Tuberous Sclerosis Complex: Sedation / Anaesthetic Considerations

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Citation

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Abstract

A 20-years-old female patient, known case of Tuberous Sclerosis Complex, was presented for sedation/ anaesthesia for radiological intervention (arterial embolization) for the control of bleeding within the renal angiomyolipoma. The sedation/ anaesthetic management of this case was tailored to the prevention of seizure activity, hypoperfusion of the main organs, avoidance of epileptogenic drugs, etc. and diagnostic features and possible complications of the disease are also discussed.

CASE HISTORY

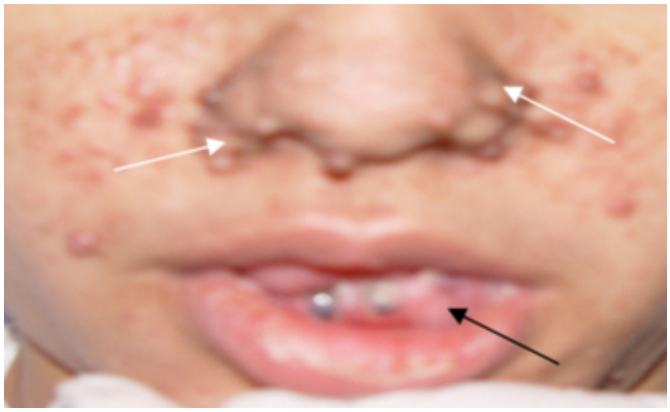
A 20 years old female, weighing 50 kg, a known case of Tuberous Sclerosis Complex, was presented in Accident and Emergency Department with history of abdominal pain, fever, vomiting and haematuria for the last 24 hours. She was then, transferred to Surgical ICU for observations and was booked for arterial embolization in Interventional Radiology Department under sedation/anaesthesia on emergency basis.

She was mentally retarded and physically handicapped and depended on others to look after her. She can only contact with her eyes when her name was called.

On physical examination, she looked pale. There were multiple angiofibromas on face particularly, the both nasolabial folds as shown in Figure 1.

Figure 1

Figure 1: Tuberous Sclerosis Complex. White arrows indicate angiofibromas on the nasolabial folds while black arrow shows gingival angiofibroma.



We faced difficulty to assess her airway anatomy but it looked normal apart from poor oral hygiene, some missing teeth and gingival angiofibromas. Her pulse rate was 115/minute, regular and low volume. Blood Pressure was 110/70 mm Hg, SpO_2 98% with face mask, O_2 being at 4L/mim. She was running temperature of 39.4 C. Respiratory rate was 22 breath/minute and regular. She had palpable renal mass on the left side of abdomen. Cardio respiratory systems were unremarkable. She was taking orally tablets carbamazipine 200 mg twice daily and phynetion 100 mg once daily for epilepsy. The last attack of seizure activity was noted 6 years ago. Her ECG showed sinus tachycardia of 109 beats/minutes and first degree heart block. Chest x-ray was unremarkable.

Complete blood examination showed WBC Count 24.4 $\times 10^9$

/L, RBC Count 2.35 $\times 10^9$ /L Platelet Count 740$\times 10^9$ /L, Haemoglobin76 g /L and Haemotocrit 21%.

Coagulation profile was PT 24.8 seconds, PT+INR 2.12 and APTT 43.9seconds.

Renal function tests, serum electrolytes and liver function tests were Urea 1.6 mmol /L, Creatinine 51µmom / L, Osmolality 286 mosm / kg, Sodium 135 mmol /L, Potassium

3.3 mmol / L, Chloride 98mmol /L and Liver Function Tests Total Bilirubin 17µmol /L, Total Proteins 57g /L, Albumin 20g /L, Alkaline Phosphatase 212 U /L, Alanine Aminotransferase 28 U /L, Aspartate Aminotransferase 89 U /L, Gamma Glutamyl Transferase 406 U /L, Globulins 37 g /L and Lactate Dehydrogenase 939U / L, respectively. Carbamazapine and phenytion blood levels were 1.0 (10-20µg/ml) and 6.0 (4-12 µg/ml).

Her CT scan Brain (Figure 2) and Abdomen (Figure 3) showed findings consistent with Tuberous

Figure 2

Figure 2: CT scan brain. Arrows showing calcified nodules on the walls of lateral ventricle.

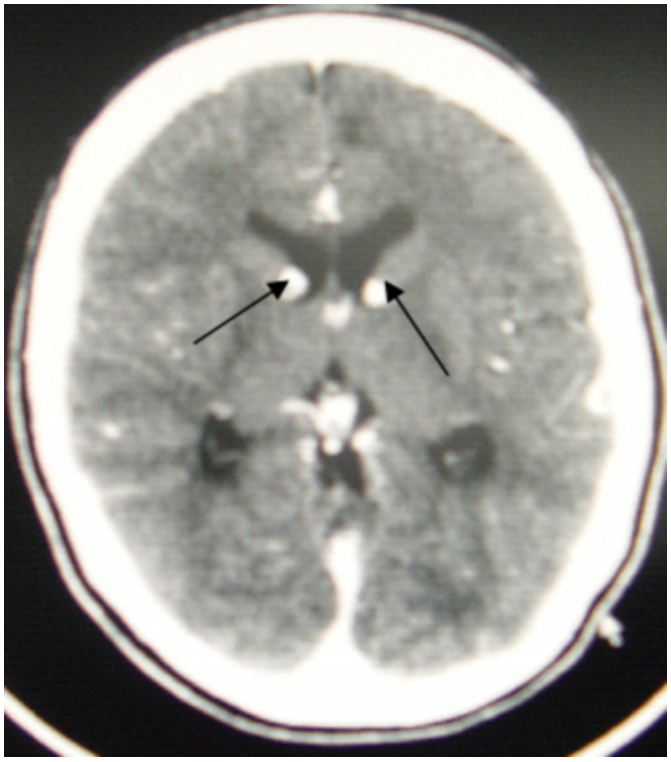
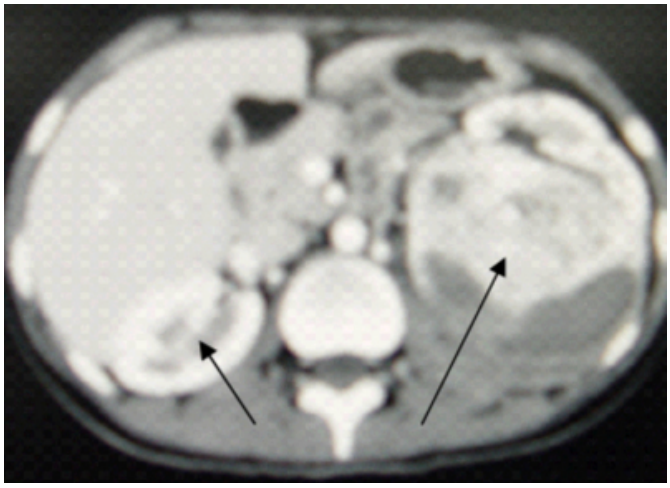


Figure 3

Figure 3: CT scan abdomen showing left renal angiomyolipoma larger than the right renal indicated by black arrows.



Sclerosis done on July 25, 2006. She received Vitamin K, potassium supplement, two units of PRBC and 6 units of FFP before going to Angio-room. Coagulation profile was now PT 16.1 seconds, PT+INR 1.25 and APTT 25 seconds.

SEDATION/ ANAESTHETIC MANAGEMENT

The patient was transferred was from SICU to angio-room accompanied by an anaesthetist and nursing staff on her SICU bed. Monitoring continued in the form of ECG, Pulse oximetry, invasive BP monitoring and urine output, etc. Our goals of management were to keep:

Patient well sedated

Mean arterial BP >60 mm Hg

SpO_2 >97%

Urine out put > 50ml/hour

Haemoglobin > 80 g /L and Haemotocrit of >25%

We started with oxygen therapy with face mask at the flow of 4-6L/minute. Injection fentanyl 50 µg and midazolam 2 mg were given intravenously in the beginning and then continued as boluses of 25 µg and 1 mg, respectively. Patient remained cold and calm during the first 3 hours and then started moving her legs. At this stage, Laryngeal mask airway(LMA) sized 3 was carefully inserted after further injecting 50 µg of fentanyl and then maintained with oxygen in air and sevoflorane 0-1 %. It further took an hour to complete the procedure. She remained haemodynamically stable throughout the procedure. During the whole

procedure, she received fentanyl 300 µg, midazolam 10 mg, Lactated Ringer's solution 800 ml, two units of PRBC and two units of FFP. Laryngeal mask airway was removed when she was fully conscious. We achieved our all goals without any complication. She was then transferred to SICU for further observations.

DISCUSSION

Patients with common or uncommon genetic disorders, with or without multiple congenital anomalies, present unique challenges to the health care provider responsible for administering sedation and anesthesia during surgical or technical procedures. Patients affected with heritable diseases often have special health-related needs requiring attention before successful sedation or anesthesia. It is important for health care providers, including nurses and physicians treating these patients, to recognize risk factors and potential complications before sedation or anesthesia Acknowledging unique anesthesia considerations is an essential part of providing adequate health care for patients with genetic diseases and can serve as a means of avoiding morbidity and mortality [1]

Tuberous Sclerosis or Tuberous Sclerosis Complex (TSC), also known as Epiloia and Bourneville disease is a rare, multi-system genetic autosomal dominant disease. Epidemiological studies report an incidence ranging between 1:10000 to 1:170000. In this disease two gene loci have been identified on chromosome 9q34 (TSC1) and 16p13.3 (TSC2) and they occur in all racial groups [2[. The diagnostic criteria for Tuberous Sclerosis Complex is shown in Table 1[3]

Figure 4

Table 1: Diagnostic criteria [] for Tuberous Sclerosis Complex (TSC)

Primary features	Secondary features	Tertiary features
Facial angiomas	Affected first degree relative	Hypomelanotic macules
Multiple ungal fibromas	Cardiac rhabdomyomas	Confetti* skin lesions
Cortical tubers*	Other retinal hamartomas	Renal cysts#
Subependymal nodule*#	Cerebral tuber	Pits in teeth enamal
Giant cell astrocytoma*	Non-calc subependymal#	Rectal polyp-hamartoma
Retinal astrocytomas	Shagreen patch	Bone cysts
	Forehead plaque	Gingival fibromas
	Pulm lymphangiomyoma*	Pulm lymphangioma*
	Renal angiomyolipomas	Hamartomas of other organs
	Renal cysts*	Cerebral heteropias
		Infantile spasms

Definite TSC. Either one primary, two secondary or one secondary plus two tertiary Probable TSC. Either one secondary plus one tertiary or three tertiary Suspect TSC. Either one secondary or two tertiary features. * Histological disgonisis # radiological diagnosis

Patients suffering from Tuberous Sclerosis Complex , whatever the age may be, may present for a variety of surgical procedures either elective or emergency as a results of the uncontrolled wide spread proliferation of hamartomas through the body. From the anaesthesiologist point of view, there are number of potential pitfalls into which they may fall. Some of them may be life threatening [3]. There is limited information available in the literature regarding the anesthetic management of patients with tuberous sclerosis [4].

Central Nervous System problems include communication problems, epilepsy and focal lesions. The uncooperative patient can be a challenge, specifically, those with mental deficiency, psychiatric diagnoses, or aberrant behavior. Special attention must be given to make the patient feel as comfortable as possible. Special behavior assessments may be required before sedation or anesthesia administration to meet or gain the trust of the patient and family and to alleviate problems. Exaggerated anxiety may lead to further tactile defensiveness, hyperactivity, attention deficits, psychomotor disturbances, and uncooperativeness. Desensitization and allaying anxiety are important key points to remember before successful sedation or anesthesia administration in patients with special needs. This is particularly important for patients with genetic diseases with neurological involvement [approximately 60% of the reported 10,000 genetic conditions have central or peripheral nervous system abnormalities [5]. Communication with the patient may be difficult since mental retardation is common in 60% of patients with Tuberous Sclerosis Complex. Hyperactivity or autistic behavior may aggravate the problem. In this regard, we might come across a lot of problems like assessment of airway, pain and sedation scores, initiating and then maintaining regional anaesthetic techniques, awake Fiberoptic intubation, incentive spirometery, and non-invasive ventilation, etc. Neurological lesions include single or multiple cerebral tubers or nodules, astrocytomas and multiple subependymal periventicular nodules. These nodules may calcify or cause hydrocephalus by obstructing the circulation of cerebrospinal fluid. Astrocytomas may cause focal neurological deficits, raised intracranial pressure, behavioral changes or loss of seizure control [3]. Epilepsy is common in 80-90% of the patients.

These patients are usually taking antileptic drugs. These drugs should be continued throughout the perioperative period. Possible drug interaction with anaesthetic agents should be kept in mind white anaesthetizing such types of patients. Epileptogenic drugs such as methohexitone, etomidate, ketamine, propofol, enflorane, atracurium and cis-atracurium due to their active metabolites, dopamine antagonists such as metoclopramide should not be used. Care should be exercised while choosing anaesthetics because of controversies and debates on such drugs and this discussion is beyond the scope of this report. Hyponatremia, hypoglycemia, hypocarbia should be avoided.

Cardiovascular manifestations can have major anaesthetic implications. Cardiac rhabdomyomas are usually asymptomatic but should be suspected in patients with arrhythmias or a localized loss of electric activity. The rhabdomyomas may be single or multiple and may occur in any chamber of heart. Up to 50-60% of patients with TSC have cardiac disease, mainly rhabdomyomas [6]. These may cause mechanical problems because of their size or because of the defects in the conducting system caused by their infiltrating nature. Aneurysms of thoracic and abdominal aortas have also been observed rarely. Hypertension may occur secondary to renal tumor or renal artery stenosis. A base line cardiac evaluation is therefore essential part of the preoperative workup even in asymptomatic patients [3].

Pulmonary manifestations include hamartomatous growth that may involve the lungs or pleura. A 33 year old woman with tuberous sclerosis and pulmonary lymphangiomyomatosis was undertaken bilateral sequential lung transplantation. Due to the progressive dyspnea and recurrent pneumothorax, she could not handle her normal daily life without oxygen supplement [7]. A preoperative chest x-ray is indicated to exclude silent pulmonary or mediastinal masses.

Gastrointestinal manifestation include hamartomatous growth like fibromata ,papillomata and pitting of teeth enemal at any level of gastrointestinal tract including mouth, esophagus, stomach, pancreas, liver or intestine. Microhamartomatous polyps are present in the rectum in 75% of cases. Hepatic hamartomas have also been reported. These may obscure the view of larynx and could be mistakenly considered to be due to intubation trauma. The may lead to delayed gastric emptying or intestinal obstruction. These may act potential source of bleeding [3].

Renal angiomyolipomas and cysts are characteristics of the disease and are present in 50-80% of affected patients. Angiomyolipoma is a benign renal neoplasm composed of fat, vascular, and smooth muscle elements [8]. The angiolipomatous process may also involve the adrenals. Spontaneous bleeding may be fatal, and these tumors are best treated by embolization. Other features may include renal cysts, polycystic kidneys, and renal carcinoma. Although an angiomyolipoma is considered benign, rare cases, possibly related to multicentric disease, have been reported regarding extension into the renal vein and/or inferior vena cava (IVC), as well as deposits in the regional lymph nodes [9]. When angiomyolipomas are symptomatic, the main presenting symptoms are related to intratumoral or retroperitoneal hemorrhage. Symptoms related to hemorrhagic complications occur in 87% of patients, and hematuria is reported in 40%.A palpable abdominal mass is present in 47% of symptomatic patients [7]. There is a case report of a 30-year-old female patient with tuberous sclerosis who underwent Laparatomy for haemorrhagic renal angiomyolipoma [10].

The characteristic cutaneous lesions are angiofibromas. These are pink or skin-colored telangiectatic papules commonly observed in the nasolabial folds and on the cheeks and chin. Other areas in which they may be observed include in and around nails (ungual fibromas), scalp, and forehead. In the oral mucosa, they may be observed in the lips, dorsa of tongue, and palate. Dental pitting occurs in about 90% of patients. Periungual fibromas (Koenen tumors) are smooth, firm, flesh-colored papules emerging from the nail folds. Shagreen patches are flesh-colored soft plaques that are frequently found in the lumbosacral area but may occur anywhere on the trunk. The surface may be pebbly (resembling pigskin or untanned leather) with prominent follicular openings. White macules are ovoid, hypopigmented, ash leaf–shaped macules that can be found on the trunks or limbs. White macules offer an excellent opportunity for early diagnosis because they may be found at birth or early infancy. A careful examination is necessary before making any firm diagnosis because hypopigmented macules may be a normal finding in newborn babies. Other skin signs include guttate leukoderma, café-au-lait macules, and poliosis. These lesions help in diagnosis [3].

Ocular involvement includes hypopigmented spots in the iris, equivalent to the ash-leaf macule in the skin. Retinal phakomas are observed as whitish-gray nodular lumps with a lump of mulberries appearance. These represent hamartomas characterized by proliferation of astrocytes. Every patient

with TSC should have a thorough ophthalmologic examination at the time of diagnosis [3].

Tuberous sclerosis Complex is diseases which affect much organ system. These patients may present for surgery at any age on the operating lists involving almost every surgical discipline. A cursory preoperative examination only reveals the tip of the ice-berg. What lies beneath may catch the unsuspecting anaesthesiologist by surprise. A potentially fatal out come may be the result [3].

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References

1. Butler MG, Hayes BG, Hathaway MM and Begleiter M. Specific Genetic Diseases at Risk for Sedation/Anesthesia Complications. Anesth Analg 2000; 91:837-855.
2. Lee JJ, Imrie M, Taylor V. Anaesthesia and tuberous sclerosis. Br J Anaesth 1994; 73:421-5.
3. Bosenberg A. Tuberous sclerosis: anaesthetic consideration. South Afr J Anaesth analg. May 2003; 4-6.
4. Ethan Bryson & Steven M. Neustein: Tuberous Sclerosis: A Case Report and Review: The Internet Journal of Anesthesiology. 2007; Volume 13, Number 1.
5. Online Mendelian Inheritance in Man, OMIMTM. Center for Medical Genetics, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Med (Bethesda, MD). Available at http://www.ncbi.nlm.nih.gov/omim
6. Schweiger JW, Schwartz RE, Stayer SA. The anaesthetic management of the patient with tuberous sclerosis complex Pediatric Anesthesia 1994; 4 (5):339-342
7. Oh YS, Park YS, Whang JW. Anesthetic Considerations in the Bilateral Sequential Lung Transplantation: A case report. Korean J Anesthesiol. 1998 Feb; 34(2):453-456.
8. Cohen MD. Genitourinary tumors. In: Cohen MD, ed. Imaging of Children With Cancer. St Louis, Mo: Mosby Year Book; 1992:552-88.
9. Baert J, Vandamme B, Sciot R, Oyen, H and Van Poppel, L. Benign angiomyolipoma involving the renal vein and vena cava as a tumor thrombus: Case Report. J Urol. Apr 1995; 153 (4):1205-7.
10. Ong EL, Koay CK. Tuberous sclerosis presenting for Laparatomy. Anaesth Intensive Care. 2000 Feb; 28(1):94-6.

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