



Case Report

A subtle case of tuberous sclerosis complex

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ABSTRACT

Tuberous sclerosis complex (TSC) is known to cause severe intractable epilepsy and mental retardation; however, diagnosis can be delayed in milder cases. We report a 26-year-old right-handed female patient who started having convulsions at age 7 days. She had several focal seizures per year that were intractable to treatment with carbamazepine or phenytoin. Her two sisters had several episodes of suspected epileptic seizures but had no symptoms related to TSC. Seizure semiology of the patient comprised of visual hallucination, loss of consciousness, and convulsive movements predominantly on the right. Physical examination revealed several small scattered angiofibromas over the nose that were histologically determined by skin biopsy. Hypomelanotic macules, shagreen patches, or periungual fibromas were not seen. Neurological examination showed mental retardation (MMSE: 23/30, WAIS-III: VIQ63, PIQ59, FIQ58) and decreased vibration sensation in both legs. Interictal EEG showed slow waves and epileptiform discharges broadly over the anterior quadrants bilaterally. Brain imaging showed multiple cortical tubers and malformation of cortical development but no subependymal nodules. Interictal IMP-SPECT showed hypoperfusion in the left frontal lobe. Cardiac rhabdomyoma was not noticed by cardiac echography. Truncal CT showed sclerosis of the bilateral lumbosacral joints. There was no abnormality in the lung, major arteries, liver, or kidneys. No hamartomas or retinal achromic patches were noticed by ophthalmologic evaluation. Administration of lamotrigine was effective for her seizures. This patient fulfilled two major features of diagnostic criteria for TSC and was diagnosed as definite TSC. Patients with mental retardation and epilepsy should be carefully evaluated for the possible diagnosis of TSC.

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1. Introduction

Tuberous sclerosis complex (TSC) is a multisystem, autosomal dominant disorder with an incidence of approximately 1 in 6000 live births [1]. Tuberous sclerosis complex usually manifests itself in early life with severe intractable epilepsy and mental retardation; however, diagnosis can be delayed in milder cases. A recent study demonstrated the importance of early diagnosis and commencement of preventative antiepileptic treatment of infants with TSC to improve neurodevelopmental and seizure outcomes [2]. Here, we present a patient with TSC with subtle cardinal manifestations. Part of this manuscript was presented at the 10th Asian & Oceanian Epilepsy Congress, Singapore 2014 and appeared in an abstract form [3].

2. Case report

A 26-year-old right-handed woman presented for a thorough evaluation of seizures that were not controlled by medical therapy. She

started having convulsions at age 7 days and had several focal seizures per year that were intractable to treatment with carbamazepine or phenytoin. Her two sisters had several episodes of suspected epileptic seizures. Her elder sister had fainting attacks probably caused by anemia. Her younger sister developed generalized convulsions when she was

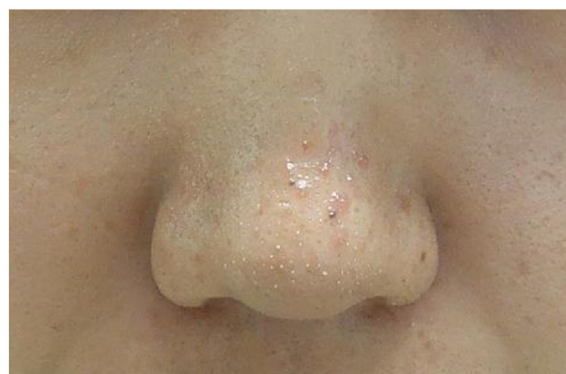


Fig. 1. Several small angiofibromas over the nose in a 26-year-old woman.

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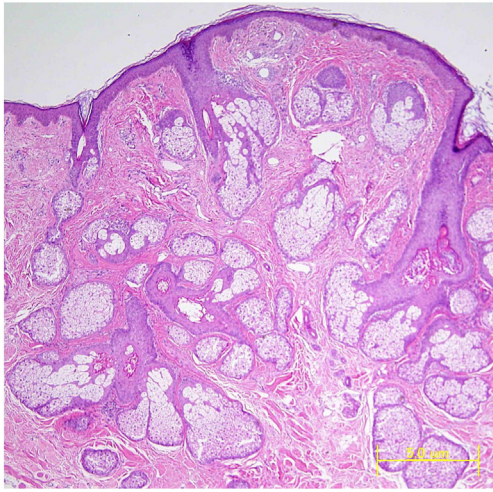


Fig. 2. A dome-shaped angiofibroma in the superficial dermis, showing a proliferation of stellate and spindle cells around blood vessels and concentric collagen bundles.

in high school, was treated with antiepileptic medication, and, after finishing therapy, has been seizure-free for more than 2 years. Both were examined in other hospitals, and no symptom related to TSC was reported.

Seizure semiology of the patient comprised of visual hallucination, loss of consciousness, and convulsive movements predominantly on the right side. Therefore we categorized her seizures as focal without initial impairment of consciousness evolving to impaired consciousness and then to bilateral convulsive seizures.

Physical examination revealed several small scattered angiofibromas over the nose (Fig. 1) that were histologically determined by skin biopsy (Fig. 2). Hypomelanotic macules, shagreen patches, or periungual fibromas were not seen. Neurological examination showed mental retardation (MMSE: 23/30, WAIS-III: VIQ 63, PIQ 59, FIQ 58) and decreased vibration sensation in both legs. Interictal EEG showed slow waves and epileptiform discharges broadly over the anterior quadrants bilaterally (Fig. 3). Brain imaging showed multiple cortical tubers and malformation of cortical development in the left cerebral hemisphere but no subependymal nodules or other calcified lesions (Fig. 4). Interictal IMP-SPECT showed hypoperfusion in the left frontal lobe (Fig. 4). Truncal CT showed sclerosis of the bilateral lumbosacral joints (Fig. 5). Cardiac rhabdomyoma was not noticed by cardiac echography. There was no abnormality of the lung, major arteries, liver, or kidneys. No hamartomas or retinal achromic patches were noticed by ophthalmologic evaluation. Administration of lamotrigine was effective for her seizures.

3. Discussion

This patient fulfilled two major diagnostic criteria for TSC, i.e., facial angiofibromas and cortical tubers, and was diagnosed as having definite TSC [4]. This patient’s epilepsy was categorized into epilepsies attributed to and organized by structural-metabolic causes, neurocutaneous syndromes, and TSC. She was devoid of calcified subependymal nodules which are known to be one of the most common features of TSC. Approximately 90% of patients have subependymal nodules in epidemiological studies among patient populations with TSC, and mainly in children (mean age of 10–11 years) [5,6], compared with 77% among those in adults (mean age of 27 years) [7]. Early recognition of TSC is important to understand the course of the disease and possible strategies to prevent progression [2].

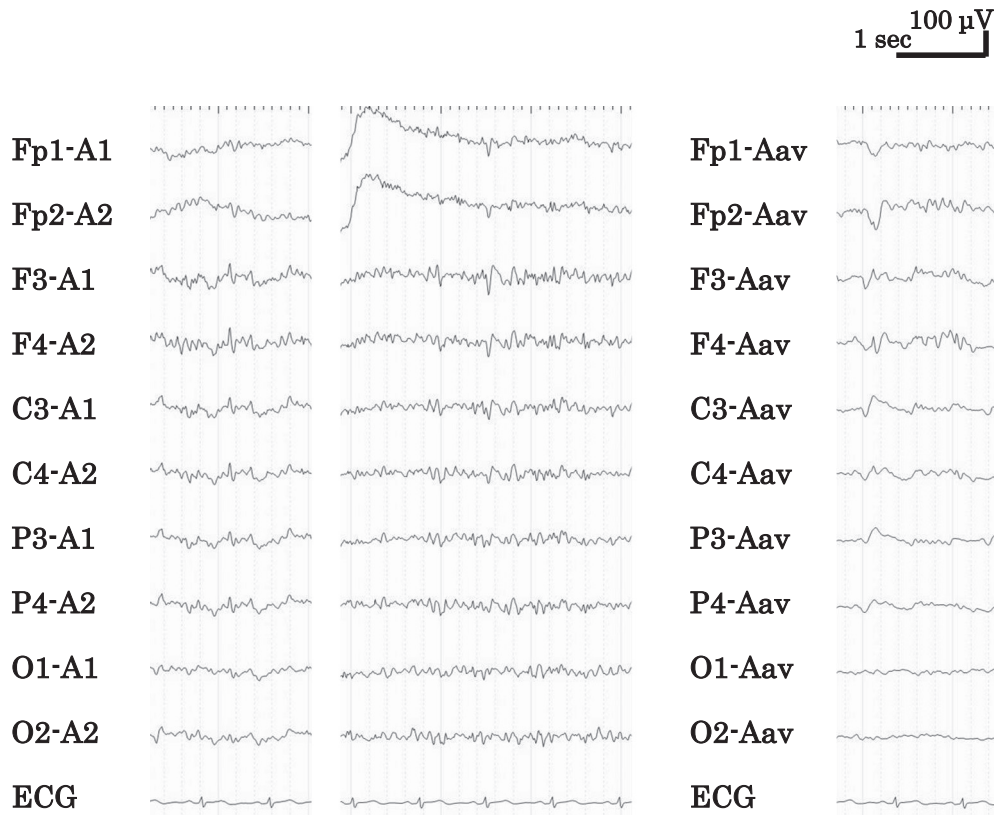


Fig. 3. Interictal EEG. Slow waves and epileptiform discharges broadly over the anterior quadrants bilaterally.

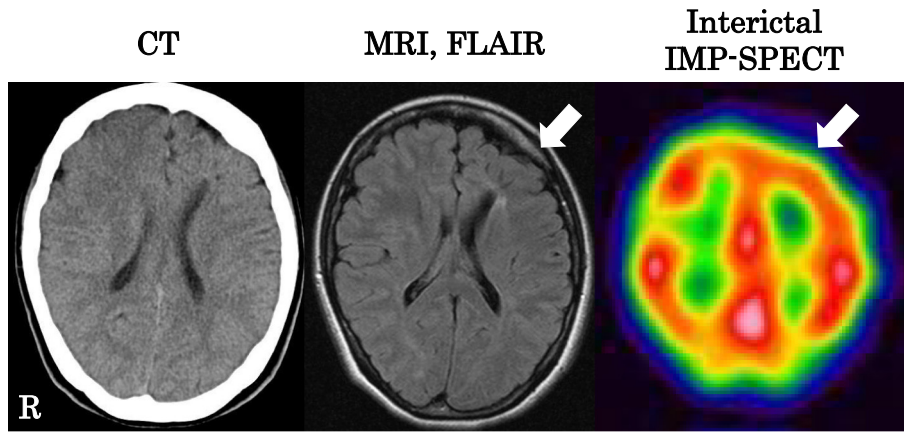


Fig. 4. Axial views of CT, FLAIR MRI, and interictal IMP-SPECT almost at the same level. Note malformation of cortical development and hypoperfusion in the left frontal lobe (arrow). No subependymal nodules or other calcified lesions were seen on CT.

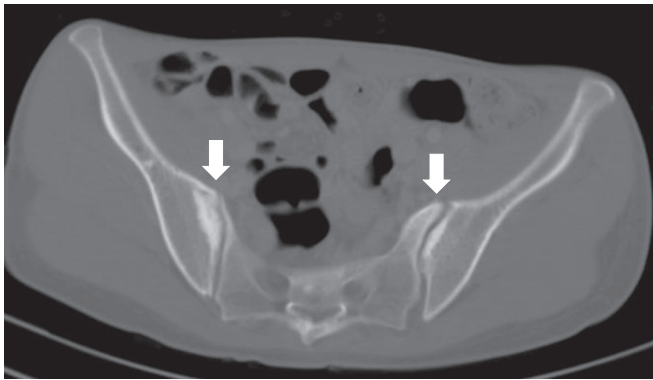


Fig. 5. Sclerosis of bilateral lumbosacral joints in truncal CT (arrows).

4. Conclusion

Patients with mental retardation and epilepsy should be carefully evaluated for the possible diagnosis of TSC, even if they lack subependymal nodules or show mild skin symptoms.

Conflict of interest

The authors declare that they have no conflict of interest.

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