



Research Article

Clinical Manifestations and MR Imaging Features In Hypothalamic Hamartomas

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Summary

Hypothalamic hamartomas (HH) are rare non-neoplastic congenital malformations. The aims of this study are to demonstrate the brain MR findings and clinical manifestations in children with HH and the literature is reviewed. We have evaluated 6 children with HH diagnosed by brain MR imaging. We analyzed age at seizure onset, seizure types, neuropsychological assessment, and the presence of precocious puberty, electroencephalogram and MR findings. Among 6 HH patients, 2 manifested precocious puberty, 2 had experienced seizures, and 1 presented with both precocious puberty and seizures, and 1 presented with hyperactivity. MR imaging showed hypothalamic mass that was isointense to brain parenchyma on T1- weighted images and isointense-or hyperintense on T2-weighted images, without contrast enhancement. The size of the lesions does not change in the course of follow-up. Typical clinical presentation, peculiar location and MR imaging features strongly favour the HH diagnosis. Accurate diagnosis and classification is important for the selection of treatment modality.

Key words: Hypothalamic hamartoma, MR imaging, gelastic seizure, precocious puberty

Hipotalamik Hamartomların Klinik ve MR Görüntüleme Özellikleri

Özet

Hipotalamik hamartomlar nadir izlenen neoplazik olmayan konjenital malformasyonlardır. Bu çalışmanın amacı hipotalamik hamartomların klinik özelliklerini ve beyin MR bulgularını literatür bilgileri ışığında değerlendirmektir. Beyin MR tetkikinde hipotalamik hamartom tanısı alan 6 olgu değerlendirildi. Olguların nöbet başlangıç yaşı, nöbet tipleri, nöropsikolojik değerlendirmeleri, puberte prekoks varlığı, EEG ve MR bulguları değerlendirildi. Olguların 2' si puberte prekoks, 2' si nöbet, 1'i hem nöbet hem de puberte prekoks ve 1 olgu hiperaktivite kliniğiyle başvurdu. T1 ağırlıklı beyin MR görüntülerde beyin parankimiyle izointens, T2 ağırlıklı görüntülerde parankimle izo-hiperintens olarak izlenen ve kontrast tutulumu göstermeyen hipotalamik kitleler saptandı. Tanımlanan lezyonların takip MR değerlendirmesinde boyut ya da morfolojik değişiklik saptanmadı. Tipik klinik prezantasyonu, lokalizasyonu ve MR özellikleriyle hipotalamik hamartom tanısı kolaylıkla konabilir. Hipotalamik hamartomları doğru tanımlamak ve sınıflandırmak tedavinin belirlenmesinde önemlidir.

Anahtar Kelimeler: Hipotalamik Hamartom, MR görüntüleme, Gelastik Nöbet, Puberte prekoks

INTRODUCTION

Hypothalamic hamartomas (HH) are rare congenital, nonneoplastic heterotopias. The characteristic clinical symptoms are precocious puberty (PP), gelastic seizure, cognitive and behavioral abnormalities. The diagnosis of HH is based on the typical MR findings. To emphasize

characteristic clinical and radiologic findings of this rare entity, we present the 6 patients with HH.

CASE PRESENTATION

The clinical and MR findings of the patients are summarized Table 1.

Table1: Clinical features and MR findings

Patients	1	2	3	4	5	6
Age/gender	7yrs/G	7yrs/B	2.5yrs/G	1.5yrs/B	7yrs/B	15yrs/B
Age at seizure onset	2yrs	-	-		7 yrs	2yrs
Seizure type	GTC	-	-	-	GTC	Gel, GTC
PP onset years	7yrs		2.5yrs	1.5yrs		
HH size	<1cm	<1cm	<1cm	<1cm	<1cm	>1cm
Cognitive function (IQ)*		Average				low average
Behavioral symptoms		ADHD				
T2 signal intensity	iso	iso	iso	hyper	iso	hyper
T1 signal intensity	iso	iso	iso	iso	iso	iso
Contrast enhancement	no	no	no	no	no	no
Follow-up MR	no change					

G, girl; B, boy; Gel, gelastic seizure; GTC, Generalized tonic-clonic seizure; PP, Precocious puberty; HH, hypothalamic hamartoma; ADHD, attention-deficit/hyperactivity disorder; *Wechsler Intelligence Scale for Children; average: 90-109; low average 80-89.

Case 1

A 7 –year-old girl presented with growth of breasts and beginning of menarche and seizures. Physical examination revealed mild enlargement of breasts, pubic hair, and prominent labia. Endocrinological studies confirmed central PP. Bone age was consistent with that of a girl 10 years old. Abdominal ultrasonography revealed that the uterus and ovaries had peripubertal

morphology. The patient had generalized tonic-clonic seizures. Seizure frequency was four per year. EEG findings consisted of epileptiform spike discharges primarily in the temporal areas. MR imaging of the brain showed a pedunculated hypothalamic mass arising from the tuber cinereum that was isointense to brain parenchyma on both T1- and T2-weighted images, 1 cm in diameter. No contrast enhancement was

seen postcontrast images (Figure 1a, b). Coronal CT of the skull base showed large craniopharyngeal canal. The patient was started on a gonadotropin-releasing hormone analogue, after which there was regression of the pubertal development. Over the following years, puberty

remained under control and the patient grew up normally. Good seizure control obtained with anticonvulsant medications. A follow up MRI after 3 years did not show any obvious change in the size or the morphology of lesion.

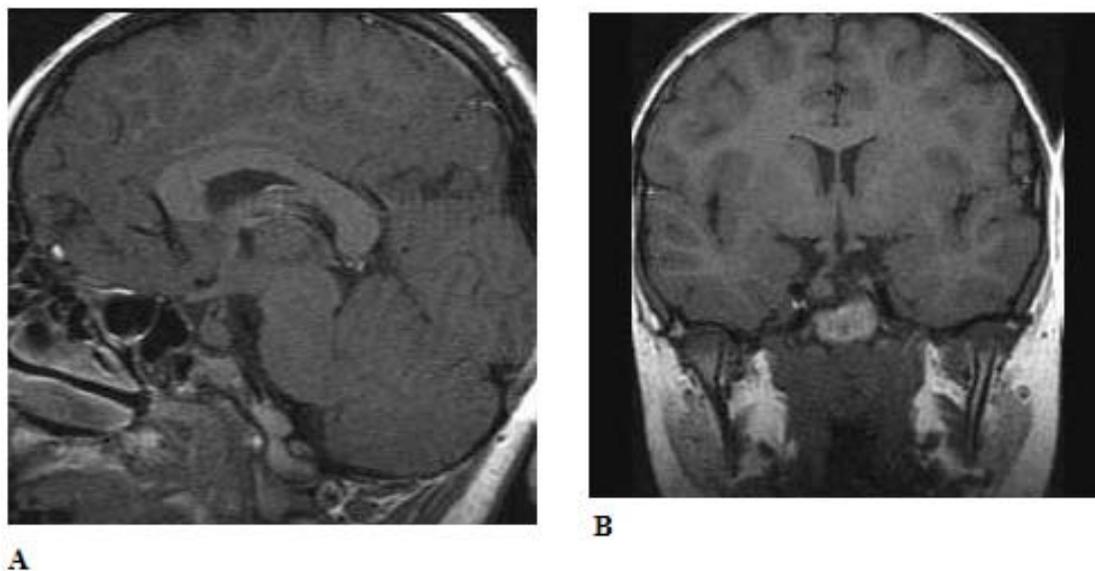


Fig 1: Sagittal (a) and coronal (b) T1-weighted image show small pedunculated hypothalamic mass arising from the tuber cinereum with suprasellar extension.

Case 2

A 7-year-old boy presented with attention-deficit/hyperactivity disorder, and aggression. No anomaly was detected on physical examination. He had no history of seizures and PP. Neurological examination was normal. IQ testing was showed normal cognitive function. An EEG finding was normal. MR imaging of the brain showed a sessile hypothalamic mass that was isointense to brain parenchyma on both T1- and T2-weighted images, < 1 cm in diameter. The mass was not enhanced after intravenous gadolinium injection. Patient was received psychotropic medication. A follow up MRI after 3 years did not show any obvious change in the size or the morphology of lesion.

Case 3

A 2.5-year-old girl presented with somatic advance. Bone age was consistent with that

of a girl 5 years old. Serum levels of sexual hormones were detected the levels of puberty. Neurological examination was normal. MR imaging of the brain showed a pedunculated mass arising from the tuber cinereum that was isointense to brain parenchyma on both T1- and T2-weighted images, <1 cm in diameter, there is no contrast enhancement. Patient responded well to medical management with gonadotropin-releasing hormone analogue. A follow up MRI after 3 years did not show any obvious change in the lesion.

Case 4

A 1.5-year-old boy presented with pubic hair and an enlarged penis. Endocrinological studies confirmed central PP. MR imaging of the brain showed a sessile mass arising from the hypothalamus that was isointense to brain parenchyma on T1-weighted images, <1 cm in diameter,

without contrast enhancement (Figure 2). The lesion appeared hyperintense on T2-weighted imaging. PP was controlled by medical treatment with gonadotropin-releasing hormone analog. MRI after 1 year did not show any obvious change in the lesion.

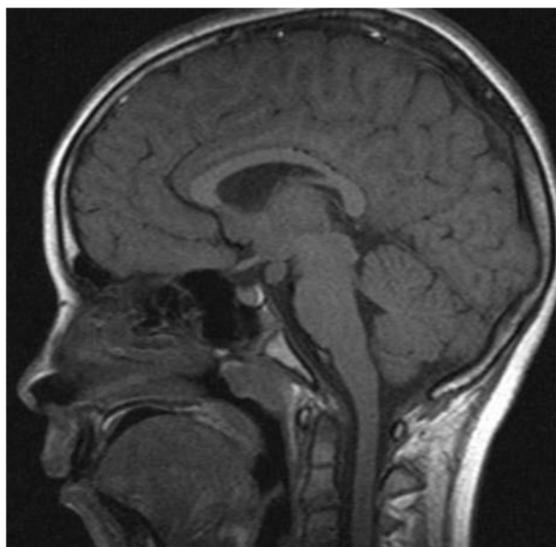


Fig 2: Sagittal T1-weighted image show sessile small hypothalamic mass arising from the mamiller body that was isointense to brain parenchyma. Note no distortion of third ventricle and hypothalamus.

Case 5

A 7 -year-old boy presented with hypertensive encephalopathy and seizure. He had chronic renal disease. Clinically his sexual characters were well ahead of those expected for his age. His interictal EEG finding was normal. MR imaging of the brain showed sessile mass arising from the tuber cinereum that was isointense to brain parenchyma on both T1- and T2-weighted images, <1 cm in diameter, lack of contrast enhancement. Seizure was controlled by medical treatment. A follow up MRI after 1 year did not show any obvious change in the lesion.

Case 6

A 15 -year-old boy presented with generalized tonic clonic seizures. Seizure frequency was one per week. Past history

revealed gelastic seizure at the age of two years. Later on, seizures became generalized. EEG findings consisted of generalized epileptiform spike discharges. He had mild cognitive function impairment. MR imaging of the brain showed sessile hypothalamic mass that was isointense to brain parenchyma on T1-weighted images, with interpeduncular, prepontine, and suprasellar extension, >1 cm in diameter, lack of contrast enhancement. The lesion appeared hyperintense on T2-weighted imaging (Figure 3). Patient was referred to an other center for surgical therapy, because of medically refractory seizure.

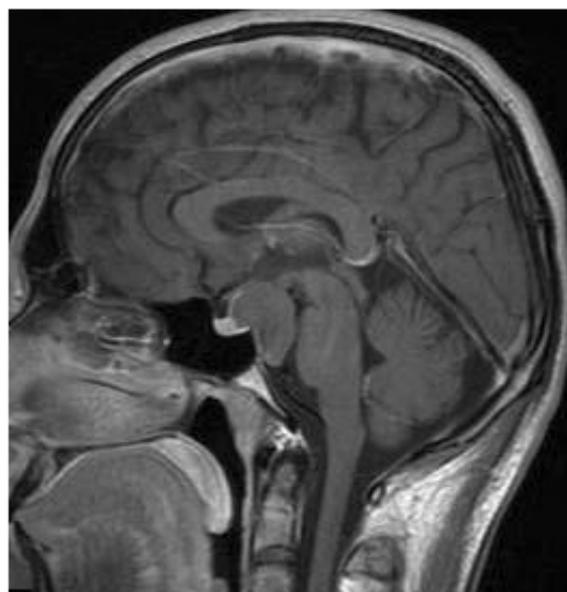


Fig 3: Postcontrast sagittal T1-weighted image show large sessile hypothalamic mass with suprasellar, interpeduncular and prepontine extention.

DISCUSSION

Hypothalamic hamartomas are relatively rare, non-neoplastic congenital malformations. They may be pedunculated, attached to the tuber cinereum or the mamillary bodies by a thin stalk, or sessile, presenting as a mass within the hypothalamus. The histologic composition of these hamartomas has been described as

consisting of neurons similar in appearance to hypothalamic neurons⁽⁶⁾.

The most common presenting symptom is isosexual PP and HH are the most common cause of central PP⁽¹⁷⁾. Precocious puberty is defined as true puberty with onset before 8 years in girls and 9 years in boys. It is relatively common in girls in whom it is usually idiopathic, and uncommon in boys in whom there is a much higher chance of finding pathology. Several studies found that children with organic lesions started their puberty earlier, more rapid advancement of pubertal signs, and had higher LH and FSH peaks compared to those with idiopathic PP^(15,8).

Seizure is the main neurologic manifestation of HH and gelastic seizures beginning early in life are the classical epileptic presentation. Gelastic seizures are epileptic events characteristic by bouts of laughter and they are rarely diagnosed at onset. They may be mistaken for normal laughter and or misdiagnosed as infantile colic. The interictal and ictal EEG is often normal⁽⁴⁾. In a proportion of patients, there is a progression through other partial seizure types to a generalized epileptic encephalopathy.

Interictal electroencephalogram may be normal in early phases, and then interictal spikes (temporal or frontal) followed by multifocal independent spikes and finally slow spike waves⁽⁷⁾.

Children with HH and seizures had high rates of the cognitive and behavioral disorders, including oppositional defiant disorder, attention-deficit/hyperactivity disorder, conduct disorder, speech retardation/learning impairment, and anxiety and mood disorders⁽²⁴⁾. Multiple factors may be contributed to the cognitive and behavioral disorders of children with HH. Although a predominant opinion is a direct effect of their seizure activity, disturbances of the hypothalamus theoretically could lead to series of cognitive and behavioral disorders⁽¹⁸⁾. Developmental delays correlate with

severity, frequency, and variety of the seizure patterns⁽⁴⁾.

HH may occur either as an isolated sporadic lesion, or may be with other anomalies, most commonly in the Pallister-Hall syndrome (PHS). PHS is characterized by HH, central polydactyly, and other abnormalities including imperforate anus, bifid epiglottis, and panhypopituitarism⁽¹²⁾. Patients with PHS-associated hamartomas may respond more readily to antiepileptic medications and rarely need surgical intervention⁽²¹⁾.

Computed tomography is not sensitive to the presence of the small HH. MRI is the study of choice for patients with clinical suspicion of HH. These lesions have typically been described as isointense to gray matter on T2-weighted and T1-weighted images, though more recent sources describe T2 hyperintensity⁽²¹⁾. More recent studies using short TE spectroscopic sequences have found an increase in myoinositol in addition to the N-acetylaspartate reduction. Elevation of myoinositol can also be seen in some cases of low-grade glioma, even without associated elevation in choline. Thus, spectral signature alone cannot reliably differentiate HH from glioma⁽²⁾. The diagnosis of HH is based on the characteristic location, isointensity to normal brain, lack of contrast enhancement of the solid portion of the mass, the absence of hemorrhage and calcification and absence of change in size and morphology of the mass at the follow-up. The association of HH and large craniopharyngeal canal has been reported^(11,14). All our patients showed a pedunculated-or sessile hypothalamic mass arising from the tuber cinereum or mamillary body that was isointense to brain parenchyma on T1- and isointense-or hyperintense on T2-weighted images without contrast enhancement. Follow-up MR in all our patients showed no change in size and morphology of the mass.

Differential diagnosis of HH may include craniopharyngioma, optic-hypothalamic glioma, Rathke cleft cyst and germinomas. These tumors have heterogeneous signal intensity and often show contrast enhancement⁽²¹⁾.

Classification of the HH is important for the management of the treatment a correlation with the clinical presentation and accurate prediction of their prognosis. Several different classifications of hypothalamic hamartoma have been proposed according to the topographic and clinical data^(6,3,9,10). Several factors contribute to the classification of hamartoma, such as the size, pedunculated or sessile, the anatomical relationship between the hamartoma and the adjacent hypothalamus and third ventricle. The pedunculated type and <1 cm size of lesion is more likely to be associated with PP, and the sessile type and >1 cm is often associated with gelastic seizures. In our series, 2 patients was found <1 cm and pedunculated HH, 3 patients had <1cm and sessile HH, and 1 patients had > 1cm and sessile HH.

Treatment options for PP associated with HH may be surgical or medical. Surgical excision of hamartoma in young children is recommended, whereas in children close to puberty, no surgical treatment is required. Medical treatment includes use of a long-acting GnRH analogue or antagonists until puberty. PP is generally controlled safely and effectively by GnRH agonist treatment^(1,9). Our patients with PP responded well to medical management.

Although there are very few reports of good seizure control obtained with various anticonvulsant medications, it is generally accepted that the gelastic seizures associated with HH are refractory to medical treatment⁽¹³⁾. Several studies have demonstrated that HH has an intrinsic epileptogenicity and that the epileptic discharges spread from the hamartoma^(16,22). Early surgical intervention is consequently recommended

in an attempt to minimize or prevent the cognitive and behavioral sequels of epileptic syndrome. Multiple treatment options are available for patients with medically uncontrolled seizures including the open surgical resection, endoscopic resection, or disconnection, radio-frequency ablation, interstitial radiosurgery, and gamma knife radiosurgery (GKS). The choice of treatment must be individualized depending on the age, the size, location, attachment, and effect of the lesion on the hypothalamus, the severity of the epilepsy, and of the cognitive/psychiatric comorbidity. Many reports of surgical cases pointed out that total or near-total resection was very important to control the seizures. The transcallosal resection of HH is an effective and safe treatment, but there is a small risk of short-term memory impairment. Gamma knife radiosurgery using higher marginal doses can be an effective and safe alternative treatment modality for HH, and is capable of achieving good seizure control and improving behavioral disorders. To date no serious complications have been reported. However, it should be remembered that higher marginal doses might injure critical surrounding structures (most important, the optic tracts). Additionally, the therapeutic effect of GKS is known to be delayed. A patient with a large HH is better suited to open surgery. The endoscopic approach is an alternative for smaller HH. An adolescent or adult HH patient with milder epilepsy and intact cognition would be better suited to GKS. A patient with a residual HH after respective surgery and ongoing epilepsy may be suited to the gamma knife^(19,20,22).

CONCLUSION

Due to advances in MR imaging, the number of cases of HH has been on the rise. Typical clinical presentation, peculiar location and MRI features strongly favour the diagnosis of HH diagnosis. Accurate diagnosis and classification is important

for the selection of treatment modality. Effective and early treatment led to the improvement or cessation of seizures and prevent the decline in their cognitive abilities and better quality of life for HH patients.

Acknowledgments

We thank Huseyin Durmaz, for their assistance with the neuropsychological assessment.

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Received by: 22 August 2008

Revised by: 22 September 2008

Accepted: 16 October 2008

The Online Journal of Neurological Sciences (Turkish) 1984-2009

This e-journal is run by Ege University Faculty of Medicine, Dept. of Neurological Surgery, Bornova, Izmir-35100TR as part of the Ege Neurological Surgery World Wide Web service.

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E-mail: editor@jns.dergisi.org

URL: <http://www.jns.dergisi.org>

Journal of Neurological Sciences (Turkish)

Abbr: J. Neurol. Sci.[Turk]

ISSNe 1302-1664

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