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INTERESTING MEDICAL IMAGE

Inappropriate Laughter in a Patient with Hypothalamic Hamartoma

Faris Al Kalbani,[1] Faraz Ahmad,[2] Alaa Elmanzalawy,[3] *Amna Al Futaisi[4]

ضحك بشكل غير لائق لدى مريض مصاب بورم عابِي وِطائِي

فارس الكلباني، فَراز أحمد، علاء المنزلاوي، آمنة الفطيسية

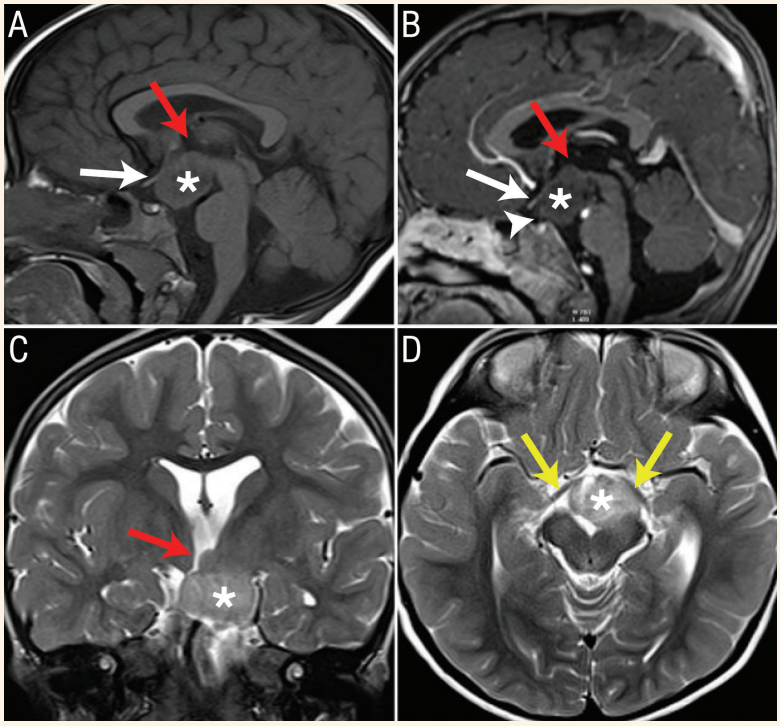

Figure 1: Sagittal T1-weighted magnetic resonance images (MRIs) of the brain of a two-year and seven-month-old boy before (**A**) and after (**B**) intravenous gadolinium contrast administration. They show a mass (asterisk) arising from the both above and below the floor of the third ventricle (red arrows). Accordingly, this mass has both vertical and horizontal planes of attachment to the floor of the third ventricle classifying it radiologically as Delalande type III. It occupies most of the suprasellar and interpeduncular cisterns. It compresses the optic chiasm (white arrows) and pituitary stalk (White arrowhead) anteriorly. Coronal (**C**) and axial (**D**) T2-weighted MRIs show the mass having a heterogenous hyperintense signal. It is seen stretching the optic tracts bilaterally (yellow arrows) in (**D**).

A two-year and seven-month-old boy presented to the Emergency Department at Sultan Qaboos University Hospital, Muscat, Oman, in 2019, with a two-day history of uprolling of eyeballs, unresponsiveness and drooling of saliva lasting for seconds. There was no abnormal limb movement or loss of tone. The episodes were followed by a postictal state that lasted 30 minutes. There were no triggers for the episodes, such as fever or intercurrent illness. The patient was born at term gestation to a consanguineous marriage. Antenatal, birth and family history were unremarkable. His developmental milestones were appropriate for his age and his immunisation was up-to-date. A sleep electroencephalogram (EEG) showed abnormal interictal generalised epileptiform discharges with no associated clinical accompaniment. There were bilateral occipital epileptiform discharges with slowing over the left

[1]*Department of Child Health, Oman Medical Specialty Board, Muscat, Oman;* [2]*Department of Child Health and* [3]*Radiology and Molecular Imaging, Sultan Qaboos University Hospital, Muscat, Oman;* [4]*Department of Child Health, Sultan Qaboos University, Muscat, Oman*
**Corresponding Author's e-mail: amnaf@squ.edu.om*

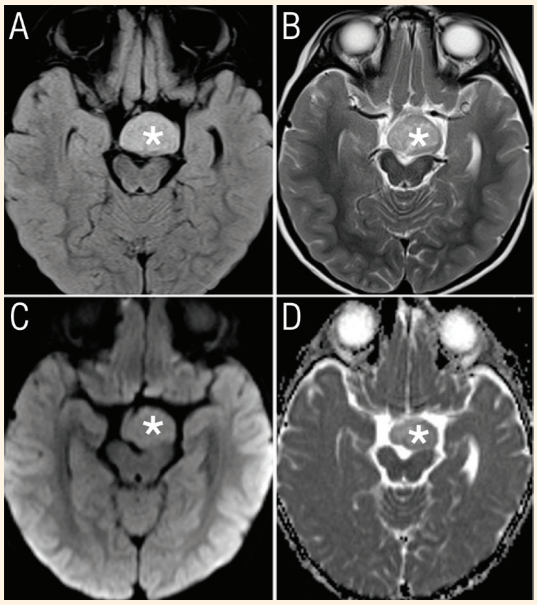

Figure 2: Magnetic resonance imaging (MRI) of the brain of a two-year and seven-month-old boy showing a hypothalamic (*tuber cinereum*) hamartoma (asterisk). It shows (**A** & **B**) hyperintense signal on fluid-attenuated inversion recovery and T2 MRIs. Axial diffusion-weighted MRI (**C**) and apparent diffusion coefficient map (**D**) images showing no evidence of diffusion restriction in this lesion.

posterior head region. In view of some lateralising features on EEG, MRI of the brain was done within three weeks of initial presentation, which revealed features of a hypothalamic hamartoma (HH; Figures 1 and 2). Formal visual field assessment was not possible due to the patient's young age. However, no visual symptoms were observed and endocrine workup was normal. Initial seizure control was achieved with levetiracetam reaching a dose of 40 mg/kg/day. Two months later, he developed multiple, sudden onset, unprovoked and uncontrollable laughing episodes that were occurring for no obvious reasons, suggestive of gelastic seizures. Postictally, he was immediately back to his baseline with no tiredness or sleepiness. Repeated routine EEG did not capture the events and showed no clear epileptiform abnormality except bilateral posterior slowing with left temporal dominance. Long-term video EEG was not performed. The episodes of gelastic seizures were difficult to control and required the administration of topiramate (6 mg/kg/day) as well as a short course of phenytoin (6 mg/kg/day) to control a cluster of focal seizures. Currently, he is on two anti-epileptic medications (levetiracetam and topiramate). Eight months later during follow-up, the father of the child reported mild hyperactivity. There was no evidence of neuroregression. During the write-up of this article, the patient was awaiting formal assessment with the developmental and behavioural paediatric team.

Although he was not yet seizure-free, the episodes were reasonably controlled with 1–2 brief daily episodes of eyelid twitching and occasional gelastic seizures once in 1–2 weeks. The parents were offered the option of surgical intervention, but decided against it.

Comment

As a rare developmental malformation, HH can display diverse clinical manifestations. It may present with intractable seizures, central precocious puberty and cognitive and neuropsychiatric disturbances. Seizures associated with HH can be of variable types and include focal seizures with impaired awareness, generalised tonic-clonic seizures, epileptic spasms, atonic, tonic, focal seizures with retained awareness and the hallmark gelastic seizures.[1] Based on the radiological features, the HH of the current patient was classified as Delalande type III.[2] The patient initially presented with focal seizure with impaired awareness and later developed gelastic seizures, which are a unique type of seizures that are usually seen in early childhood. Gelastic seizures are characterised by frequent brief attacks of inappropriate laughter.[3] The EEG during a gelastic seizure is usually normal or may show non-specific abnormalities, which may contribute to the difficulty in establishing the diagnosis when gelastic seizures are the sole presentation. The seizures in HH are thought to be due to either the intrinsic epileptogenicity of the hamartoma itself or contributed by the extensive epileptogenic networks and possible kindling-like relationship between the HH and the cortex.[4,5] This epileptogenic spread could possibly explain the EEG findings in the current patient.

Most patients with epilepsy secondary to HH develop an associated mood disorder, behavioural issues and/or cognitive delay. A significant proportion of patients with HH and epilepsy may present with central precocious puberty. However, growth hormone deficiency, hypothyroidism and adrenal insufficiency are rare. Although diabetes *insipidus* is not seen in non-operated HH, it is frequently seen postoperatively.[6]

Treatment of HH-associated epilepsy is challenging and complete seizure freedom with anti-seizure medications is rarely achieved. Behavioural and learning difficulties as well as cognitive delay lead to an overall developmental impairment contributing to the increased morbidity associated with HH. Treatment strategies in such cases of progressive encephalopathy associated with HH should be based on multidisciplinary care, including neurologists,

neuropsychologists and neurosurgeons. Therapeutic options include anti-seizure medications, ketogenic diet therapy and vagal nerve stimulation. Neurosurgical options include microsurgical resection, endoscopic disconnection, stereotactic laser ablation therapy, gamma knife surgery and laser interstitial thermal therapies. Although surgical intervention remains the best treatment option for achieving seizure control in drug refractory cases, it is associated with a high risk of postoperative long-term endocrine dysfunction, especially with disconnection surgeries. Newer surgical techniques—including stereotactic radiofrequency thermo-coagulation, gamma knife surgery and laser interstitial thermal therapies—are reported to have better outcomes, though long-term follow-up of such patients is needed to monitor the neurodevelopmental and endocrine functions.[7] Therefore, multidisciplinary care with regular follow up and monitoring is recommended in such cases to make timely decisions based on individual case progress and evolution.[8]

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