Case Report

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Late diagnosis of tuberous sclerosis complex in a 40-year-old female presenting with abdominal pain: a case report

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Abstract

Tuberous sclerosis (TS) is a rare autosomal-dominant neurocutaneous disorder that is characterized by hamartomas affecting a variety of organs, including the brain, heart, kidneys, skin, lungs, and liver. TS can emerge in a wide variety of clinical and phenotypic forms at any age, all with varying degrees of severity, and is brought on by mutations in the tumor suppressor genes *TSC1* or *TSC2*. This case report is about a 40-year-old female with facial angiofibromas and abdominal symptoms who was referred to the radiology department of our hospital for ultrasonography of the abdomen, which revealed echogenic mass lesions/angiomyolipomas in bilateral kidneys. Subsequent contrast-enhanced computed tomography of the abdomen revealed large fat-attenuating mass lesions which were confirmed to be angiomyolipomas. Similarly, noncontrast computed tomography of the head showed multiple calcified nodules/tubers in subependymal, subcortical, and cortical locations of the brain. High-resolution computed tomography of the chest showed multiple cystic lesions in bilateral lungs suggestive of lymphangioleiomyomatosis. The aim of this case report is to highlight the late presentation of tuberous sclerosis complex.

Keywords: angiomyolipomas, cortical tubers, facial angiofibromas, lymphangioleiomyomatosis, subependymal tubers, tuberous sclerosis

Introduction and importance

Tuberous sclerosis complex (TSC) is a progressive neurocutaneous disorder with an estimated incidence and prevalence of 1 in 6000–10,000 live births and 1 in 20,000 individuals, respectively[1]. It is a multisystem illness that may present with varying clinical manifestations ranging from severe mental retardation and intractable seizures to normal intellect and absence of seizures that becomes apparent only in late childhood[2]. It occurs due to mutation in *TSC1* and *TSC2*, leading to the formation of multiple benign hamartomas of the brain, eyes, heart, lung, liver, kidney, and skin[3].

This case report has been reported in line with the Surgical CAse REport (SCARE) Criteria[4].

HIGHLIGHTS

- Tuberous sclerosis (TS) is a rare autosomal-dominant neurocutaneous disorder that is characterized by hamartomas affecting a variety of organs, including the brain, heart, kidneys, skin, lungs, and liver.
- TS can emerge in a wide variety of clinical and phenotypic forms at any age, all with varying degrees of severity.
- This case report is about a 40-year-old female with facial angiofibromas and abdominal symptoms who was referred to the radiology department of our hospital for ultrasonography of the abdomen, which revealed angiomyolipomas in bilateral kidneys.
- Subsequent contrast-enhanced computed tomography of the abdomen revealed large fat-attenuating mass lesions which were confirmed to be angiomyolipomas. Similarly, noncontrast computed tomography of the head showed multiple calcified nodules/tubers in subependymal, subcortical, and cortical locations of the brain. High-resolution computed tomography of the chest showed multiple cystic lesions in bilateral lungs suggestive of lymphangioleiomyomatosis.
- This spectrum of findings is consistent with TS.
- The aim of this case report is to highlight on the late presentation of tuberous sclerosis complex.

Case presentation

A 40-year-old female presented to our hospital with complaints of abdominal pain, abdominal fullness, and episodes of vomiting for the previous 1 month. The patient tried over-the-counter

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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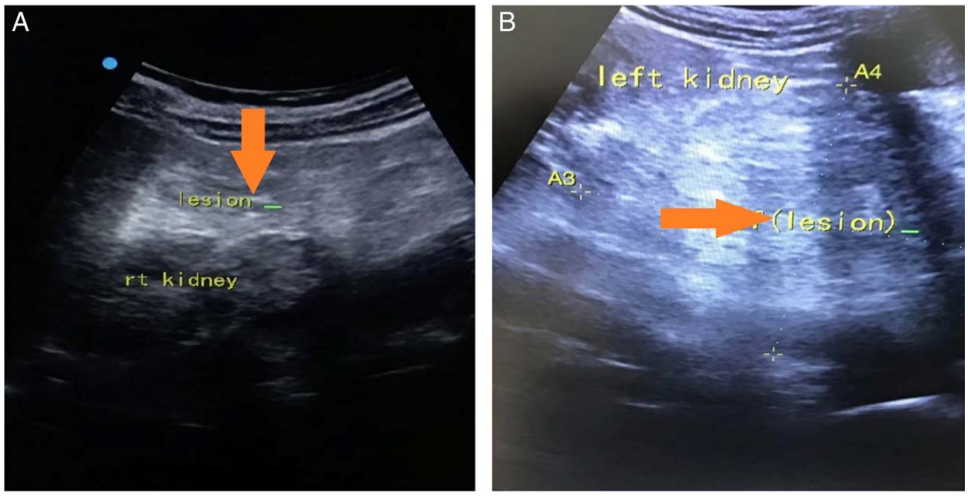

Figure 1. Ultrasound of the right kidney (A) and left kidney (B) shows echogenic mass lesions/angiomyolipomas bilaterally (red arrows in A and B).

proton pump inhibitors and antiemetic medications to relieve her symptoms, but her symptoms persisted with no significant improvement. She was then advised for ultrasonography of abdomen which revealed large echogenic lesions arising from bilateral kidneys (Fig. 1).

On physical examination, multiple small pinkish erythematous papules, with some of them coalescent and forming plaques, were noted in the central part of her face, especially affecting the nasolabial folds, cheek, and nose. The patient reported that these growths appeared at an early age, for which she had been undergoing treatment with topical creams for quite a long time without much improvement (Fig. 2).

Few reddish brown nodular growths were noted in her nail folds, suggestive of periungual fibromas. The patient reported an increased number of such nodules during the winter months.

Contrast-enhanced computed tomography abdomen and pelvis revealed large lobulated heterogeneous exophytic fat-attenuating mass lesions in bilateral kidneys suggestive of angiomyolipomas (AMLs). Few other fat-attenuating lesions were also noted in the left kidney (Figs 3, 4).

High-resolution computed tomography chest findings showed multiple smooth, round thin-walled cystic lesions in the random distribution in bilateral lungs, suggestive of lymphangioleiomyomatosis (LAM) (Fig. 5).

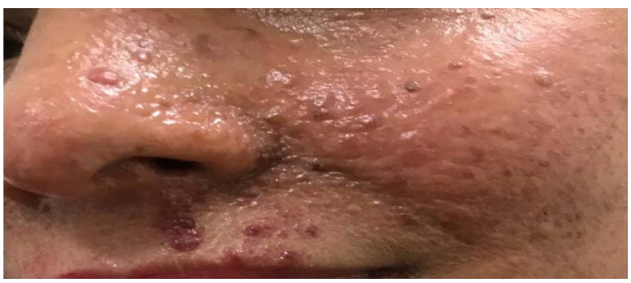

Figure 2. Multiple red papules (angiofibromas) on the face, especially on the nasolabial folds, cheek, and nose.

Reconstructed computed tomography (CT) images in the bone window showed multiple sclerotic lesions in the lumbar and lower dorsal vertebrae (Fig. 6).

Noncontrast computed tomography head revealed calcified nodules in subependymal, cortical, and subcortical regions of the brain (tubers) (Fig. 7).

She also underwent an ophthalmologic examination which revealed a refractive error in bilateral eyes for which she has been wearing power glasses. No retinal abnormalities and visual field defects were detected. Echocardiography findings and baseline laboratory findings were normal.

Considering all the imaging findings and cutaneous manifestations, a definitive diagnosis of tuberous sclerosis (TS) was made. The patient was planned for chemoembolization for renal lesions and was advised for a dermatological and neurological consultation.

Clinical discussion

TSC is a multisystem progressive neurocutaneous autosomal-dominant condition that occurs due to inactivating mutation either in *TSC1* located in the long arm of chromosome 9 encoding hamartin or in *TSC2* located in the short arm of chromosome 16 encoding tuberin[3]. *TSC2* is three times more prevalent and has significant deletions and missense mutation resulting in more severe neurodevelopmental abnormalities, whereas the majority of *TSC1* mutations are minor and result in the production of a truncated protein[1]. The mutations in *TSC1* and *TSC2* lead to the formation of hamartomas in various organs. Cortical tubers, subependymal nodules, and subependymal giant cell astrocytomas can be present in the brain. Similarly, other manifestations include renal AMLs, LAM in the lung, rhabdomyomas in the heart, nontraumatic ungual or retinal nodular hamartomas, intraoral fibromas, and dental enamel pits. Cutaneous manifestations include angiofibromas, Shagreen patches, and hypomelanotic macules[5,6]. Almost all TSC patients show visible skin or dental disease signs on physical examination. Thus, it is important to highlight dermatological manifestations to further investigate the presence of TSC[7].

Although TSC is an autosomal-dominant disease, a high rate of spontaneous mutation can occur; thus, as in our case, nearly two-thirds of the patients do not have a positive family history[8]. The

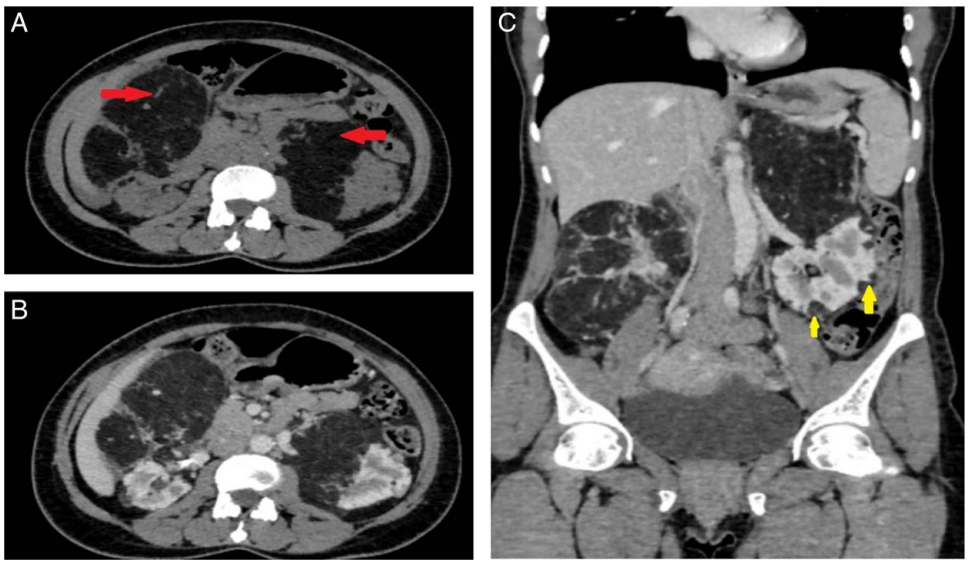

Figure 3. Noncontrast computed tomography (A) and contrast-enhanced computed tomography (B) images of the abdomen in axial plane shows well-defined large, lobulated, exophytic, heterogeneous fat-attenuating mass lesions arising from bilateral kidneys (inter/lower pole of the right kidney and upper pole of the left kidney; denoted by red arrows in A and B), in keeping with renal angiomyolipomas. Contrast-enhanced computed tomography (C) images of the abdomen in coronal plane shows multiple other fat-attenuating lesions in the left kidney (yellow arrows in C).

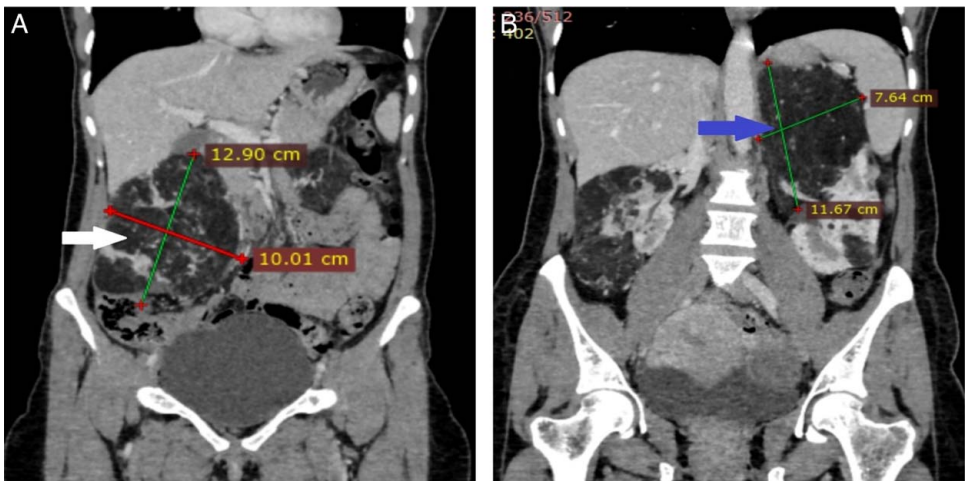

Figure 4. Contrast-enhanced computed tomography images of the abdomen in the coronal plane (A and B), the lesion in the right kidney measures ~12.90 × 10.01 cm and on the left measures ~11.67 × 7.64 cm. The lesions do not show enhancement in postcontrast studies.

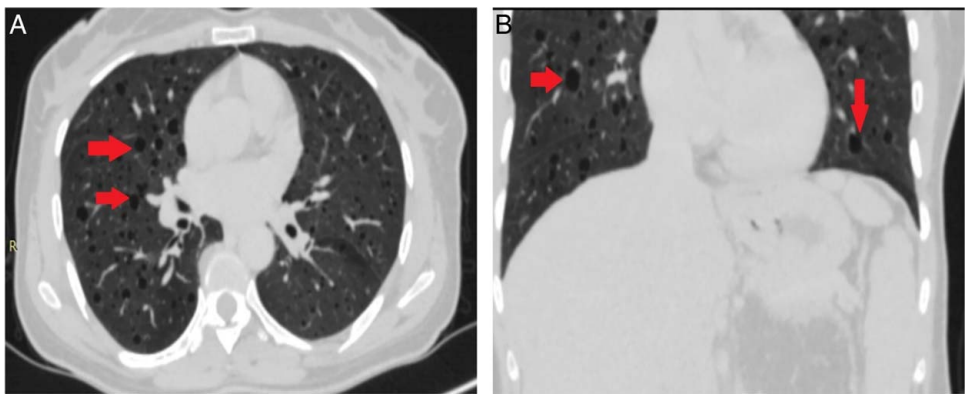

Figure 5. High-resolution computed tomography images in the axial plane (A), and coronal plane (B) shows multiple round thin-walled cystic lesions in random distribution in bilateral lungs. These findings are consistent with lymphangioleiomyomatosis.

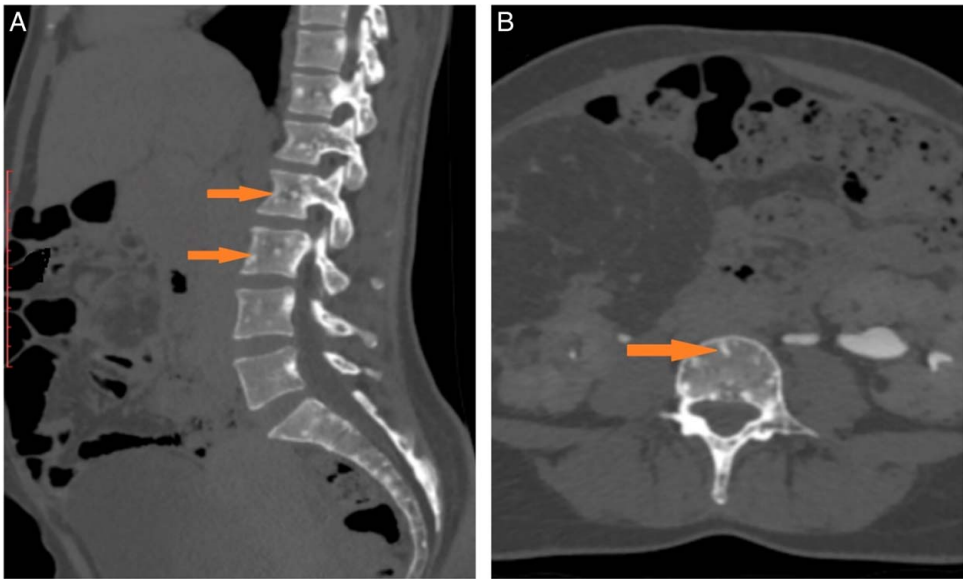

Figure 6. Multiple sclerotic lesions noted in visualized lumbar and lower dorsal vertebrae (orange arrows in A and B).

Vogt triad of mental retardation, seizure, and facial angiofibromas is typical of TS; nevertheless, nearly half of TS patients have normal intellect, and a quarter do not have seizures[5]. Out of these three manifestations, our patient had facial angiofibromas.

The presence of subependymal, cortical and subcortical tubers, LAM, multiple bilateral renal AMLs, facial angiofibromas, and ungual fibromas in our patient confirmed the diagnosis of TS. However, genetic analysis was not done.

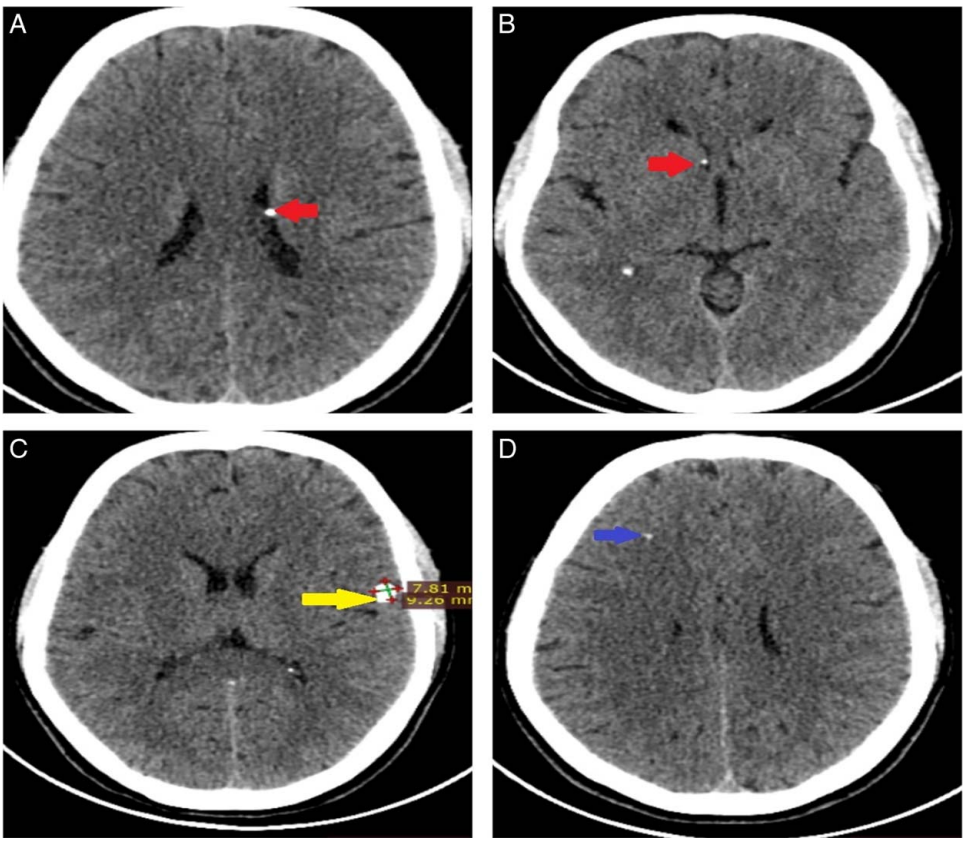

Figure 7. Noncontrast computed tomography images of the head in the axial plane (A–D) shows calcified subependymal nodules in the left lateral ventricle (A) and the frontal horn of right lateral ventricle (B). Approximately 9.2 × 7.8 mm-sized calcified cortical tuber is also noted in the left frontal lobe (yellow arrow in C), and a tiny calcified subcortical tuber is noted in the right frontal lobe (blue arrow in D).

Imaging is crucial for the diagnosis of TS. CT is an effective modality for the detection of subependymal nodules because they are commonly associated with calcification. Although MRI has been found to be more effective than CT at detecting cortical tubers and subependymal giant cell astrocytomas, CT can still detect cortical tubers. By assessing intratumoral fat density (density < – 20 HU), CT can identify AML. Chest CT can also quickly diagnose chest symptoms such as LAM[9].

Conclusion

TS is a uncommon neurocutaneous disorder with a progressive clinical course. Not all TS presents with the classic clinical triad, and in some cases, diagnosis is delayed for a prolonged period of time. Hence imaging, in addition to clinical manifestations, plays a crucial role in the diagnosis. A multidisciplinary approach is required for the appropriate management and to reduce morbidity and mortality.

Ethical approval

Ethical approval was not required for a case report.

Patient consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Patient perspective

The patient was anxious about the condition. However, she felt a lot better after proper counseling and advice.

Sources of funding

No funding was received in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Author contribution

Sajiva Aryal – analyzed and interpreted the patient data and was a major contributor in writing the manuscript. S.S. – contributed in writing the manuscript, editing the manuscript, and organization of images in the manuscript. Saman Aryal – contributed in writing the manuscript and literature review. V.B. – contributed in writing the manuscript and literature review.

Conflicts of interest disclosure

There are no conflicts of interest among the authors to disclose.

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