**CLINICAL VIGNETTE**

# Anesthesia Considerations for a Pediatric Patient with Tuberous Sclerosis

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## *Introduction*

Tuberous sclerosis (TS), also known as Bourneville disease, is a progressive autosomal dominant neurocutaneous disorder characterized by hamartoma formation in a variety of organs including, but not limited to, the brain, heart, liver, lungs, kidneys and skin.[1] The hamartoma itself is a benign tumor-like malformation of local tissue, however, it can have significant clinical effects based on location and compression of local structures. Approximately 1,000,000 individuals are affected globally with an incidence of 1/10,000 cases per year.[1,2] One third of these cases are due to an autosomal dominant mutation while the remainder are sporadic cases.[1] This medical condition is predominately caused by inactivating mutations of the TSC1 gene for hamartin protein on chromosome 9q34 or TSC 2 gene for tuberine protein on chromosome 16p13.3.[2] These proteins normally trigger a GTP-ase protein Rheb, which acts on mTOR, an important regulator of cell growth, differentiation, migration and proliferative cell processes.[2] Dysregulation of mTOR via inactivation of both alleles of hamartin or tuberine protein result in hamartoma formation.

Clinical manifestation of tuberous sclerosis is highly variable. The traditional Vogt triad of angiofibromas, mental retardation, and intractable epilepsy is only seen in 30% of patients.[1,2] Cutaneous manifestations are present in 90% of patients with TS and may appear as ash leaf spots, facial angiofibromas, Shagreen patches and skin tags.[2-5] Neurological pathologies are also present in 90% of patients and include glioneuronal hamartomas (cortical tubers), subependymal nodules, seizures, mental retardation, mental delay, and autism.[1-3] Mental delay is the most common neurological manifestation, and it can be seen in 70-80% of patients, while infantile spasms are present in 30-40% of patients with TS. [1-3] Cardiovascular rhabdmyomas are present in 40-60% of patients and may result in cardiac dysfunction.[1,2] Renal angiolipomas occur in 80% of patients and are typically bilateral, with increased risk of renal cell carcinoma and autosomal dominant polycystic kidney disease.[3] Retinal hamartomas occur in 40-50% of patients.[2,3] Given the broad expression of TS, patients typically require in depth workup for possible manifestations. Treatment of TS is focused on organ specific symptomatic findings, and patients typically require multidisciplinary management.

## *Case Report*

A 3-year-old boy with tuberous sclerosis presented to the Anesthesia clinic for preoperative anesthesia evaluation for a MRI brain under monitored anesthesia care. Patient had a history of developmental delay with complex partial seizures, and a known left retinal hamartoma. The MRI was scheduled to evaluate for possible cerebral pathology given patient's persistent seizures. The patient's seizures were medically managed with Lamotrigine and Rufinamide. The patient's weight was 14.1 kg, height was 95 cm, and he had a BMI of 15.6 (37$^{th}$ percentile for age). Patient's complete blood panel and complete metabolic panel including BUN and creatinine were within normal limits for age. A pre-operative electrocardiogram (EKG) revealed a normal sinus rhythm with a heart rate of 116. A prior renal ultrasound showed no evidence of hydronephrosis or renal mass. Patient was instructed to continue oral antiepileptic medications preoperatively.

On the day of the procedure, the patient was given oral midazolam as an anxiolytic. After the child was relaxed, a peripheral intravenous catheter was placed. Standard monitors were placed, and supplemental oxygen via face mask was started. Patient was sedated with a continuous infusion of intravenous propofol. An oral airway was placed to relieve partial airway obstruction without event. The MRI scan took a total of 40 minutes. During the course of the anesthetic, the patient remained hemodynamically stable with spontaneous respirations. At the end of the procedure, the propofol infusion was discontinued, and the patient was transported to the post-anesthesia care unit room (PACU) in stable condition. The patient remained in the PACU for approximately one hour and was later discharged home. The MRI brain later revealed subependymal nodules in the cortical regions, a common central nervous system finding of TS patients.

## *Discussion*

There are several considerations when administering anesthesia to patients with tuberous sclerosis. Preoperatively, these patients should be evaluated for a history of common neurological, cardiovascular, pulmonary, and renal symptoms secondary to hamartoma formation. Symptomatic patients should undergo further workup.[3,4] Prior to surgery, all patients should have BUN, creatinine, and electrolytes evaluated to assess for possible renal lipomas resulting in renal dysfunction.[4]

Approximately half of patients with TS will develop rhabdomyosarcoma over the course of their life.[1,4] As a result, preoperative evaluation of these patients should include a

transthoracic echocardiogram.[2,4] Symptomatic patients may present with congestive heart failure, conduction abnormalities, or hemodynamic abnormalities.[2,4]

While in the operating room, all patients should be monitored with standard anesthesia monitors including blood pressure, EKG, pulse oximetry, and capnography. Patients with severe symptomatic cardiac disease may require an intra-arterial catheter for hemodynamic monitoring.[1,3,4] For patients with a history of seizures, special consideration should be taken to prevent seizures peri-operatively. Patients should continue anti-seizure medications during the day of surgery.[2,4] Ketamine should be used judiciously, as it can lower the seizure threshold and increase ICP.[2]

Female patients of child bearing age with TS are more likely to develop lymphangioleiomyomatosis, which has been associated with recurrent pneumothoracies.[3,4] In this subset of patients, high peak airway pressures should be avoided to prevent pneumothorax during positive pressure ventilation.[3,4]

This pediatric patient with mainly neurological manifestations of tuberous sclerosis, was completed with monitored anesthesia care without complications.

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