

Pediatric Clips

Tuberous sclerosis complex

By Pedro Weisleder, MD, PhD

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Pediatric Clips from The Children's Medical Center of Dayton are quick reviews of common pediatric conditions.

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CASE STUDY

A 6-year-old boy was admitted to the hospital secondary to new onset seizures. The child's mother indicated on the day of admission, the patient was in his usual state of health. Suddenly, he began exhibiting tonic-clonic activity of left side extremities associated with loss of consciousness. The abnormal activity lasted approximately five minutes and subsided spontaneously. Mom suspected the child had a seizure and dialed 911. Emergency medical technicians described the child as stable but confused. He was taken to the emergency department (ED) for

further evaluation. The ED physician learned the child had an unremarkable past medical history. Two unanticipated issues were: he was receiving special education services in school and mom had a history of seizures in her youth. The physical exam revealed the following abnormalities: several hypopigmented macules over the child's abdomen, an area of thickened skin above the right buttock and a growth in the right index's periungual region with fingernail deformity. The neurology service was consulted and the boy was admitted to the hospital. The

next day he underwent MRI of the brain, which revealed a hypointense mass on T-1 weighted images in the cortical region of the right temporal lobe. The mass was hyperintense both on T-2 weighted and fluid attenuation inversion recovery (FLAIR) images. Finally, an ultrasound revealed several cystic lesions in the renal parenchyma of the child's kidneys. The diagnosis of definite tuberous sclerosis complex was made. The boy was prescribed antiseizure medication and discharged from the hospital with instructions to follow up in the pediatric neurology clinic.

CASE DISCUSSION

Tuberous sclerosis complex (TSC), formerly known simply as tuberous sclerosis, is one of the more than 10 neurocutaneous syndromes or phakomatosis. This is a group of hereditary or congenital diseases that have in common the presence of hamartomas in the tissues involved. Hamartomas are nonneoplastic masses composed of disorganized cells native to the organ where they are found. The word phakoma is of Greek origin and means tumor.

TSC is a multisystem disease that occurs in approximately one in 8,000 individuals.¹ The condition is characterized by the presence of hamartomas in several tissues including the brain, eye, skin, heart, lungs and kidneys. TSC is inherited in an autosomal dominant fashion, but approximately 60% of cases are consequence of *de novo* mutations.² TSC occurs as a consequence of mutation in one of two genes: TSC1 or TSC2. TSC1 is found on chromosome 9q34.3 and encodes for the protein hamartin. TSC2 is found on chromosome 16p13.3

and encodes for the protein tuberin. Hamartin and tuberin work together to regulate cell growth and differentiation. Because the proteins work in conjunction, mutations of either gene generate the same disease. TSC has significant phenotypic variability.

Major features of TSC in the brain include cortical tubers (**Figure 1**), subependymal nodules, subependymal giant-cell astrocytomas (**Figure 2**) and white-matter radial migration lines. The most common manifestation of these abnormalities is seizures. Other neurological manifestations of the disease include hydrocephalus, developmental delay, mental retardation and autism-spectrum disorders.³ Major features of TSC outside of the brain include retinal hamartomas, hypomelanotic macules, facial angiofibromas, ungual fibromas, Shagreen plaques, cardiac rhabdomyomas and renal angiomyolipomas.¹ Minor features of TSC include retinal hypomelanotic plaques, dental enamel pits, gingival fibromas, confetti-like skin lesions, renal cysts and cystic bone lesions.

The diagnosis of TSC is made in the following fashion:

- Definite: two major features + one minor feature or one major feature + two minor features
- Possible: one major feature + one minor feature
- Probable: one major feature, or two or more minor features

The evaluation of a patient with TSC includes:

- EEG to investigate the possibility of seizures
- Neurodevelopmental evaluation searching for cognitive impairments
- MRI of the brain to identify cortical tubers or giant-cell astrocytomas
- Echocardiography searching for rhabdomyomas
- Ultrasound to evaluate the patient's kidneys

Treatment is directed towards abnormalities found on these tests. Finally, genetic counseling and parental examination are essential components of the comprehensive management of TSC patients.

Continued from the front.



Figure 1. Brain MRI of a patient with TSC revealing cortical tubers in both temporal lobes (coronal sections, FLAIR sequence).

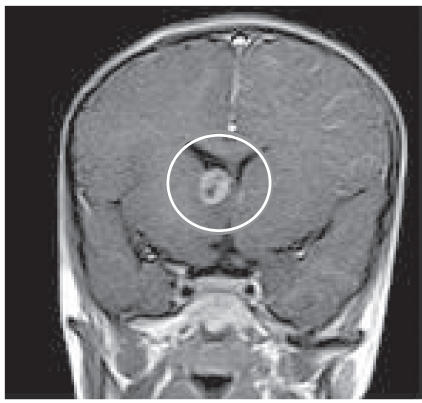


Figure 2. Brain MRI of a patient with TSC revealing a subependymal giant-cell astrocytoma in the right hemisphere (coronal sections, contrast enhanced T-1 weighted image).

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FEATURED SPECIALIST



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NEUROLOGY AT DAYTON CHILDREN'S

The department of pediatric neurology provides care for infants through adolescents with a variety of neurological disease

including Tourette syndrome, cerebral palsy, headache and seizure disorders. The neurology department offers advanced multidisciplinary diagnostic and therapeutic management 24 hours a day, and the inpatient/outpatient EEG lab performs all modalities of electroneurodiagnostic testing, including video EEGs. For more information on neurology at Dayton Children's, call 937-641-3080. To refer a patient, call 937-641-4000 or fax the appropriate referral form to 937-641-4500.

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