential about the seizure provoking nature of certain anaesthetic drugs that are best avoided in such patients. Further the factors triggering the epileptogenic crises should be kept in mind while dealing with such patients. Thus, adequate knowledge of the disease is imperative and a meticulous perioperative anaesthetic care is mandatory throughout the course.

Index Terms- Tuberous sclerosis, epilepsy, anaesthetic implications, antiepileptic drugs

I. INTRODUCTION

Tuberous sclerosis is an autosomal dominant[1] rare multisystem syndrome characterized by hamartomatous tumours of the brain, skin, viscera, and eye. Bourneville, in 1880, coined the term *tuberous sclerosis.*[2] In 1908, Vogt first proposed epilepsy, mental retardation, and the skin lesions of adenoma sebaceum as a diagnostic triad for tuberous sclerosis.[3] The primary features that are considered to be very specific for tuberous sclerosis include facial angiofibromas (pathognomonic), multiple ungual fibromas, histologically confirmed cortical tubers, histologically confirmed subependymal nodule(s), multiple retinal astrocytomas, and radiologic evidence of multiple calcified subependymal nodules protruding into the ventricle.[4] Tuberous sclerosis is now referred to as *tuberous sclerosis complex*, emphasizing the variance of the clinical symptoms.[5]

The disease is a result due to inactivating mutations in either the TSC1 gene, located on chromosome 9q34 or the TSC2 gene on chromosome 16p13.[6]

II. CASE REPORT

An eight year old female patient, a known case of tuberous sclerosis, was scheduled to have left eye lensectomy under general anaesthesia for a subluxated cataract in left eye.

She suffered from seizure disorder, delayed milestones, caries teeth and adenoma sebaceum on face with shagreen patches on the skin of lumbosacral region. (Figure 1)

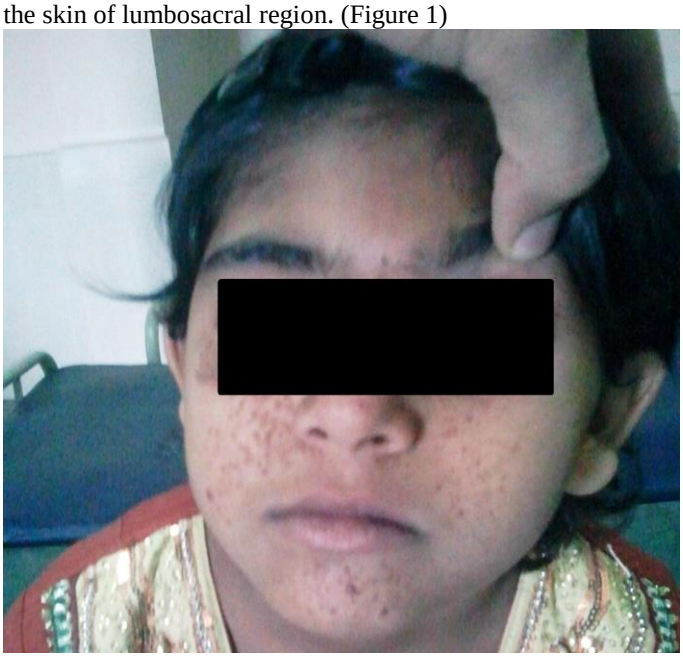

Figure 1: Photograph shows multiple erythematous facial papules known as adenoma sebaceum

Patient had multiple calcified subependymal nodules and calcified cortical tubers on computerized axial tomography (CT). (Figure 2)

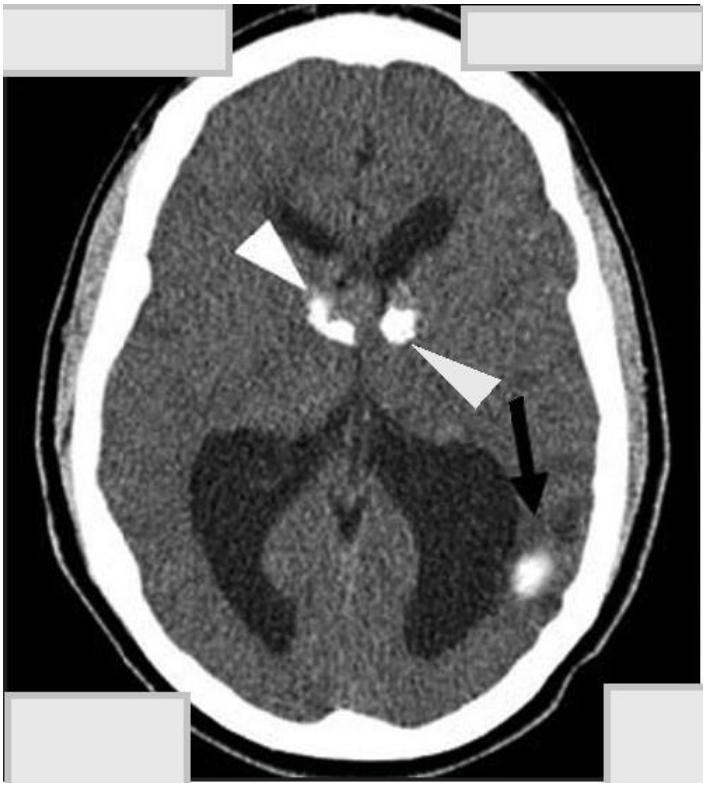

Figure 2: Transverse section CT brain shows multiple calcified cortical tubers in caudate nucleus (arrow heads) and left periventricular white matter (arrow).

Workup:

A complete history and physical examination are essential as organs affected by TS vary greatly from one patient to the other. In addition to routine investigations of blood and urine, chest radiograph, electrocardiogram, echocardiogram, serum electrolytes, blood urea and creatinine were done which were found to be within normal limits. CT scan revealed multiple calcified cortical tubers in the caudate nucleus and periventricular white matter. Histologically, these cortical tubers are glioneuronal hamartomas which are focal developmental malformations of the cerebral cortex, characterized by the proliferation of glial and neuronal cells and exhibiting loss of the 6-layered structure of the cortex and bizarre-appearing giant cells, dysplastic neurons, and astrocytes.[7,8] Subependymal nodules are hamartomas typically seen in the subependymal wall of the lateral ventricles and may protrude into the ventricular lumen. Together with the cortical tubers, they are present in approximately 90% of children with TSC.[9]

III. ANAESTHETIC TECHNIQUE

- Patient was posted for a left eye cataract surgery.
- Antiepileptic drug (tablet carbamazepine 100mg BD) was continued till the day of surgery.
- Premedication was done with injection midazolam 0.5mg, injection glycopyrrolate (0.01mg/kg) and injection fentanyl (1 mcg/kg), 45 minutes before the surgery.
- Induction was done with injection thiopentone sodium 4mg/kg body weight following preoxygenation with 100% oxygen for 3 minutes.
- Injection rocuronium bromide (1 mg/kg) was given to facilitate endotracheal intubation and airway secured with 5 sized cuffed endotracheal tube at 16 cm after confirming bilateral equal air entry.
- Anaesthesia was maintained with intermittent positive pressure ventilation under sevoflurane in gas oxygen mixture.
- Mannitol was infused to keep the intraocular pressure to the optimum level.
- Injection ondansetron 2 mg was given intravenously at the conclusion of surgery to prevent postoperative nausea and vomiting.
- The residual neuromuscular blockade was reversed with a mixture of pyridostigmine (0.2 mg/kg) and glycopyrrolate (0.01mg/kg).
- The course and conduct of anaesthesia was uneventful and the patient could be discharged following uneventful recovery.

IV. DISCUSSION

A complete history and physical examination are crucial since the organs affected by TS can vary to a great extent from one patient to the other.

Tuberous sclerosis is rare disorder and involves multiple organs. Such cases demand thorough history, examination and investigation in order to know the severity of disease and possible on table anaesthesia complications. Epileptogenic drugs like enflurane[10], methohexitone[11], ketamine[12], etomidate[13,14], morphine[15], meperidine, vecuronium should be avoided. Further hypoxia and hypercapnea which precipitate seizures is avoided. Benzodiazepines[16], sevoflurane, isoflurane[17], desflurane[18], fentanyl[19] and nitrous oxide can safely be used. If renal and hepatic function of patient is affected then mivacurium and cisatracurium may be the safest choices. Post operatively patient should be monitored for seizure activity and adequate pain relief should be provided.

In such patients with well controlled epilepsy, all efforts should be made to avoid interruption of antiepileptic medication perioperatively. Anticonvulsant therapy should be optimized prior to the procedure and continued until the morning of surgery and throughout the perioperative period.[20] Our patient was on carbamazepine that changes the ionic conductance to sodium with a membrane stabilizing effect. In addition to accelerating its own metabolism, Carbamazepine exacerbates hepatic oxidation and conjugation of other liposoluble drugs. Due to its potent enzyme inducing properties, carbamazepine reduces the plasma concentrations of thiopental, propofol, midazolam, opioids and neuromuscular non depolarizing blockers. There is risk of hepatotoxicity after anaesthesia with halothane, enflurane, and possibly with sevoflurane.[21] Thus, a notable pharmacokinetic and pharmacodynamic interactions exist between antiepileptic drugs and the drugs commonly used in anaesthesia, and these

interactions affect both drug efficacy and seizure risk intraoperatively.

The premedication was carried out with the use of a benzodiazepine, midazolam, as it is widely used due to its potent anticonvulsant and anxiolytic effects. During maintenance of anaesthesia, sevoflurane was administered because at concentrations of less than 1.5 MAC (avoiding hyperventilation) it is safe in the epileptic patients.[22]

The need for intraoperative invasive monitoring depends on the severity of the cardiovascular or cerebrovascular pathology and the type of procedure. Short surgical procedures as that of a cataract surgery or minor procedures like imaging does not demand invasive monitoring. Postoperatively, a short observation period is adequate following minor procedures in mildly affected patients.

Thus, several specific considerations exist that an anesthesiologist must consider when managing an epilepsy patient. The ability of the anaesthetics to modulate or potentiate seizure activity is to be kept in mind. Also, the effects of anti-epileptic drugs and interaction with anaesthesia should be considered. The presence of concomitant medical problems occasionally associated with epilepsy should be evaluated. The first generation anti-epileptic drugs (which was being used in our patient), such as carbamazepine, phenytoin and phenobarbital are resistant to the effects of neuromuscular-blocking agents. These drugs also enhance cytochrome P450, which affects the metabolism of other drugs and may necessitate dose adjustments of anaesthetic drugs like propofol, muscle relaxants and opioids. Hence, epileptic patients receiving anti-epileptic drugs require higher doses of fentanyl to maintain a comparable depth of anaesthesia.

V. CONCLUSION

Although the surgery was uneventful with smooth anaesthetic outcome, the probability for anaesthetic complications due to TS remains high throughout the procedure. A general awareness is essential about the seizure provoking nature of certain anaesthetic drugs that are best avoided in such patients. Further the factors triggering the epileptogenic crises should be kept in mind while dealing with such patients. Thus, adequate knowledge of the disease is imperative and a meticulous perioperative anaesthetic care is mandatory throughout the course.

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