Magnetic resonance imaging findings of hypothalamic hamartoma correlated with clinical features

Xiao-Ming Qiu, *MD,* ***Hong Wang,*** *MD,* ***Fei Wei,*** *MD,*
Jian Zheng, *MD, PhD.*

Hypothalamic hamartoma (HH) is a rare congenital malformation composed of a haphazard assembly of neurons. It locates in the mamillary bodies, tuber cinereum, rarely within the hypothalamus itself, which is a well-defined, solitary mass projecting from the base of the brain into the suprasellar and interpeduncular cistern. It usually remains stable in size, increasing over time up to 4 cm in diameter. It mainly occurs in babies <2 years of age.[1] Clinical signs such as central precocious puberty, gelastic seizures, developmental delay, and cognitive deficits are observed. However, gelastic seizures are rarely diagnosed at onset, and may be mistaken by normal laughter or misdiagnosed as infantile colic.[1-3] Despite its rarity, the diagnosis is impeded by "silent" medical imaging mimicking the normal gray matter of the hypothalamus. Familiarity with key MRI features, in addition to clinical findings at presentation, is helpful in developing the differential diagnosis for lesions involving the hypothalamic region. Herein, we described one case of HH in an 8-year-old girl with gelastic seizures to enhance physicians' awareness of this situation.

This patient presented to the neurologists with intermittent gelastic seizures several times per year since age 2. The forced laughing did not provoke the attention of parents and local doctors for the features of transient attack (lasting 30 seconds, full recovery). One month before presentation she developed more frequent attacks of 3-5 fits per month, and had one episode of secondary generalization, which consisted of tonic-clonic movements of extremities and forced upward eye deviation for 1-2 minutes. Physical examination and neuropsychiatric examination were not noteworthy. The laboratory studies including the endocrine profile were unremarkable. Radiographic bone age was consistent with that of a girl 8 years old. Ictal EEG findings included discharges originating in the fronto-temporal regions or bilateral synchronous generalized slow waves. During drowsiness or sleeping, bilateral generalized spike and wave activity were recorded.

A homogeneous isodense suprasellar nodular mass was disclosed in the axial non-enhanced CT imaging. The mass was approximately 1.5 cm x 1 cm, and MR imaging demonstrated a sessile mass of the posterior hypothalamus arising from the region of the tuber cinereum and joining mainly in the left mammillary body. Its signal intensity was generally homogeneous and isointense relative to gray matter on T1-weighted images (T1WI), and slightly hyper-intense on T2-weighted images (T2WI) with a fluid-attenuated inversion recovery (FLAIR) sequence. The lesion did not gain enhancement on T1WI following intravenous contrast injection (**Figure 1**). It was diagnosed as HH.

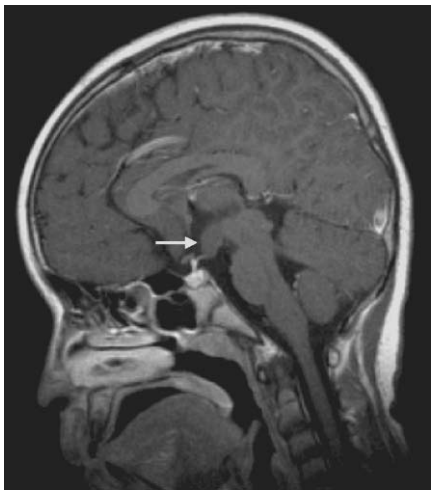

Figure 1 - The sagittal T1-weighted image showing no enhancement of nodular mass posterior to the enhancing pituitary gland and stalk in the suprasellar region (arrow).

Hypothalamic hamartoma can be asymptomatic, which has been confirmed by autopsy. Symptomatic HH is associated with the triad of precocious puberty, gelastic seizures, and developmental delay. The true iso-sexual precocious puberty is the most frequent clinical sign, which did not occur in this girl. The associated features include larger hamartoma size and contact with the pituitary stalk. Hypotheses on true precocious puberty include stimulation of anterior hypothalamus, mechanical interference with the posterior hypothalamus or release of luteinizing hormone-releasing hormone.[1]

Gelastic seizures may be the only initial presenting feature, as in our patient, with an uncoupling of emotional experience from the expression of affect during the ictal phase. They are progressive, commencing in infancy, deteriorating into a more complex seizure disorder resulting in intractable epilepsy. Patients may experience several types of seizures including gelastic, dacrystic, complex partial seizures, generalized tonic-clonic seizures, drop attacks, and infantile spasms. A pedunculated, parahypothalamic HH may not present with seizures, but only with precocious puberty, while the sessile or intrahypothalamic HH is apt to have gelastic seizures as indicated in our patient. Electrophysiological and pathophysiological studies have confirmed the intrinsic epileptogenicity of the HH and propagation from the HH through the fornix to the temporal-frontal lobes.[1-3] Progressive cognitive deficits,

and important psychiatric comorbidity were described in patients with HH. Seizure severity and frequency correlated with severity of cognitive deficits.[1-3] In our patient, the secondary generalized epilepsy seemed not to have deteriorated her cognition and memory.

Around 5% of HH cases are associated with Pallister-Hall syndrome, a rare developmental disorder marked by a spectrum of features ranging from mild extra fingers or toes to severe laryngotracheal cleft. Other permanent neurological deficits are observed with hemiparesis and partial unilateral third nerve paresis. The manifestations caused by pressure on the surrounding structures include hydrocephalus, visual disturbances, pituitary hormonal deficiency, and a rare diencephalic syndrome (failure to thrive, vomiting, and emaciation).[1] None of these occurred in our patient.

A well-defined round pedunculated or sessile mass suspended from the tuber cinereum/mamillary bodies, isointense on T1WI and iso-/slightly hyperintense on T2WI (imaging characteristics of gray matter), and no gadolinium-enhancement is the signature MR imaging indicator of HH. Such findings associated with clinical features allow differentiation of HH from other suprasellar and sellar neoplastic entities. The isointensity helps differentiate HH from gliomas, metastases, and encephalitis, all of which are hypointense on T1WI and hyperintense on T2WI. Classically, the characteristic of no gadolinium-enhancement distinguishes HH from craniopharyngioma (irregular enhancement with cystic and solid components, and calcifications, accounting for approximately 50% of suprasellar masses in children), hypothalamic gliomas (moderately heterogeneous enhancement, occurring in approximately one tenth of children with neurofibromatosis), and sarcoidosis (leptomeningeal enhancement with multiple foci of parenchymal enhancement). It also helps differentiate HH from germinomas and suprasellar meningiomas, both of which are near isointensity relative to the brain, but have a homogeneous enhancement. A thickened infundibulum enhancement is demonstrated in the germ cell tumors, lymphocytic hypophysitis, and Langerhans cell histiocytosis granulomas. Other dynamic typical features and enhancement patterns may appear in hemangioblastomas, adenohypophysitis and all kinds of cysts. Imaging with a FLAIR sequence depicts the lesions with fluid-like contents such as arachnoid or epidermoid cysts. In general, most of these lesions are more anteriorly located than the tuber cinereum hamartomas. If they extend into post-chiasmatic and interpeduncular cisterns, the suprasellar components usually are so large that structural changes warrant a diagnosis of suprasellar lesions with posterior extension, rather than HH.[4,5]

In management of HH, MR imaging is the most precise method of detecting HH for the superior details over CT. Careful examination of location and the symptom-time sequence provides anatomical-clinical correlations, and is even determinative of the diagnosis. In our patient, subtotal removal of the hypothalamus was carried out, and the intractable epilepsy stopped. Early control of HH may cease the development of serious symptoms including cognitive deficits and poor quality of life.

In conclusion, physicians should be aware of this rare but important disease, particularly in patients with gelastic seizures and a suprasellar mass.

Received 14th March 2010. Accepted 20th April 2010.

From the Department of Radiology (Qiu, Wang), the Huangshi Center Hospital, and the Department of Neurology (Wei, Zheng), Xinqiao Hospital, Third Military Medical University, Chongqing, China. Address correspondence and reprint requests to: Dr. Fei Wei, Xinqiao Street, District Shapingba, Chongqing, 400038, P.R. China. Tel. +86 (023) 68774642. Fax: +86 (023) 65317511. E-mail: fei.wei@gmail.com

References

1. Arita K, Kurisu K, Kiura Y, Iida K, Otsubo H. Hypothalamic hamartoma. ***Neurol Med Chir (Tokyo)*** 2005; 45: 221-231.
2. Téllez-Zenteno JF, Serrano-Almeida C, Moien-Afshari F. Gelastic seizures associated with hypothalamic hamartomas. An update in the clinical presentation, diagnosis and treatment. ***Neuropsychiatr Dis Treat*** 2008; 4: 1021-1031.
3. Castro LH, Ferreira LK, Teles LR, Jorge CL, Arantes PR, Ono CR, et al. Epilepsy syndromes associated with hypothalamic hamartomas. ***Seizure*** 2007; 16: 50-58.
4. Freeman JL, Coleman LT, Wellard RM, Kean MJ, Rosenfeld JV, Jackson GD, et al. MR imaging and spectroscopic study of epileptogenic hypothalamic hamartomas: analysis of 72 cases. ***AJNR Am J Neuroradiol*** 2004; 25: 450-462.
5. Saleem SN, Said AH, Lee DH. Lesions of the hypothalamus: MR imaging diagnostic features. ***Radiographics*** 2007; 27: 1087-1108.