Neurosciences Quiz

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Seizure and skin lesions

Case Presentation

A 20-year-old man presented with a history of generalized tonic-clonic seizures from age 4. His seizures were controlled with carbamazepine. On clinical examination, he was mentally subnormal, but there were no focal neurological deficits. Dermatological assessment revealed certain findings in his face and trunk (**Figure 1**), and brain magnetic resonance imaging is shown in **Figure 2**.

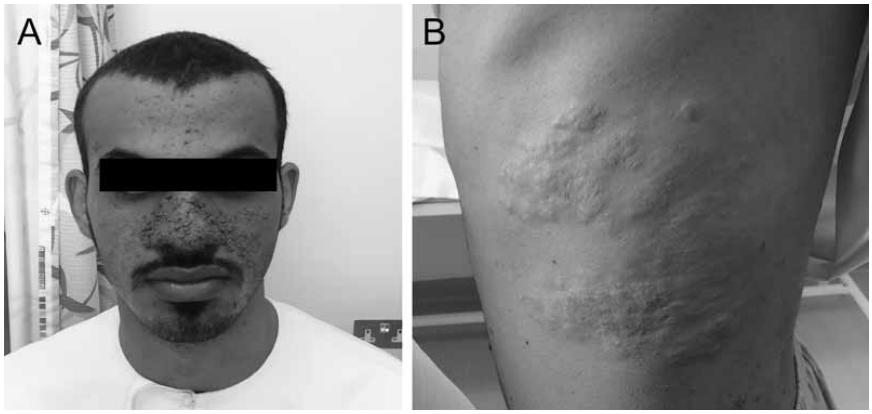

Figure 1 - Photographs of patient's face **A**) and trunk **B**) demonstrating certain cutaneous signs/findings.

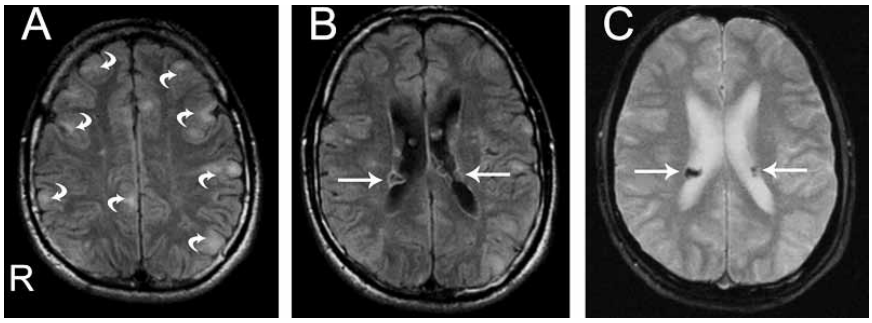

Figure 2 - Axial fluid attenuated inversion recovery magnetic resonance imaging of brain **A** & **B**) and T2 gradient recall echo sequence **C**).

Questions

1. What abnormalities are observed in **Figure 1**?
2. What findings are seen in **Figure 2**?
3. What is the clinical diagnosis?
4. How will you manage this patient?

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Answers & Discussion

1. *Clinical findings.* The clinical photograph of the patient's face shows multiple, small papular lesions over the nose, nasolabial folds, and forehead that are typical of adenoma sebaceum or angiofibromas. The raised skin lesions over the lateral aspect of the trunk/flank are characteristic of shagreen patches.

2. *MRI findings.* Brain MRI shows cortical tubers (curved arrows, **Figure 2A**) and calcified subependymal nodules (straight arrows, **Figures 2B and 2C**). **Figure 2C**, a T2 weighted gradient recall echo image shows the presence of calcification as striking hypointense lesions (arrows).

3. *Clinical diagnosis.* The presence of 4 major features namely, adenoma sebaceum, shagreen patches, cortical tubers, and subependymal nodules favors the diagnosis of definite tuberous sclerosis complex.[1]

4. *Management.* The patient had generalized seizures (this could be primary generalized seizure or partial seizure with secondary generalization, the onset of which he could not describe in detail) and the habitual seizures were well controlled with carbamazepine. Hence, the anticonvulsant was continued. He should be educated on potential seizure triggers such as missing or discontinuing anticonvulsants, sleep deprivation, and fasting. He needs regular follow-up in the neurologic clinic for ascertaining seizure control; adjustment of medications if there are breakthrough seizures (his baseline EEG showed intermittent generalized epileptiform discharges), and regular follow-up neuroimaging scans for detecting the early appearance and interval progression of subependymal giant cell astrocytoma. Everolimus or neurosurgical procedure is indicated for progressive subependymal giant cell astrocytoma (see the discussion below). He also requires work-up for other organ lesions such as echocardiography or MRI for cardiac rhabdomyoma, renal ultrasound (or CT of abdomen/pelvis) for renal angiomyolipoma or renal cysts, and ophthalmologist consultation for retinal hamartoma.

Tuberous sclerosis complex (TSC) is an autosomal dominant neuro-cutaneous disorder that manifests with seizures, mental subnormality, autism, attention deficit hyperkinetic disorder, subependymal giant cell astrocytoma, and retinal hamartomas.[1] There is a spectrum of ictal manifestations in TSC ranging from symptomatic epileptic spasms, Lennox Gastaut syndrome to focal seizures, complex focal seizures, and generalized seizures.[2] The hallmark lesion, namely, cortical tubers, consists of dysplastic neurons, abnormal lamination, and astrogliosis. Tuberous sclerosis complex is caused by a mutation in the TSC1 gene on chromosome 9q34 (leading to truncation of hamartin protein) or TSC2 gene on chromosome 16p13.3 (leading to loss or truncation of tuberin protein).[3] These tumor suppressor genes and their encoding proteins are crucial for cellular proliferation, growth, and protein synthesis. Recently, in an open label study, Everolimus, a drug that acts by inhibiting mammalian target of rapamycin (mTOR) complex 1 has been shown to result in regression of subependymal giant cell astrocytoma and reduction in the frequency of seizures.[4] For epileptic spasms related to TSC, the drug of choice is vigabatrin and hence, the importance of making the diagnosis in that setting. As our patient's seizures (primary generalized seizure or probably partial seizure with secondary generalization) were well controlled with carbamazepine, he was continued on it. Follow-up brain imaging permits recognition of interval progression or regression of subependymal giant cell astrocytoma and the use of mTOR inhibitors or neurosurgical procedure as indicated. Patients on vigabatrin should have serial assessment of visual fields. Identification of the characteristic extra-neural signs such as dermatological manifestations (adenoma sebaceum, shagreen patches, hypomelanotic macules, non-traumatic ungual fibromas, and fibrous facial plaques) provides useful clues to the underlying phakomatosis such as TSC, and would aid in the proper interpretation of neuroimaging scan, as in this patient.

References

1. Roach ES, Sparagana SP. Diagnosis of tuberous sclerosis complex. ***J Child Neurol*** 2004; 19: 643-649.
2. Chu-Shore CJ, Major P, Camposano S, Muzykewicz D, Thiele EA. The natural history of epilepsy in tuberous sclerosis complex. ***Epilepsia*** 2010; 51: 1236-1241.
3. Hoogeveen-Westerveld M, Wentink M, van den Heuvel D, Mozaffari M, Ekong R, Povey S, et al. Functional assessment of variants in the TSC1 and TSC2 genes identified in individuals with Tuberous Sclerosis Complex. ***Hum Mutat*** 2011; 32: 424-435.
4. Krueger DA, Care MM, Holland K, Agricola K, Tudor C, Mangeshkar P, et al. Everolimus for subependymal giant-cell astrocytomas in tuberous sclerosis. ***N Engl J Med*** 2010; 363: 1801-1811.