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What is the classic triad of clinical symptoms for tuberous sclerosis?
Seizures, mental impairment, and adenoma sebaceum. Note that this triad is not obligatory for tuberous sclerosis diagnosis and many patients with tuberous sclerosis do not demonstrate all three of these clinical symptoms. It is important to be aware of this triad for board preparation purposes as these symptoms, in a question stem, may guide you toward recognition that tuberous sclerosis is being tested.

True or false? Identification of a Tuberous Sclerosis Complex (TSC) 1 or 2 genetic mutation is sufficient to diagnoses tuberous sclerosis.
True. Of interest, TSC1 encodes hamartin and TSC2 encodes tuberin and is more common. Both are part of the mTOR pathway, and both impair tumor suppressor genes.

True or false? Genetic testing that reveals no TSC 1 or 2 genetic mutation excludes the possibility of tuberous sclerosis.
False. Up to 25% of tuberous sclerosis complex patients will not show a TSC 1 or 2 mutation upon testing. Therefore, lack of a TSC 1 or 2 gene does not rule out or exclude tuberous sclerosis.

If the classic clinical triad of tuberous sclerosis or genetic testing of TSC1 or TSC2 genetic mutations do not identify all tuberous sclerosis patients, how is the diagnosis of tuberous sclerosis confirmed in all cases?
This is a complicated answer, but to simplify for radiology board exam purposes there are major and minor criteria that have been developed for tuberous sclerosis diagnosis. A diagnosis of definite tuberous sclerosis complex is made if one has 2 major or 1 major and 2 minor criteria. Possible tuberous sclerosis complex diagnosis is made if there is 1 major or at least 2 minor criteria present.

What are the major criteria for diagnosis of tuberous sclerosis complex?
Three or more angiofibromas, 2 or more angiomyolipomas, 2 or more ungual/periungual fibromas, lymphangioleiomyomatosis, 3 or more hyperpigmented macules, a cardiac rhabdomyoma, a collagenoma, also termed a shagreen patch which is a subepidermal collagenous nevus, a subependymal giant cell astrocytoma, or a subependymal hamartoma, multiple retinal hamartomas, and, finally, cortical tubers and other cortical dysplasias including so called cerebral white matter migration lines.

What are the minor criteria for diagnosis of tuberous sclerosis complex?
Multiple renal cysts, multiple dental enamel pits, multiple intraoral fibromas, extrarenal hamartomas, a retinal chromic patch, and so-called confetti skin lesions which are small hypopigmented macules scattered over the arms, legs, and other regions of the body.

True or false? Tuberous sclerosis is an autosomal dominant condition.
The answer is true AND false. This is a trick question. Most cases of tuberous sclerosis result from spontaneous mutations but about one-third of cases are inherited in an autosomal dominant manner.

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What is the HAMARTOMAS mnemonic for tuberous sclerosis?
H=hamartomas (skin, eyes, CNS)
A=angiofibromas of face/adenoma sebaceum
M=mental impairment
A=angiomyolipoma of the kidney
R=rhabdomyoma of the heart
T=tubers (cortical/subcortical)
O=oral fibromas and dental enamel pits
M=migration anomalies of white matter/multiple tumors of various organs
A=ash-leaf spots (hypomelanotic macules)
S=seizures, shagreen patches

Various forms of this exist. I've made a few of my own modifications to this mnemonic to make it more accurate/potentially helpful. However, this is not an all-inclusive list of pathology for tuberous sclerosis!

What are the highest-yield CNS tumors to remember for tuberous sclerosis for board exams?
Subependymal giant cell astrocytomas: Classic imaging features are an intensely enhancing intraventricular mass near the foramen of Monro with frequent calcifications on CT, that are somewhat large at presentation, enlarge over time, and present in older children/teenagers. These are benign tumors and are highly associated with tuberous sclerosis. These can cause obstructive hydrocephalus.

Subependymal hamartomas: Classic imaging features are that of small calcified irregular intraventricular masses (subependymal giant cell astrocytomas are classically over 1 cm in size and these are classically under 1 cm in size) with variable enhancement patters presenting in very young patients, typically within 1st 6 months of life. These may progress in time to become subependymal giant cell astrocytomas.

Cortical/subcortical tubers: These are often seizure generating lesions that are present in nearly all tuberous sclerosis patients. Imaging classically shows triangular-shaped lesions in a cortical/juxtacortical distribution, most commonly in the frontal lobes. Most of these do not enhance but can be detected based on T1 hypointensity and T2/FLAIR signal hyperintensity outside of the neonatal period. These are often somewhat calcified on CT.

What are the highest-yield renal tumors to remember for tuberous sclerosis on board exams?
Renal angiomyolipomas: Benign and seen with several phakomatoses (including neurofibromatosis type I and von Hippel-Lindau), but classically associated with tuberous sclerosis. CT shows macroscopic fat in many but not all cases and tend not to calcify. MRI also often shows internal fat using fat saturation and/or in phase and out of phase sequences. These are hypervascular masses and can show a sunburst appearance on initial enhancement and onion peel appearance on more delayed post-contrast imaging. Remember risk of spontaneous hemorrhage which can be severe. If you see a fat-containing renal lesion with calcifications, think renal cell carcinoma first rather than a renal angiomyolipoma.

Renal cysts: Often multiple and bilateral with tuberous sclerosis.

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What are some other abdominal lesions associated with tuberous sclerosis?
Several exist. These include hepatic angiomyolipomas and retroperitoneal lymphangiomyomatosis with multiple retroperitoneal cystic lesions like lymphangioleiomyomatosis (LAM) of the lungs which can cause chylous ascites.

True or false? A cardiac rhabdomyoma is the most common cardiac tumor in a fetus.
True. In fact, cardiac rhabdomyomas represent most pediatric cardiac tumors overall with most of these diagnosed in the first year of life. These can be either single or multiple. On ultrasound expect a solid hyperechoic mass or masses within or near the myocardium that on MRI are T1 hypointense and T2 hyperintense.

True or false? Cardiac rhabdomyomas often spontaneously regress.
True. Cardiac rhabdomyomas often spontaneously regress and often require no treatment unless there is something like ventricular outflow obstruction, valvular impairment, uncontrolled arrhythmias.

What is the prognosis of tuberous sclerosis?
Mortality is roughly 40% at about age 40. I would remember 40% at age 40 for board exams.

What imaging surveillance may be indicated for individuals with tuberous sclerosis?
Intensive imaging surveillance has been recommended by certain groups for tuberous sclerosis.

Brain MRI: For asymptomatic under 25 years of age, brain MRI every 1-3 years. Those with asymptomatic subependymal giant cell astrocytomas may need more frequent brain MRI than this for monitoring. Periodic imaging into adulthood with brain MRI, as clinically directed.

Echocardiography: Every 1-3 years until regression of any cardiac rhabdomyomas is documented.

Abdominal MRI: Every 1 to 3 years.

High resolution chest CT: Starting at age 18 in adult females, screening for lymphangioleiomyomatosis every 5-7 years until menopause.

Additional non-imaging screening for various complications/associations of tuberous sclerosis has been proposed with EKG, renal function monitoring, dental evaluation, eye screening, etc.

True or false? mTOR inhibitors can be used for treatment of several tuberous sclerosis complications.
True. mTOR inhibitors can be helpful for things like enlarging subependymal giant cell astrocytomas and renal angiomyolipomas.