A Case of Tuberous Sclerosis and Rhabdomyoma in a Neonate

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BACKGROUND

Tuberous sclerosis complex (TSC) describes a neurocutaneous disorder causing pleomorphic features, tending to affect multiple organ systems often in the form of benign hamartomas. Organ systems often affected are the skin, renal and pulmonary systems. It is inherited in an autosomal dominant manner, with pathologic genotypes involving mutations in the TSC1 or 2 genes. De novo mutations do occur in up to 80% of cases. Regardless of cause, the expression of the disease is variable. The rarity of this disease paired with the potential severity of its expression makes understanding its presentation an important endeavor to recognize the disease and give appropriate treatment.

UNIQUENESS

This case is unique due to the overall rarity of the disease’s presentation. It is somewhat rare, occurring in between 1/5000–1/10000 live births. Therefore, a provider may only be expected to encounter a handful of cases in their career.

CASE DESCRIPTION

A seronegative, GBS negative G2P1 mother initially presented with concern for an abnormal fetal US suspicious for rhabdomyoma, possible renal failure and pylonephritis. Follow up fetal ECHO demonstrated 2 intracardiac masses (RV apex, LVOT). Fetal MRI was suspicious for subependymal nodules. This clinical picture in context of a consanguineous pregnancy raised suspicions for tuberous sclerosis complex prenatally. NICU team was made aware of case prior to presentation.

INTERVENTIONS & TIMELINES

At delivery, patient was initially brought to the warmer, dried and stimulated. APGARs 9/9. Patient was placed NPO while pending initial cardiac clearance. Prenatal diagnosis of cardiac rhabdomyoma was confirmed with postnatal ECHO. This demonstrated more than 5 and possibly up to 10 various tumors. They involve the RV free wall extensively, moderator band, the RV apex, the ventricular septum on both RV and LV sides as well as the mitral valve papillary muscles. Another tumor in the LVOT was found to be causing moderate obstruction with peak gradient 49 and mean gradient 29 mmHg.

MRI brain revealed numerous cerebral tubers and subependymal nodules, consistent with tuberous sclerosis. Routine EEG on DOL 1 was normal. Prolonged EEG was also without abnormal findings. Genetic testing was obtained to confirm the strong clinical suspicion of tuberous sclerosis. Testing confirmed the diagnosis of tuberous sclerosis complex with a positive TSC2 mutation noted. Patient was started on PGE initially, which was subsequently discontinued. Sirolimus 0.1mg was started while patient was admitted for treatment of rhabdomyoma. Patient’s diet was advanced with cardiology clearance, and was on POAL feeds by the time of discharge. Patient was set to follow up with the Lurie’s TSC interdisciplinary clinic, urology, and cardiology.

OUTCOMES

In outpatient follow up, patient has thus far been progressing well, feeling and growing appropriately. Per documentation, patient has been compliant with their sirolimus regimen. Patient has been referred to EI due to risk of developmental delay.

EEG was performed outpatient at the TSC clinic at Lurie’s Children’s hospital, most recent results read as “Rare epileptiform discharges over the left posterior temporal region. No seizures.” Vigabatrin was added in light of abnormal EEG.

Nephrology appointment is pending for 6 months of life.

DISCUSSION & CONCLUSION

Tuberous sclerosis is an autosomal inherited genetic disorder, causing an increased predisposition to the formation of hamartomas. Prenatally, it is common for the only presenting signs to be cardiac rhabdomyomas or cortical tubers, with osseous, renal, or pulmonary lesions more commonly diagnosed in adulthood. Skin findings are present in about 90% of cases. Hypopigmented macules are usually present in early childhood, with ungual fibromas and facial angiofibromas typically manifesting around puberty. Diagnosis is established when 2 of the major criteria, or 1 major and 2 minor diagnostic criteria are met, with confirmation with genetic testing recommended. There are two known genetic causes of the condition, TSC 1 and 2 mutations. TSC1 mutation occurs on chromosome 9 and is related to hamartin protein production. TSC2 is on chromosome 16 and affects tuberin protein production. Hamartin and tuberin are both thought to play important roles in cell division, with dysregulation thought to cause tumor formation due to aberrant mTOR signaling as detailed above. It may also cause regression of cardiac rhabdomyomas in infants, potentially circumventing the need for surgery later on in life.

Neurologic complications are the most common and usually the most impairing aspect of TSC. Much of this stems from structural neurodevelopmental abnormalities include cortical tubers (seen in our patient) and subependymal nodules. Epilepsy is frequently the most challenging aspect of TSC from a neurologic point of view. Patients are at risk of seizure of all types, with mood and anxiety disorders also frequently associated with the condition. Our patient was placed on Vipmat following surveillance EEG as prophylaxis against this. Intellectual disability has a prevalence of 40%-50% in TSC; 30% are severely affected with IQs in the very low range.

Regardless of the manifestations, the 2012 TSC consensus recommends lifetime surveillance in order to monitor symptoms progression. Prognosis is difficult to discuss, depending on each individual's manifestations of disease.

REFERENCES