TUBEROUS SCLEROSIS

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CASE HISTORY

An 11-year-old boy, whose father was known to have tuberous sclerosis (TS), presented with a first fit. On examination he had characteristic facial changes of adenoma sebaceum and a subungual fibroma. Neurological examination was unremarkable and there was no convincing evidence of raised intracranial pressure. MRI brain scan confirmed the diagnosis of tuberous sclerosis, showing subependymal nodules and a tumour arising from the left foramen of Munro, confirmed to be a giant cell astrocytoma following surgery (Figure 1).

DISCUSSION

Tuberous sclerosis, otherwise known as Bourneville's disease or epiloia, is a neuroectodermal familial disorder. Though autosomal dominant it has a low penetrance and variable expressivity, with a prevalence of 1 in 34,000-100,000.[1] The disease is characterised by a classical triad of seizures, mental retardation and adenoma sebaceum, as described by Volt in 1908, leading to the popular mnemonic 'zits, fits and nitwits'. This, however, represents only part of the clinical spectrum of disease manifestation much beloved of postgraduate examiners. This condition lends itself to many characteristic radiological features, and increasingly diagnosis is being confirmed earlier by radiological criteria as changes may be apparent earlier radiologically than clinically.[2]

CENTRAL NERVOUS SYSTEM MANIFESTATIONS

Central Nervous System (CNS) involvement is identified in most patients presenting clinically with myoclonic seizures and progressive mental retardation. There are a number of well-defined radiological findings.

Tubers are cortical hamartomas formed by clusters of atypical glial cells surrounded by giant cells and give their name to the disease. They are said to occur in up to 95% of patients, being multiple in approximately 75%.[3] Over the age of two, they are frequently calcified which makes their identification straightforward on CT. Without calcification identification can be more difficult, with lesions seen as hypodense regions of abnormal myelination within widened cortical gyri. MRI is a more sensitive imaging method for tubers[4] though the appearances change with age. In neonates the lesions are low signal on T2-weighted MRI which changes to high signal in adulthood as the white matter myelinates.

Subependymal nodules are identified in more than 90% of patients,[3] most of which calcify. They are found typically on the ventricular surface of the caudate nucleus and along the ventricular surface of the lateral ventricle where they are described as 'candle drippings'. They also occur just posterior to the foramen of Munro, and because of their calcification, may be identified on plain films. On CT they are easily visible as calcified nodules (Figure 2). On MRI they may enhance following administration of gadolinium; their subependymal nature is more apparent and they can be seen protruding into the ventricle itself (Figure 3).

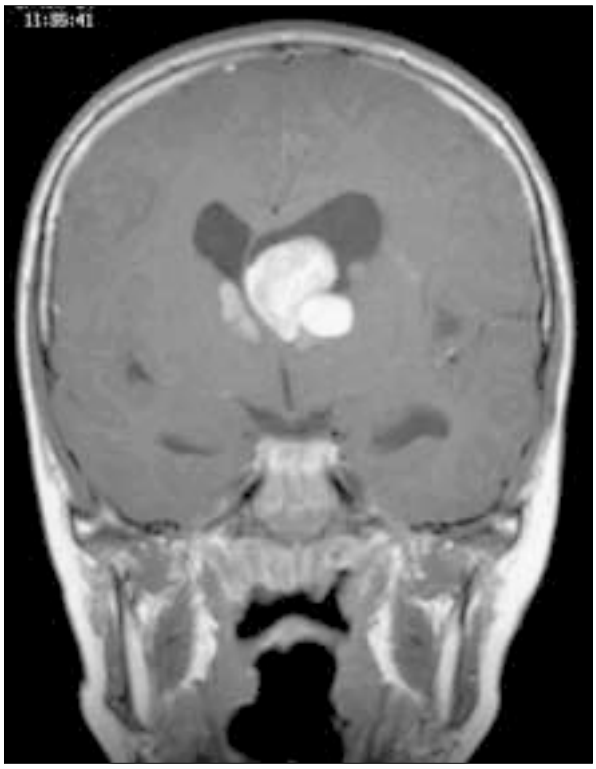

FIGURE 1
MRI brain (post contrast) showing subependymal nodules and a mass obstructing the left foramen of Munro.

Giant cell astrocytomas are the most commonly seen tumours in tuberous sclerosis (Figure 1). They are located near the foramen of Munro and tend to enlarge, growing into the lateral ventricle, often causing hydrocephalus by obstructing the CSF drainage. They are usually partially calcified. On CT they are rounded and often hypo-dense or occasionally iso-dense with the surrounding tissue. MRI appearances can be varied, with many tumours showing flow void due to dilated vessels.[4] The only reliable feature that differentiates them from subependymal nodules, however, is a change in size. Most of the tumours are low grade astrocytomas, though they can degenerate into higher grade tumours.

RENAL INVOLVEMENT

Although renal involvement leading to renal failure is rare, benign mesenchymal tumours known as angiomyolipomas (AML) are common, occurring in 80% of those with TS.[5] These are hamartomata comprised of fat, smooth muscle cells and blood vessels. In TS they are frequently large, bilateral and multiple. AML may be the only evidence of

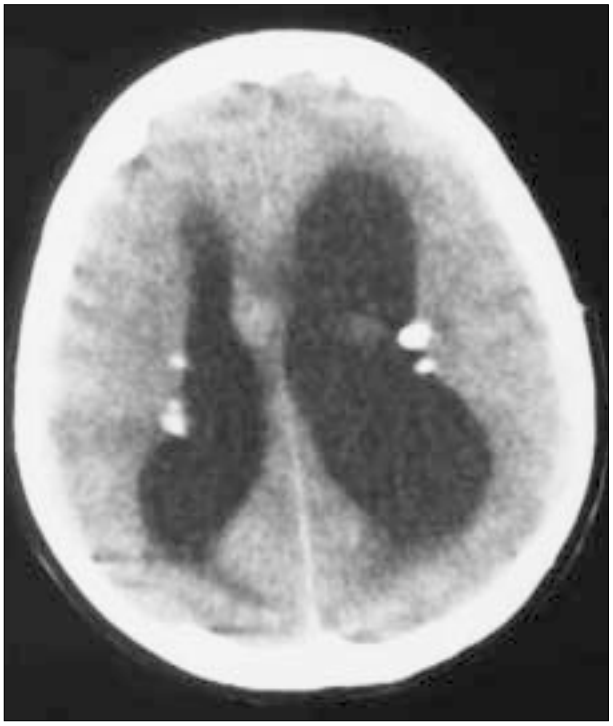

FIGURE 2
CT of brain in tuberous sclerosis demonstrating calcified subependymal nodules along the walls of the lateral ventricles.

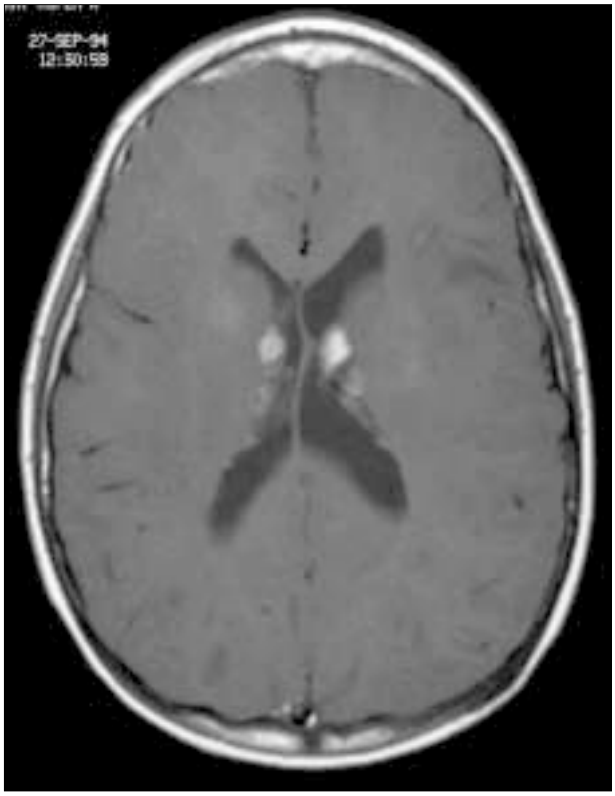

FIGURE 3
Axial MRI brain demonstrating enhancing subependymal nodules.

TS, and although only 40% of those with AML have TS, incidental diagnosis (for example at ultrasound) should alert the clinician to the underlying condition. Small lesions are asymptomatic though approximately 90% present with abdominal or flank pain due to their ready propensity for intra-lesional haemorrhage. This can occasionally be massive and life-threatening, requiring angiography with subsequent embolisation of the angiomatous tissue. The imaging appearances depend largely on the relative amounts of the component tissues. Up to 10% may be identified on plain film as a lucent mass because of the high fat content. Initial diagnosis is often suspected on ultrasound with the identification of a hyperechoic tumour, though haemorrhage and necrosis can alter this appearance. CT should always be considered, as a renal cell carcinoma can appear hyperechoic at ultrasound in 5% of cases. On CT, AML is usually seen as a well encapsulated cortical tumour. Its appearance is heterogenous, though in most cases areas of fat attenuation[6] are found which are virtually pathognomonic. Enhancement is variable depending on the amount of angiomatous tissue within the tumour (Figure 4). Similarly, the amount of vascular tissue determines the angiographic appearance: the aneurysmally-dilated vessels may give the tumour a 'whorled' appearance, but there are no specific imaging features to distinguish it from a renal cell carcinoma, thus limiting angiography as a primary diagnostic tool. Patients with tuberous sclerosis may also present with multiple simple renal cysts and there is a mildly elevated risk of developing renal cell carcinoma.

PULMONARY INVOLVEMENT

Pulmonary involvement occurs in 1% of patients with TS resulting in diffuse interstitial changes in the lung fields, manifesting radiographically as reticular nodular shadowing.[7] As the disease progresses, honeycomb and cystic changes may develop. Unlike most interstitial lung diseases, the lung fields tend to increase due to small airway obstruction, focal emphysema and cyst formation. Lymphangioleiomyomatosis (LAM) is a 'form fruste' of TS, occurring almost exclusively in females.[8] The pathological and radiological features are similar to pulmonary TS except that lymphatic involvement is a major feature of LAM, resulting in chylothorax and mediastinal lymph nodal enlargement in a significant number of patients. Clinically

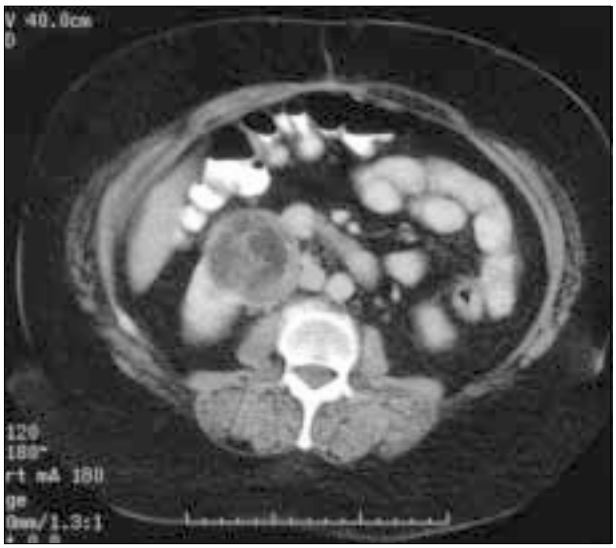

FIGURE 4
CT abdomen showing angiomyolipoma of the right kidney.

it differs from pulmonary TS in that it is not hereditary and patients do not have the neuro-cutaneous manifestations of TS. High resolution CT shows characteristic thin-walled cysts scattered throughout the lung parenchyma (Figure 5). Spontaneous pneumothorax occurs frequently with this condition and occasionally cor pulmonale develops.

OTHER SYSTEMS

Many other organs systems are also involved in tuberous sclerosis:[9] retinal hamartomas or phakomas occur in more than 50% of patients; cardiac rhabdomyoma of the heart is a well-recognised association occurring in 5% of cases. Other visceral organs may also be involved, principally with the development of adenomas. Bone involvement is not often recognised though frequently occurring, with bone islands in both the axial and appendicular skeleton, and bone cysts in the small bones of the hands and feet.

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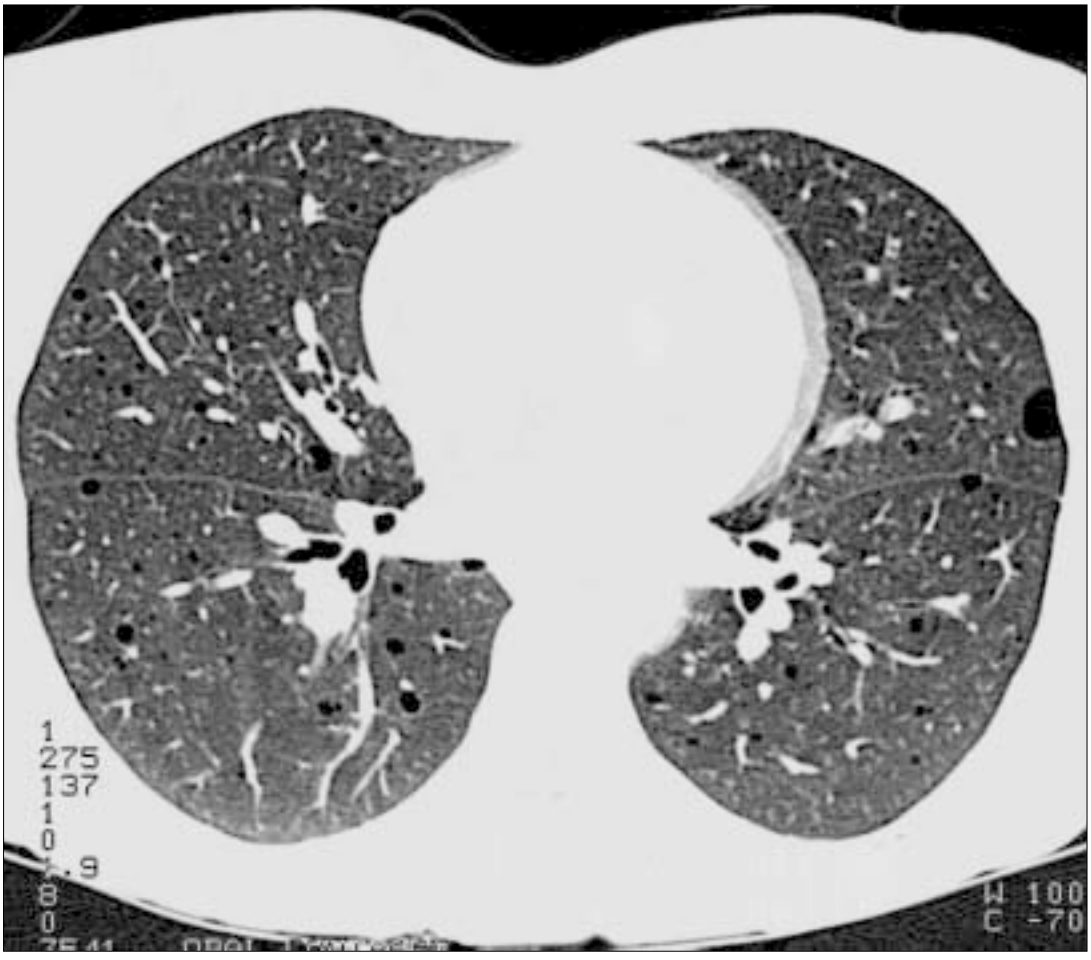

FIGURE 5
High resolution CT of chest in LAM with multiple thin-walled cysts seen scattered throughout the lung parenchyma.