Giant Hypothalamic Hamartoma Treated with Thermocoagulation: A Case Report and Literature Review

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บทคัดย่อ

ไฮโปธาลามิกฮามาร์โตมาเป็นพยาธิสภาพที่เป็นมาแต่กำเนิดซึ่งผู้ป่วยมักมาด้วยอาการชักเชาว์ปัญญาผิดปกติและเข้าสู่วัยหนุ่มสาวก่อนก่อนกำหนด โดยที่การชักมักเป็นชนิด gelastic ซึ่ง เป็นลักษณะเด่นของพยาธิสภาพชนิดนี้และการตรวจโดย electroencephalogram มักยืนยันว่าการชักกำเนิดมาจากก้อนไฮโปธาลามิกฮามาร์โตมา

ทางเลือกหนึ่งสำหรับผู้ป่วยชักที่ดื้อยาคือการรักษาด้วยการผ่าตัดโดยที่แนวทางการผ่าตัดพิจารณาจากขนาดและตำแหน่งของฮามาร์โตมาเป็นสำคัญ ไฮโปธาลามิกฮามาร์โตมาจัดเป็นขนาดยักษ์ เมื่อมีขนาดมากกว่า 3 เซนติเมตรซึ่งโดยส่วนใหญ่มักไม่สามารถผ่าตัดออกได้หมด ในบทความนี้ผู้เขียนรายงานเด็กหญิงอายุ 5 ขวบซึ่งมาด้วย gelastic seizure ที่ดื้อต่อยาและ การตรวจเครื่องสะท้อนสนามแม่เหล็ก พบฮามาร์โตมาขนาด 37 × 27 × 23 มิลลิเมตร ซึ่งได้รับการรักษาด้วยการจี้ด้วย radiofrequency thermocoagulation หลังผ่าตัดผู้ป่วยอาการชักลดลง 90% บทความนี้ยังได้นำเสนอการผ่าตัดชนิดต่างๆที่ใช้ในการรักษาไฮโปธาลามิกฮามาร์โตด้วย

Abstract

Hypothalamic hamartomas (HH) is a rare congenital nonneoplastic developmental lesion which often presents with intractable seizure, cognitive impairment, precoccious puberty and delay development. Gelastic seizure is the hallmark and epileptiform discharges are electrographically confirmed to originate within the hamartoma[1]. Surgical intervention for complete removal or disconnection is typically needed for seizure control. Size and anatomical features of HH play an important role for surgical considerations.

Giant hypothalamic hamartomas (GHH) are defined when their dimensions exceed 30 mm^2. Most of them are unable to be completely resected. Authors present a case of a 5-year-old girl with intractable gelastic seizure. Magnetic resonance imaging (MRI) of the brain revealed 37 x 27 x 23 mm giant hypothalamic hamartoma. Post stereotactic radiofrequency thermocoagulation, the patient had 90% seizure reduction. Review literature of various surgical interventions of HH is also presented.

Introduction

Hypothalamic hamartoma (HH) is a rare congenital nonneoplastic developmental lesion composed of ectopically located normal neurons and glia, resembling the normal hypothalamus[3]. The estimated incidence is 1 per 50,000 to 100,000[4]. Patients with HH often present with intractable seizure, central precocious puberty and cognitive impairment. Gelastic seizures are the hallmark and HH is likely to be diagnosed in the early childhood. The seizures are generally refractory to standard medical treatments.

Surgical removal of the lesion has been reported to be effective treatment to control the seizure but could potentially damage hypothalamus and cranial nerves especially in giant hypothalamic hamartoma[5]. The average size of HH ranges from 17.9-18 mm and when their dimensions exceed 30 mm, they are classified as giant hypothalamic hamartoma (GHH)[6].

Authors present a case of giant HH treated by stereotactic radiofrequency thermocoagulation and literature review.

Case report

A 5-year-old girl presented with gelastic seizure which began at the age of 4 months. She was normally delivered at term but had respiratory distress (APGAR 5-7-8) which was diagnosed as transient tachypnea of newborn (TTNB). She also had developmental delay after the age of 4 months. She has been having 40 gelastic seizures per day even after being treated with multiple antiepileptic drugs. Electroencephalogram revealed normal awake and sleep patterns. Brain MRI showed a well-defined intra axial mass (37 x 27 x 23 mm) occupying suprasellar and interpeduncular cisterns originated from inferior wall of the third ventricle. The mass showed iso-signal intensity on T1WI and hyper signal intensity on T2WI without enhancement on postcontrast images.

Due to its size and adherence to the surrounding structures of GHH, stereotactic radiofrequency thermocoagulation was considered for controlling intractable seizure (Figure 1). The 18 thermocoagulation targets under Leksell frame-based stereotactic guidance was performed by heating of the tip for 60 seconds at 74-76 degree celsius. After treatment, 90% seizure reduction was achieved without complication. HH size decreased from 37 x 27 x 23 mm to 29 x 18 x 15 mm (Figure 2).

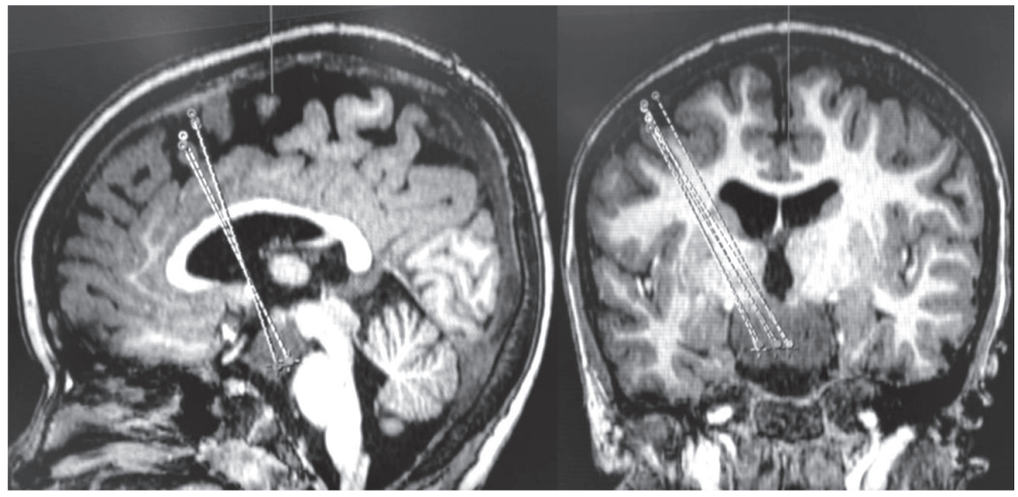

Figure 1: Stereotactic radiofrequency planning.

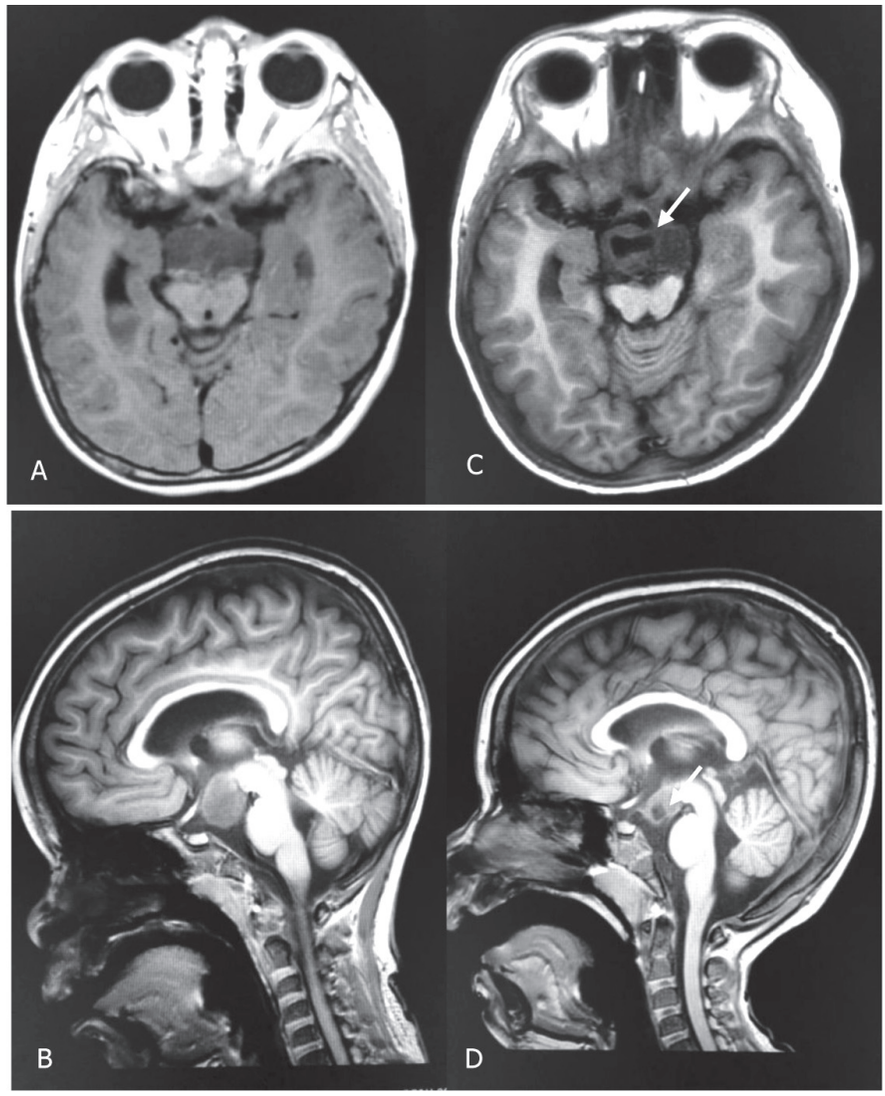

Figure 2 A, B) T1WI pre and C,D post radiofrequency thermoablation. Note treatment cavity on the right side of HH (arrow)

Discussion

The term "hamartoma" derives from the Geek word "hamartia" which means mistake or error. It was first used in 1904 by Eugen Albrecht and later Willis used this term to define congenital noneoplastic developmental lesions that are normal in structure but ectopic in location[3].

Most of the sporadic HH cases present with various types of seizure in 61% (92% had Gelastic seizure), central precocious puberty (CPP) in 63%, and developmental delay in 49% of 277 cases reported since 1950. All of developmental delay patients suffered from seizure and 25% of patients had both CPP and seizures[4].

In the review of 11 GHHs by Alves et al, 63.6% of the patients had seizure similar to non-giant HHs but only 36.3% had precocious puberty. The lower incidence of precocious puberty in GHH is most likely due to predilection of intrahypothalamic subtype[6].

The anatomic relationship of HH and surrounding structures can be divided into parahypothalamic subtype which is attached to the floor of the third ventricle with a short or broad base without third ventricular displacement. Precocious puberty without seizure and

developmental delay often occurs in this subtype. Another subtype is intrahypothalamic which is embedded in the hypothalamus with third ventricular displacement. This subtype is associated with seizure and developmental delay[7].

HH typically presents by constellation of clinical features including gelastic seizure, central precocious puberty (CPP), developmental delay. Scalp electroencephalogram (EEG) shows no change in majority of the gelastic seizure. Brain MRI usually shows hyperintense on T2 weight image (93%), hypointense on T1 weight image(74%) and 100% is not enhanced by contrast[8].

Delalande and Fohlen[11] classified HH into 4 types for determining surgical approach. Type I: Parahypothalamic type (Horizontal or lateral orientation to hypothalamus without intraventricular component). Type II : Intrahypothalamic type (Vertical orientation with intraventricular extension). Type III: combined type I and type II, Type: IV : Giant hamartoma (picture 3)

In this report HH was classified as type IV Giant HH (size 35 x 25 mm) which involved hypothalamus, 3rd ventricle and basal cistern. Therefore, complete surgical resection could not be achieved without complication, and as a result, stereotactic radio frequency thermocoagulation was considered.

Gelastic seizures and other types of seizure from HH are often refractory to medical treatment whereas precocious puberty can be successfully treated with gonadotropin releasing hormone analog (GnRH). Recent evidence from functional MRI and intracranial EEG suggest that seizures originate in the hamartoma, in contrast to the previous theories[1,9]. Prolong intractable seizure may cause epileptic encephalopathy but from the recent data, HH is believed to be one of the causes of reversible epileptic encephalopathy. Surgi-

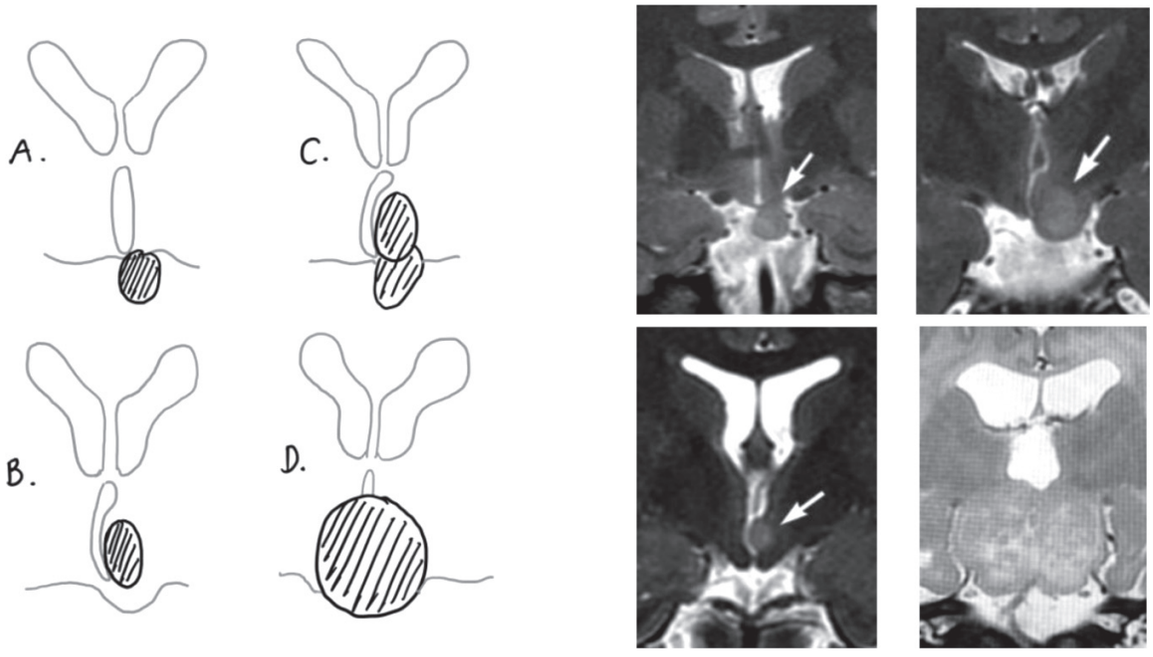

Figure 3 Delalande and Fohlen classification for determining surgical approach (A) type I: parahypothalamic type, (B) type II: Intrahypothalamic type with intraventricular extension, (C) Type III: Combined type I and II, (D)Type IV: Giant type

Table 1 Comparison of surgical interventions

Treatment modality	Number of studies (Number of patients)	Seizure free (%)	Seizure reduction (%)	Cognitive improvement (%)	Memory deficit (%)	Focal neurodeficit (%)	Endocrine deficit (%)
TAIF	5(72)	59	37	52	23	5.5	41
Endoscopic surgery	6(122)	37.7	28.6	9	7	9	29
Pterional, Translamina terminalis, OZ	11(48)	27	52	54	0	18	10.4
GKS	10(81)	28	59	56	1.2	1.2	0
SRT	5(33)	69	30	78	6	0	36
SLA	5(21)	57	38	4.7	9.5	0	4.7
VNS	3(26)	0	57	69	0	0	0

TAIF: Transcallosal anterior interforniceal approach, GKS: Gamma knife surgery, OZ: Orbitozygomatic, SRT: Stereotactic radio frequency thermocoagulation, SLA: Stereotactic laser ablation, VNS: Vagus nerve stimulation.

Table 2 Comparison of various surgical interventions

Treatment modality	Advantage	Disadvantage
TAIF	– complete resection: Most likely for intrahypothalamic and ventricular extension type (type II, III)	– Memory deficit – Invasive
Endoscopic	– Useful for type II, III	– Less memory deficit – Complete resection: Less likely
Pterional, OZ,	– Useful for type I, III	– Higher rate of focal neurodeficit
Translamina terminalis	– Complete resection: Less likely – No memory deficit	
GKS	– Minimally invasive – Useful for inoperable case, Type IV	– Delayed onset of action – Transient effect – Less likely to achieve seizure freedom
SRT	– Minimally invasive – Useful for Type IV	– Transient symptoms from localized edema
VNS	– Useful for inoperable case – Not achieve seizure free	– Expensive and need long term maintenance

cal resection is effective not only in seizure control but also in reversal of cognitive dysfunction[5,10]

Main goal of surgical treatment is to remove or disconnect hamartoma from the hypothalamus and mammillary body. Disconnection may be sufficient for seizure control but no study has compared directly between complete removal and disconnection[8].

Approach for surgical resection can be divided into 2 types

1. Top-down operation: Transcallosal anterior interforniceal approach(TAIF) and endoscopic transventricular approach are suitable for intraventricular extension type (Type II, III). TAIF outcomes from 5 studies (72 patients) revealed 59% seizure free, 37% seizure reduction and 52% cognitive improvement with only 5.5% of focal neurological deficit. However, memory deficit is a major disadvantage for this approach which occurs in 23% compared with 7% in endoscopic transventricular approach[5]. Total of 122 HH patients from 6 studies, underwent endoscopic transventricular approach resulted in 37.7% seizure free, 28.6% seizure reduction, 9% cognitive improvement and 9% of focal neurological deficit[5].

2. Bottom-up operation: Pterional approach, translamina terminalis approach and orbitozygomatic approach are suitable for parahypothalamic type (Type I, III). There is less data from these approaches than top-down operation. Conbined 48 patients from 11 studies revealed 27% seizure free, 52% seizure reduction and 54% cognitive improvement without new memory deficit.

Gamma knife surgery is a less invasive procedure. It is useful for inoperable case especially for type IV but onset of action is delayed. In large retrospective multicenter series of 30 patients by Regis et al treated with 17 Gy via GKS showed favorable outcome. Eighteen (60%) patients achieved significant seizure reduction and 7 (23%) patients were seizure free[12,13].

Stereotactic radiofrequency thermocoagulation (SRT), first reported by Fukuda, is another less invasive procedure. Depth electrodes were placed to monitor epileptiform discharge after which the tip of the electrode was heated for 60 seconds at 74 degree of celsius[9]. The patient had completely seizure freedom 14 months later. Compared with GKS, SRT appeared to have a faster onset of action without radiation effect.

Vagus nerve stimulation (VNS) is an alternative treatment for intractable epilepsy. Combined 26 patients from 3 studies achieved 57% seizure reduction and 69% of cognitive improvement without seizure freedom.

Conclusion

When hypothalamic hamartomas (HH) present with medically intractable epilepsy various surgical options are available for consideration. Selecting one of these options largely depends on anatomical location of the HH. In case where surgical resection deemed hazardous, particularly a giant HH, stereotactic radiofrequency thermocoagulation can offer good seizure control with low complication rate.

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