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## Case Report

# MR imaging of hypothalamic hamartoma in a patient with gelastic seizures ☆,☆☆

Wan Ahmad Firdaus Wan Chek, MD<sup>a</sup>, Yong Guang Teh, MD, DrRad<sup>a,b,\*</sup>, Dian Noriza Eddy Suryono, MB BCh BAO, MMed(Rad)<sup>a</sup>, Chiak Yot Ng, MBBS, MMed(Rad)<sup>b</sup>, Selim Ahmed, MBBS, FCPS, MPH<sup>b</sup>

<sup>a</sup>Department of Radiology, Sabah Women & Children's Hospital, Kota Kinabalu, Sabah, Malaysia

<sup>b</sup>Faculty of Medicine & Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

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## ABSTRACT

Hypothalamic hamartomas (HHs) are non-neoplastic malformations that occur in the region of the hypothalamus. HH is the leading cause of gelastic seizures in children and adolescents, where laughing is characteristically manifested. However, these patients can also experience different forms of complex or generalized tonic-clonic seizures that can obscure the diagnosis of HHs. We present a case of a 10 year-old boy that experienced several seizure types, but was subsequently diagnosed with HH after MR imaging was performed. This case highlights the complementary role of MR imaging in ascertaining seizure etiology when the clinical history and EEG findings are non-specific. The importance of early diagnosis with MR imaging is further underscored by the fact that patients diagnosed with HH usually develop drug resistance towards antiepileptic drugs, mandating neurosurgical assessment and intervention.

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## Introduction

Hypothalamic hamartomas (HHs) are benign neoplastic malformations that typically occur in the region of the hypothalamus, near the infundibular recess and mammillary bodies. The prevalence of HH is estimated at 1:50000 to 1:100 000 [1]. Young patients usually suffer from gelastic seizures,

precocious puberty, progressive behavioral and cognitive difficulties.

Gelastic seizures are characterized as pressure to laugh. These seizures are typically short in duration (2-30 seconds) and are exceedingly difficult to distinguish from normal laughter in infants and young patients. However, it is not uncommon for young children to also display crying-like behavior instead of laughing (ictal crying or dacrycystic crying) [2]. There are also cases of patients with HH who suffer from

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\* Corresponding author.

E-mail address: [tehyongguang@ums.edu.my](mailto:tehyongguang@ums.edu.my) (Y.G. Teh).

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other types of epileptic episodes such as complex partial and generalized seizures [3].

Obtaining accurate clinical history plays an important role in diagnosing HHs. However, the non-specific and evolving seizure semiology in HH may pose a formidable challenge when endeavoring to establish a diagnosis. The electroencephalogram (EEG), while useful in diagnosing other seizure types, has a limited ability to detect the specific epileptiform activity of HH. As such, MR imaging has an important role in the diagnosis HH especially when the clinical history and EEG findings are equivocal. The importance of MR imaging is further underscored by the fact that patients diagnosed with HH usually develop drug resistance towards antiepileptic drugs which necessitate subsequent neurosurgical assessment and intervention [4].

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## Case Report

A 10 year-old boy presented with fitting episodes for 7 months. The fitting episodes initially manifested as tonic movement of the limbs, and subsequently progressed to generalized tonic-clonic seizures. At the onset, these fitting episode occurred once every two days but gradually became more frequent, reaching a maximum frequency of twice in a day. Due to the increasing frequency of the fits, the boy's parents sought treatment at a local District Hospital. The patient was then referred to a paediatric neurologist for further assessment. During the first visit, the neurologist documented a significant delay in achieving age-appropriate developmental milestones. He was unable to read, write or converse normally. According to his parents, despite attending a special school since he was 6 years old, he was having difficulty with his school work. Otherwise, there was no history of fever or trauma that could be have precipitated the fitting episodes. There was no family history of epilepsy.

On clinical examination, he did not have any neurological deficits and he was able to walk and run normally. His physical appearance was normal and he did not have dysmorphic facial characteristics such as hypertelorism, low sets of ears, or single palmar creases. His height and weight were normal when plotted on a standardized growth chart. EEG showed non-specific, intermittent focal epileptic discharges. The boy was treated as having partial complex seizures and was prescribed two types of anti-epileptic drugs.

MRI brain was performed and revealed a non-enhancing lesion within the third ventricle, with its base sited at the floor of the third ventricle between the mammillary bodies. The lesion was isointense to gray matter on T1- and T2-weighted images (Fig. 1). This lesion projected into the suprasellar cistern, displacing the optic chiasm and pontine cisterns (Fig. 2), suggestive of a sessile-type HH.

Further history was then obtained after the MRI examination. The parents revealed that they had noticed persistent laughing behavior since he was 9 years old, consistent with gelastic seizures. Pre-ictally, the patient would have a brief episode of laughter which then developed into a tonic-clonic seizure lasting for a few seconds. Post-ictally, the boy was

usually drowsy for up to 2-3 minutes. These episodes occurred at random intervals.

Neurosurgical assessment was scheduled to plan further treatment. However, the neurosurgical appointment had to be delayed due to the COVID-19 pandemic. The boy has been on antiepileptic medication while awaiting assessment by the neurosurgical team.

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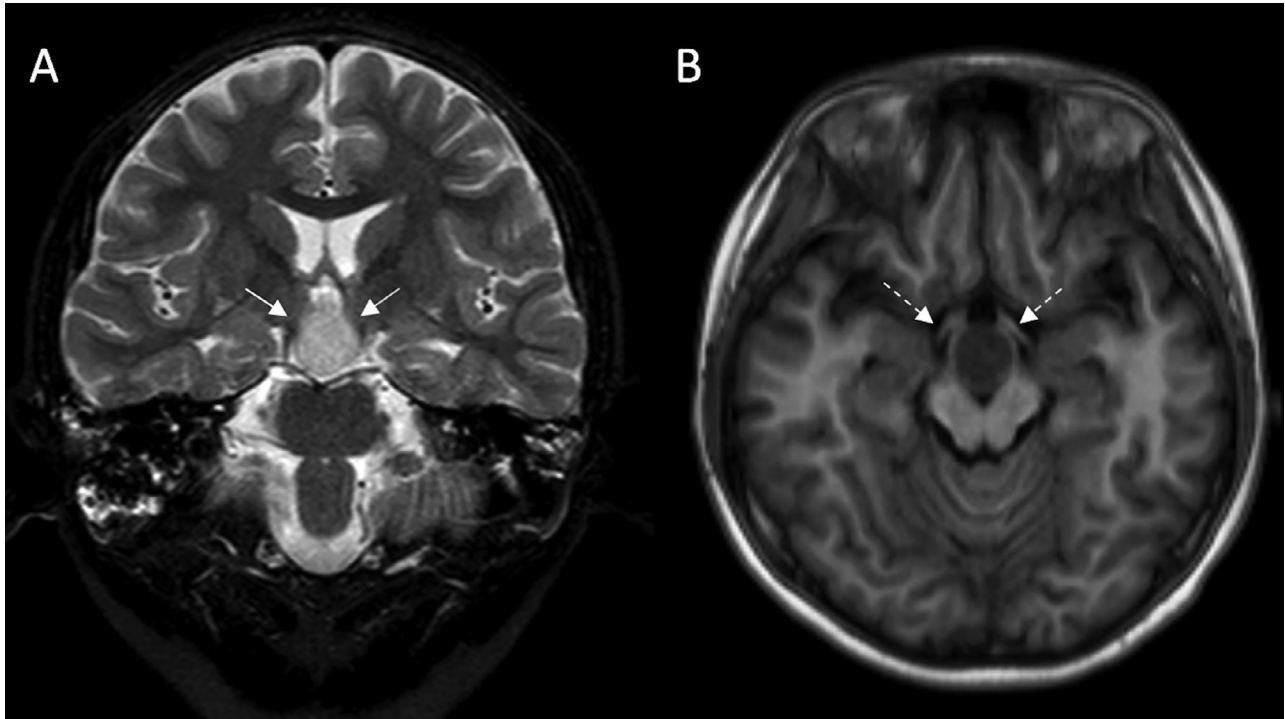
## Discussion

The hypothalamus is a complex structure that contains multiple interconnections between both cerebral frontal cortices and the limbic system. It controls essential functions such as sleep, appetite, body temperature, reproduction, and sexual behavior [2]. HHs are non-neoplastic heterotopias in the brain that usually measure between 0.5 cm to 2.0 cm in diameter [2]. It is typically found at the base of the brain in the third ventricular floor, near the tuber cinereum and the mammillary bodies.

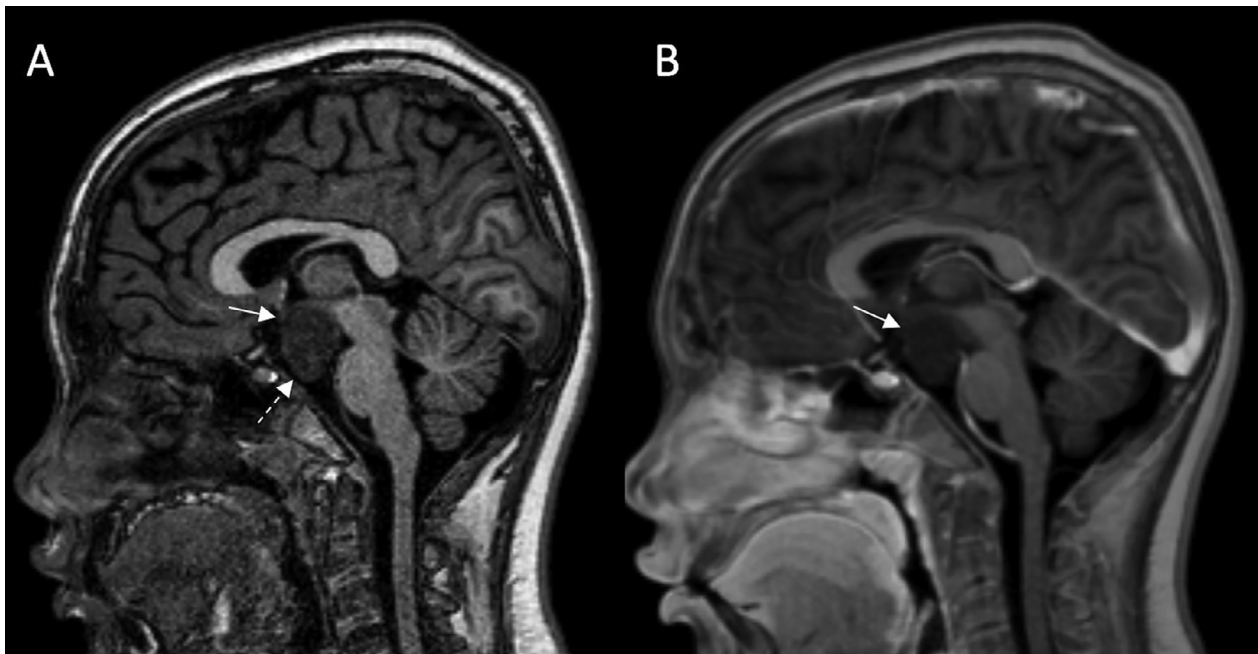
MRI plays a crucial role in differentiating the subtypes of HH and it provides the clinician with detailed anatomical information. The most commonly used classification is morphological, which divides the hamartomas into sessile and pedunculated types [5]. These two subtypes have distinct clinical presentations. Patients with the pedunculated (parahypothalamic) type usually develop precocious puberty between the age of 3 months and 9 years old [5]. No behavioral dysfunction, mental retardation, or other neurological symptoms are seen in this type of HH. Conversely, in the sessile (intrahypothalamic) type, precocious puberty is rarely seen; patients usually develop gelastic or other types of seizures [6].

MRI has been shown to be superior to CT scan in detecting small hamartomas [7]. HHs are uniformly isointense to grey matter on T1-weighted MR images and the lesion demonstrates corresponding homogeneous high signal on T2-weighted images. The hyperintensity demonstrated on T2-weighted images in small hamartomas may result in decreased conspicuity of the hamartoma [7,8,9]. The sagittal plane is important to evaluate the extension through, or displacement, of the floor of the third ventricle, which would enable differentiation of HH subtypes [5]. Sessile HHs have a partial or complete base of attachment that is within the third ventricle. Pedunculated HHs, on the other hand, are attached only to the floor of the third ventricle by a pedicle; the lesion itself is located external to the third ventricle. No enhancement is seen after intravenous administration of gadolinium-based contrast agents in MR studies [9].

Gelastic seizure is the most common seizure semiology that occurs in the sessile type of HH. These seizures are seldom accompanied by altered consciousness in infancy but may alter the consciousness in older patients [5]. It usually presents as a short, stereotypical, and frequent episodes of unprovoked laughter. This automatic laughter is without a sense of joy, and is without loss or reduction in consciousness, and is accompanied by autonomic signs such as tachycardia, respiratory disturbance, facial flushing, and pupil dilatation [2,7]. In some patients, gelastic seizures coexist with involuntary crying, in which the patient begins with whimpering



**Fig. 1 – (A)** T2-weighted coronal image demonstrates a well-defined, lobulated lesion arising from the tuber cinereum and extending into the third ventricle (solid white arrows) with iso- to high signal intensity. **(B)** T1-weighted axial image demonstrates the extension of the lesion into the interpeduncular cistern and it abuts the optic radiation bilaterally (white dashed arrows)



**Fig. 2 – (A)** T1-weighted sagittal image shows the lesion projecting into the suprasellar (solid white arrow) and pre-pontine (dashed white arrow) cisterns. **(B)** Post-contrast sagittal image shows non-enhancing hypothalamic hamartoma (solid white arrow)

that rapidly progresses to crying and orofacial automatism. Additionally, other types of epileptic manifestations, such as complex partial seizures or generalized seizures, can be seen concomitantly [3].

Diagnosing our patient was challenging because the seizure semiology was initially non-specific. The parents did not offer the history of persistent laughing before the MR study because they did not recognise that as abnormal behaviour. They simply thought it was their child's way of expressing pleasure and happiness. The EEG also did not provide additional information in this case. EEG has limited diagnostic sensitivity and specificity due to the deep location of HHs and the complex neuronal connections of HH with adjacent brain tissue [7]. Tissue biopsy is seldom attempted as there is significant risk of subsequent morbidity and neurological deficit [9].

Developmental delay is the commonest presentation in patients with sessile HHs especially when seizures occur at an earlier age [2]. Multiple studies have shown that epilepsy associated with HHs, especially gelastic seizures, are resistant towards anti-epileptic drugs [2]. Patients usually require multiple drugs to control the seizure. In our patient, successful seizure control was achieved with two anti-epileptic agents. Surgical intervention should be considered in patients who develop drug resistance, progressive cognitive impairment, or behavioral problems [4].

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### Patient consent

Written informed consent was obtained from the patient's parent for the publication of this case report.

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### Ethical approval

Not required.

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