Rare disease

Tuberous sclerosis complex presenting as bilateral large renal angiomyolipomas

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Summary

Tuberous sclerosis is an inherited disorder that can present with seizures, mental retardation, cutaneous lesions and visceral hamartomas, but can be entirely asymptomatic. The disease occurs in 1:100 000 persons in all races with nearly equal distribution between the sexes. Tuberous sclerosis is often associated with renal angiomyolipomas (AMLs), which occur in up to 80% of these patients. Here we report a case of a patient who presented with bilateral large renal AMLs and was detected to have tuberous sclerosis complex.

BACKGROUND

Tuberous sclerosis complex (TSC) or Bournville-Pringle disease is a rare genetic condition characterised by seizures, mental retardation and facial angiomas (Vogt's triad).¹ It is a genetic disorder affecting cellular differentiation and proliferation, which results in hamartoma formation in many organs (eg, skin, brain, eye, kidney, heart). Newer understandings of the inheritance and pathophysiology of TSC led to revised diagnostic criteria in 1998 and the recognition that the condition has a wide range of clinical features; covering the spectrum from profound physical and mental abnormalities to completely asymptomatic cases.²⁻³ Renal angiomyolipoma (AML) is a rare finding, comprising only 0.3% of all renal neoplasms.⁴ Two types are described: isolated AMLs and AMLs associated with tuberous sclerosis. AMLs associated with tuberous sclerosis are typically larger, bilateral and multiple than isolated AMLs. Up to 80% of patients with tuberous sclerosis will have AMLs. Herein, we describe case of a young patient who presented with abdominal masses, which were found to be bilateral large AMLs of kidneys. On further work up, patient was detected to have TSC with bilateral renal angioliipomas, adenoma sebaceum, subependymal calcification and superficial retinal haemorrhages.

CASE PRESENTATION

A 22-year-old man presented to our institution complaining of vague dull abdominal pain and distension of flanks since 5–6 months. There was no history of fever, weight loss, altered bowel habits, burning micturition or haematuria. On clinical examination, the patient was pale, his face showed reddish, shiny papular and plaque-like lesions on nose, cheeks and forehead consistent with adenoma sebaceum (figure 1). Other skin lesions of tuberous sclerosis such as periungual fibromas, ashleaf spots and shagreen patches were not evident. Abdominal examination revealed firm ballotable masses bilaterally in the flanks occupying almost the entire abdomen. Cardiovascular, respiratory and central nervous system examination were normal.

On investigations, his haemoglobin was 6.9 g%. Rest of the blood investigations—renal functions (blood urea nitrogen, serum creatinine and electrolytes), liver functions and urine examination—were normal. Ultrasonography of the abdomen showed bilateral, predominantly hyperechoic masses occupying the renal fossae. CT of abdomen showed both kidneys to be markedly enlarged and both kidneys were replaced by large masses of fat and vascular structures with few areas of normal renal parenchyma interspersed. Right mass measured $19 \times 9.5 \times 13.1$ cm and left mass measured $16.4 \times 9.4 \times 9.7$ cm. These masses were suggestive of bilateral large AMLs of kidney (figure 2). CT of the chest was normal.

On questioning, the patient did not give any history of seizures. With suspicion of tuberous sclerosis the patient was

Figure 1 Adenoma sebaceum.

Figure 2 Bilateral large angiomyolipomas of kidney.

investigated for other organ involvement, CT of the brain was done which showed calcified density along right lateral ventricle consistent with subependymal nodule or tuber (figure 3). On Ophthalmic examination, right eye fundus showed superficial flame shaped haemorrhages, though no retinal hamartomas were found. Two-dimensional ECHO of heart and cardiac MRI was normal.

Based on the findings of adenoma sebaceum, bilateral renal AMLs, subependymal tuber and retinal haemorrhages, the patient was diagnosed as a case of TSC. The patient was advised embolisation for AMLs and was referred for the same. He was advised regarding genetic studies, but due to financial constraints and lack of facilities at our institute it could not be done.

Figure 3 CT of the brain showing calcified density along right lateral ventricle consistent with subependymal nodule or tuber.

DISCUSSION

Von Recklinghausen first described tuberous sclerosis in 1862. Bourneville coined the term *sclerose tubereuse*, from which the name of the disease has evolved. TSC follows an autosomal-dominant inheritance pattern. As many as 60% of people with TSC do not have any family history of the condition; they have a *de novo* (new) mutation in the TSC1 or TSC2 gene and affects approximately 1 in 100 000 people with equal distribution in both sexes.² The pathophysiology of tuberous sclerosis can include glial tumours of the brain, adenoma sebaceum of the skin, rhabdomyoma of the heart and hamartomatous tumours of the thyroid, retina, liver, pancreas, lung, kidney, adrenals and ovaries. The clinical features of TSC depend on the target organ (mainly brain, skin, kidneys, lungs and heart) or organs affected and the extent of damage due to the lesions.³

AML is a benign renal neoplasm composed of fat, vascular and smooth muscle elements. The most important association of this tumour is with tuberous sclerosis. This tumour is one of the major diagnostic criteria of the disease. Overall, however, there are four times as many sporadic AMLs as there are cases associated with tuberous sclerosis. Histologically, AML is composed of a mixture of three tissue types: smooth muscle, thick-walled blood vessels and mature fat. The smooth muscle cells are benign in appearance and are arranged in sheets and bundles. The blood vessels in AML are characterised by thick, muscular walls, which lack elastic lamellae. The fat cells are mature and normally developed. Typically, the renal lesions remain silent and are incidental findings at autopsy. However, they may present with gross haematuria, flank pain, abdominal pain, nausea, vomiting, fever, abdominal distension or simply as a mass.⁵

The natural history of renal AML is unknown. Patients who have renal AMLs with tuberous sclerosis are distinctly different from those without tuberous sclerosis. Patients with tuberous sclerosis present at a younger age are more likely to be symptomatic and have large bilateral tumours that are more likely to grow and therefore more frequently require surgery. In the series by Steiner *et al*⁶ the average size of AML in patients with tuberous sclerosis is 9.6 ± 4.8 cm, and in those without tuberous sclerosis is 4.1 ± 3.4 cm. AML may grow to be large and bulky and extend into the perirenal space, which sometimes makes it difficult to differentiate from perirenal liposarcoma. However, perirenal liposarcoma is unilateral and usually will not invade the kidney because it arises from retroperitoneal fat. In comparison, renal AML arises from the renal parenchyma and involves the kidney itself.⁷ Our patient was diagnosed late at the age of 22 years because of delayed presentation to a tertiary centre and he presented with abdominal distension and anaemia.

The adipose component of AMLs helps make the diagnosis radiologically, since it is easily identified on CT. The demonstration of fat on renal ultrasound and CT can accurately diagnose AML in 95% of the cases. The radiographic features of AMLs on ultrasound examination (echogenic areas) or CT scanning (areas of fatty tissue; -20 to -60 Hounsfield units) are pathognomonic. In our case, diagnosis of AML was made on the basis of CT findings.

Most tumours can be managed conservatively, particularly if they are asymptomatic. Nephron conservation is

of even greater importance in tuberous sclerosis, in which tumours are often bilateral. Partial nephrectomy is ideal for masses with a diameter smaller than 3 cm, and partial nephrectomy may be possible in masses with a diameter smaller than 5 cm that do not abut the hilum. For lesions greater than 3.5–4 cm in size, the risk of haemorrhage and hypovolaemic shock is critical and they need to be explored. When the lesions are greater than 10 cm, the preferred route of treatment is partial nephrectomy or selective arterial embolisation.^{5 6}

Our patient presented with anaemia, flank pain and abdominal distention due to large renal AMLs filling the entire abdomen and replacing the renal parenchyma bilaterally. Usually patients present much earlier, before the AMLs reach the size seen in our patient, with symptoms such as haemorrhage, flank pain, renal failure, anaemia or palpable mass. To our knowledge, only few published case reports of such large bilateral AMLs have been presented in the literature.^{8–10} Renal cysts and AMLs are significant causes of morbidity and mortality in TSC due to renal failure or acute bleeding. Regular screening of TSC patients with renal ultrasound or CT scanning has been recommended to facilitate early surgical removal of enlarging lesions before they can cause haemorrhage or potentially dangerous distortion of renal architecture. AMLs are usually benign from the onset and growth and metastasis of these lesions are very rare, but malignant change has also been reported in renal TSC lesions.¹¹ This case illustrates the association of renal AML in a patient with tuberous sclerosis and that renal AMLs may grow substantially. Early recognition of the disease in childhood can prevent fatal complication at the adult stage.

Learning points

- Dermatological manifestations may be the only diagnostic clue to the diagnosis of tuberous sclerosis. But as illustrated in our case, in incidental finding like bilateral large renal angiomyolipomas (AMLs), one should strongly consider the diagnosis of tuberous sclerosis.
- Renal AMLs can grow substantially.
- Regular screening of TSC patients with renal ultrasound or CT is recommended to facilitate early surgical removal of enlarging lesions before they can cause haemorrhage or potentially dangerous distortion of renal architecture.

Competing interests None.

Patient consent Obtained.

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