World Journal of Surgical Procedures

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5412/wjsp.v5.i1.65

World J Surg Proced 2015 March 28; 5(1): 65-74
ISSN 2219-2832 (online)

REVIEW

How would we deal with hypothalamic hamartomas?

Kyu Won Shim, Eun Kyung Park, Ju Seong Kim, Dong-Seok Kim

Kyu Won Shim, Eun Kyung Park, Ju Seong Kim, Dong-Seok Kim, Department of Pediatric Neurosurgery, Severance Children's Hospital, Yonsei University College of Medicine, Brain Korea 21 Project for Medical Science, Seoul 120-752, South Korea
Author contributions: All authors contributed to this work.
Conflict-of-interest: There is no conflict of interests

Correspondence to: Dong-Seok Kim, MD, PhD, Professor, Department of Neurosurgery Pediatric Neurosurgery, Severance Children's Hospital, Yonsei University College of Medicine, Seoul 120-752, South Korea. dskim33@yuhs.ac
Telephone: +82-2-22282150
Fax: +82-2-3939979
Received: September 28, 2014
Peer-review started: October 10, 2014
First decision: December 17, 2014
Revised: December 26, 2014
Accepted: January 15, 2015
Article in press: January 19, 2015
Published online: March 28, 2015

Abstract

Hypothalamic hamartoma (HH) is usually associated with refractory epilepsy, cognitive impairment, and behavioral disturbance. There is now increasing evidence that HH can be treated effectively with a variety of neurosurgical approaches. Treatment options for intractable gelastic seizure in HH patients include direct open surgery with craniotomy, endoscopic surgery, radiosurgery with gamma knife and stereotactic radiofrequency thermocoagulation. Selection of treatment modalities depends on type and size of the HH and the surgeon's preference. Two surgical techniques, resection and disconnection, had been described with favorable outcomes. Pretreatment evaluation, patient selection, surgical techniques, complications, and possible selection of treatment are discussed.

Key words: Hypothalamic hamartoma; Epilepsy; Gelastic seizure; Transcallosal resection; Endoscopic surgery; Radiosurgery; Stereotactic radiofrequency ablation

Core tip: Neuronavigation-assisted neuroendoscopic surgery has been remarkably advancing. Furthermore high definition video recording system becomes its basic visualization system to facilitate the differentiation between normal tissue and abnormal tissue of hypothalamic hamartomas. Neuroendoscopic disconnection has been suggested to reduce the Gelastic seizure by the isolation of hypothalamic hamartomas (HHs) from surrounding structures. We are getting more powerful tools for performing sophisticated endoscopic disconnection surgery. Neuroendoscopic disconnection surgery used to be an optional surgery, but it becomes the first choice of surgery for HH with Gelastic seizure.

Shim KW, Park EK, Kim JS, Kim DS. How would we deal with hypothalamic hamartomas? *World J Surg Proced* 2015; 5(1): 65-74 Available from: URL: http://www.wjgnet.com/2219-2832/full/v5/i1/65.htm DOI: http://dx.doi.org/10.5412/wjsp.v5.i1.65

INTRODUCTION

The compulsive bursts of laughter were first introduced at 1873. Since Gumpert *et al*[1] described the feature of gelastic seizure (GS) Gascon *et al*[2] suggested the diagnostic criteria of gelastic epilepsy. Gelastic seizures represent the most common clinical expression of epilepsy and cause the patient to present sudden,

brief, uncontrollable attacks of laughter. These gelastic attacks progress as the patient ages, and other types of seizure, cognitive deterioration, and behavioral problems appear, frequently developing late in first decade of life, together with drop attacks and other secondary generalized epilepsy symptoms[3]. It has been demonstrated that epileptic focus originates from the hamartoma and from neocortical foci strictly related to Hypothalamic hamartomas (HHs)[4,5]. HHs are rare non-neoplastic congenital lesions of the inferior hypothalamus and consist of an abnormal mixture of neuronal and glial tissue. They issue from the floor of the third ventricle, tuber cinereum, or mammillary bodies. Hypothalamic hamartoma can be classified as sessile or pedunculated, depending on the width of their attachment to hypothalamus. Various symptoms have been associated with the sessile type of HH, including refractory epilepsy, central precocious puberty, intellectual impairment, and behavioral problems[6]. On the other hand, HHs causing isosexual precocious puberty are more likely to be pedunculated lesions that "hang" below the tuber cinereum. Close anatomic connections between HH and diencephalic hypothalamic structures also explain the autonomic, mainly sympathetic, symptoms and hormonal changes that accompanying GS[7-9]. GS appears in early childhood and quickly becomes refractory to medical treatment. The severity of the syndrome might depend, at least in part, on the size (small *vs* large), localization (tuber cinereum *vs* mamillary bodies), type of attachment (pedunculate *vs* sessile) and degree of hypothalamic displacement of the HH (lacking *vs* marked)[10-13]. Since Paillas *et al*[14] reported successful seizure outcome after resection of HHs in some patients in 1969, surgical intervention for these lesions has been attempted with variable seizure outcome[14]. Since 2000 the understanding and management of HH has increased dramatically especially in terms of intractable epilepsy. The state of the art of magnetic resonance imaging (MRI) and neuronavigation have developed synchronously by the turn of the millennium. Eventually we can have the tools for the safe and effective treatment of lesions in critical areas of the brain and without physically demonstrable borders between the offending lesion and critical areas of the brain such as the hypothalamus[15].

Focal (frontal or temporal) resections have never resolved GS, even when associated with depth electrode studies[16-19], whereas surgical and gamma-knife ablation, and radiofrequency coagulation of HH resulted in good seizure control[4,18-25]. Four surgical treatments have been introduced to treat HH: direct open surgery with craniotomy, endoscopic surgery, radiosurgery with gamma knife (GKS), and stereotactic radiofrequency thermocoagulation. Two techniques for HH surgery are used: resection or disconnection of hamartoma. The concept of disconnection had been introduced by Delalande *et al*[26] and it showed dramatic improvement in the patient. The technique disconnects the connecting tract between the hamartoma and the surrounding normal tissue.

Between 1990 and 2000, case reports on the successful surgical management of HH began to surface. These reports presumably reflected the increasing availability of contemporary imaging techniques. The first computed tomography (CT) scanner was installed in the United States in 1973[15]. A neurosurgeon removing or disconnecting an HH sees tissue that looks just like normal brain. The ability to identify the HH-brain interface depends on the subtle differences in signal intensity seen on MRI and shown by the navigation system. The surgical view is through the microscope, utilizing the endoscope or stereotactic equipment for Gamma Knife or the implantation of radiofrequency electrodes. The surgical approach to the lesion should be tailored to each case. No single approach is best for every patient.

Presurgical evaluation includes routine electro-encephalographic (EEG) monitoring and video-EEG monitoring with scalp electrodes, interictal and ictal 99m-Tc hexamethylprophyleneamine oxime single photon emission CT, MRI, neuropsychological evaluation, ophthalmological assessments with perimetry, and endocrinological investigations. The dimensions of the HHs and the anatomy surrounding the tuber cinereum can be seen clearly by high-resolution coronal and sagittal T1-weighted MRI. Endocrine assessment includes measurement of basal gonadotrophin and growth hormone levels, thyroid function, prolactin level, and cortisol reserve with glucagon stimulation. Deep electrode insertion into the HH with EEG monitoring may be necessary in some cases. Intractable seizure of the predominant gelastic type is an indication for surgical treatment. Gelastic seizures refractory to medication, neurobehavioral deterioration and direct or indirect evidence of hypothalamic seizure origin, and the absence of a cortical lesion on MRI are recommended for surgical treatment. The potential risks to memory, endocrine function, behavior, and vision have to be explained to the parents[25,27,28].

Endoscopic surgery

In patients with gelastic epilepsy-HH syndrome, the hamartoma is usually sessile; pedunculated HH is an occasional finding or may be related to endocrinological disturbances and/or to visual impairment[13,29]. Choi *et al*[27] suggested the modified classification of sessile HH, which was introduced by Delalande *et al*[26] (Figure 1). Small HHs (< 20 mm) were classified as midline (Type Ⅰ), lateral (Type Ⅱ), or intraventricular (Type Ⅲ) according to the location of the HH relative to the hypothalamus and third ventricle. A large hamartoma (> 20 mm) was de fined as giant HH (Type Ⅳ). Delalande *et al*[26] first reported on the use of endoscopic disconnection only for intraventricular

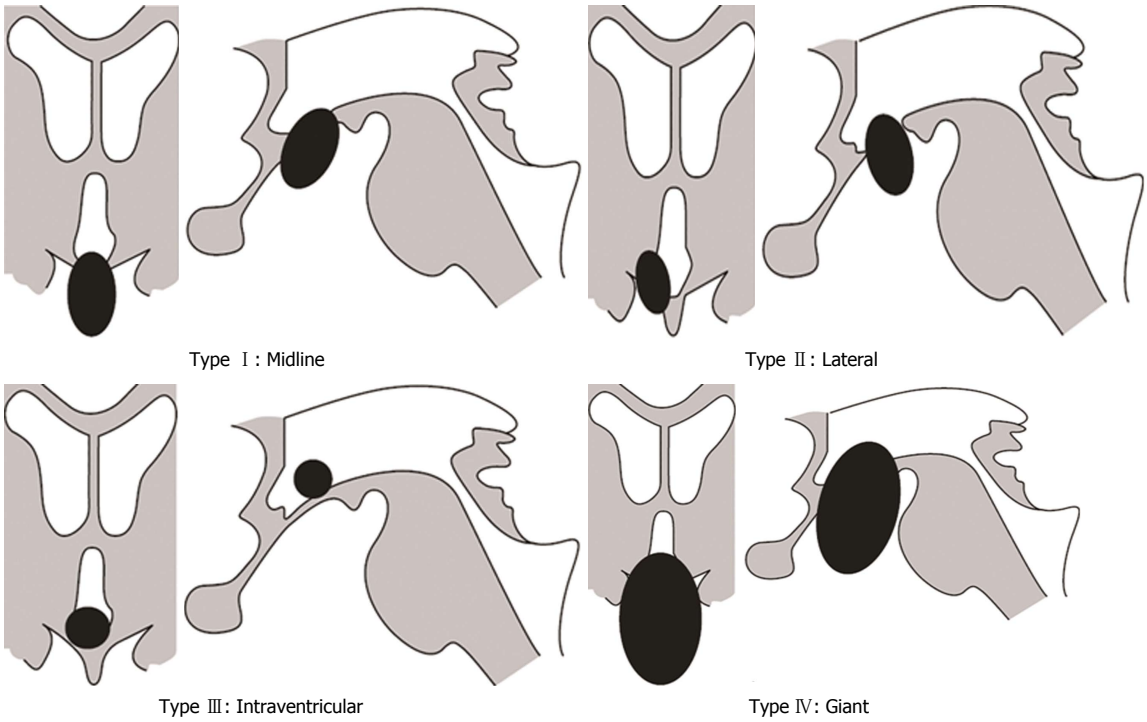


Figure 1 Classification of sessile hypothalamic hamartoma. (Modified by Choi *et al*[27] from that proposed by Delalande *et al*[26]). The hypothalamic hamartomas (HHs) were divided into four categories based on MRI findings demonstrating the relationship between the hamartoma and hypothalamus or the third ventricle. A large hamartoma (> 20 mm) was defined as a giant HH (Type Ⅳ). Small HHs (< 20 mm) were classified as midline (Type Ⅰ), lateral (Type Ⅱ), and intraventricular (Type Ⅲ) according to their relative location to the third ventricle. MRI: Magnetic resonance imaging.

type of hamartoma (Type Ⅲ) in 2003[3]. They also did endoscopic procedures in addition to conventional open surgery to treat other types of hamartoma. However, Choi *et al*[27] had tried endoscopic disconnection for Type Ⅰ, Type Ⅱ, and Type Ⅲ as the primary option of treatment and also used endoscopic surgery as an additional procedure for Type Ⅳ HH. Since Choi *et al*[27] suggested this approach Rekate *et al*[30] have found that most HHs within the third ventricle are excellent candidates for this type of excision[27,31]. Even the seizure returns redo endoscopic disconnection can be an effective rescue. Pati *et al*[32] reported their experience of repeat HHs surgery that they did re-endoscopic surgery for 8 of 21 patients and 50% of success rate.

Shim *et al*[25] (the authors' group) reported their experience with endoscopic disconnection in 11 patients in 2008. Six of 11 patients were seizure-free (Engel's class 1) immediately after surgery. Improvement in behavior was also noted in these patients after 2 mo. Outcome in three patients was class 2. In two other complicated cases which were treated with gamma knife surgery previously, seizure control was not satisfactory (class 3 or 4), but most cases showed complete resolution or a reduction of gelastic seizures. Procaccini *et al*[33] (the Delalande group) reported the results of 13 patients treated with frameless stereotactic endoscopic surgery in 2006[33]. Seizure-free recovery (Engel class 1) was achieved in 54% of the patients, and 46% of the patients showed improvement (Engel class 3). For the intraventricular type of HH, 90% of patients became seizure-free postoperatively. Ng *et al*[31] reported their experience with endoscopic removal in 44 patients based on early results. Ideal candidates for this surgery have been those with a lesion smaller than 1.5 cm in diameter. Patients with larger lesions also may be candidates as long as 6 mm of clearance is present to the top of the third ventricle. By the advance of high resolution of neuroimaging and technology of neuronavigation system the size of HHs might not be a critical point of decision for endoscopic surgery any more even though most of HHs patients have small ventricle[25,34]. In the Ng *et al*[31]'s report among 37 patients who underwent endoscopic resection 18 patients (48.6%) were seizure free at last follow-up (median 21 mo, range 13-28 mo). Seizures were reduced in 34 of 37 patients (91.9%)[30]. For giant HHs staged endoscopic disconnection becomes a one of the choice of treatment by the advent of neuronavigational neuroendoscope with high definition visualization system. The entry point, trajectory, and entry for small ventricle can be guided perfectly by this system. High definition visualization system can show a distinct cleft or indentation, the border of the HH attachment to the hypothalamus[25].

In Rekate's series, early complications occurred in 11 (25%) of 44 patients but resolved within 3 mo in all but three patients (6.8%), including one patient with postoperative hemiparesis and two patients with

short-term memory loss. Early complications included transient short-term memory loss, weight gain, thalamic infarction with memory loss, and hemiparesis[31,35]. Five of the 37 patients (13.5%) treated endoscopically experienced immediate short-term memory loss and permanent short term memory loss in 3 patients (8.2%) in endoscopic surgery group in Ng *et al*[31]'s series[30]. Choi *et al*[27] observed postoperative disconnection-like syndrome in three patients, which included mental dullness, verbal anomia, unilateral tactile anomia, and lack of somesthetic transfer. This disconnection-like syndrome disappeared spontaneously within 10 d. Even with multiple staging endoscopic disconnection the morbidity has been acceptable[25,32,36]. For minimizing complications proper trajectory directly to HHs, no anterior wiping motion of endoscope, not breaching arachnoid or pia mater keeping within third ventricle, and keep disconnection margin straight are very essential instructions. If the piarachnoid membrane was breached unilateral thalamic infarction can be resulted in about 30%[30]. However, many of these patients are so clinically and socially impaired that clinically significant damage to a mammillary body or fornix would not be evident. For this reason, it is reasonable to be more aggressive in pursuing resection or disconnection and in tolerating damage to relieve epilepsy in severely affected patients[36].

Although not all lesions are possibly deal with the endoscopic disconnection the feasibility of successful disconnection depends on a number of factors, including the plane and extent of attachment of the HH to the hypothalamus[37]. Some large lesions may require a multistep approach in which several disconnective procedures are used, or a combination of microsurgical resection and endoscopic disconnection. Larger lesion (> 15 mm) has been reported as an invincible with endoscopic disconnection. If you want to remove the HH completely, it will be nearly impossible with an HH that is over 1.5 cm. However, as we have reported, disconnection of the lesion from the brain is possible. The size of the lesion is not a major problem in disconnecting the lesion from the brain[25].

Open surgery with craniotomy

Multiple surgical approaches to the resection of HH have been described. Transbasal approaches with variations, such as the standard pterional approach, extended pterional approach with orbitotomy, and subfrontal approach, were reported but unfortunately many of these techniques were associated with high complication rates, including infarction of the internal capsule and thalamus, cranial nerve palsy (third nerve, olfactory nerve, and optic nerve), endocrinopathy, and memory loss. There also were difficulties in completely excising the lesion which extended into third ventricle[15,25,28]. Through these approaches, it was difficult or impossible to remove or disconnect the part of the mass that lay within the third ventricle, even after the lamina terminalis was opened[15]. The exposure is usually inadequate, and critical tissue borders are not readily apparent. Seizures were cured or reduced in 52% of patients undergoing approaches from below[6]. Delalande *et al*[26] introduced disconnecting surgical treatment for extraventricular HH in 2003. Dramatic improvement in 53% of those who underwent the procedure using pterional approach was reported. Two of 14 disconnection surgeries showed ischemic complications.

Rosenfeld *et al*[38] reported their experience with the transcallosal interforniceal approach in 2000[38,39]. Complete or nearly complete resection of HHs can be safely achieved *via* this approach with the possibility of seizure freedom and neurobehavioral improvement[39-41]. This approach can be used alone to treat large type Ⅱ and Ⅲ lesions. Many type Ⅳ lesions require a staged approach. If the lesion is entirely medial to the line of sight down the wall of each hypothalamus, then a large type Ⅲ or Ⅳ lesion can be disconnected during 1 operation[28,36]. Wait *et al*[36] described this approach at length.

Rosenfeld *et al*[21] reported complete or near total resection (> 95%) of HH in about 62% of the patients and 75%-95% resection was possible in about 24% of the patients. Harvey *et al*[42] reported that transcallosal resection of HH was effective treatment for intractable epilepsy, with 54%-76% of the patients being seizure-free or having a > 90% reduction in seizures. There also were improvements in behavior and cognition in 65%-88%. With univariate analysis, the likelihood of a seizure-free outcome correlated with younger age, shorter lifetime duration of epilepsy, smaller volume of HH, and total HH resection[42]. Postoperative complications were stroke, short-term memory disturbance, weight gain, diabetes insipidus, and other endocrine disturbances. Stroke is probably the result of injury of perforating vessels surrounding HH and short-term memory disturbance is due to surgical trauma of the septal, forniceal, or mammillary body. Five of the 37 patients (13.5%) treated endoscopically experienced immediate short-term memory loss, compared with 15 of 26 transcallosal patients (57.7%; $P = 0.7281$, Fishers exact test) in Ng *et al*[31]'s series[30] and permanent short term memory loss in 3 patients (8.2%) in endoscopic surgery group. Endocrinological morbidity is likely due to injury of neurovascular structure or pituitary stalk. Injuries to the optic tract and cranial nerve were rare with the transcallosal approach, but these injuries have been reported more with the traditional pterional and subfrontal approaches[43]. If the laterobasal approach is desired the orbitozygomatic approach should be preferred. Orbitozygomatic approach provides minimal brain retraction, maximum working space and light, and more favorable approach angle to HHs[44,45]. For lesions with ipsilateral attachment, the supraorbital eyebrow

approach may be sufficient[36]. Transcallosal anterior interforniceal approach used to resect HHs seems to be associated with a higher risk of postoperative memory difficulty than are approaches from below. The risk of endocrinological and hypothalamic damage may be higher, evidenced by diabetes insipidus, hypothyroidism, changes in appetite, decreased energy, and lethargy. This risk may reflect the potential for bilateral hypothalamic damage when approaching from above and midline compared with laterobasal access[40]. Potential long-term endocrinological deficits consist of permanent diabetes insipidus and hypothyroidism, which reported exclusively in patients after transcallosal anterior interforniceal approach approaches[40]. It is tremendously important to identify and follow the piarachnoid membrane 360° to disconnect HHs completely and avoid injury to critical structures, optic tract and perforating arteries of the basilar and posterior cerebral arteries. The overall rate of major permanent hypothalamic complications appeared to be slightly lower for the orbitozygomatic osteotomy group[40]. However there is a report for good cognitive outcomes with proper surgical resection for HHs of younger patients with relatively normal intelligence prior to surgery and shorter duration of epilepsy in case of no surgical complication[46].

Radiosurgery

Destruction of the HH lesion using focused ionizing radiation (gamma knife) is an attractive approach that does not require invasive surgery. Although a delayed (4-6 mo) response to gamma knife treatment is expected, early results suggest variable outcomes. Régis *et al*[47] reported excellent early seizure response. However, results in terms of long-term seizure freedom are not clear. The treatment goal of radiosurgery for HH is to deliver doses high enough to affect epileptogenesis without exceeding the tolerance of nearby critical structures. Modern radiosurgical devices such as Gamma Knife (Elekta AG), Cyber Knife (Accuray Inc.), and Novalis (BrainLab AG) can deliver conformal high-dose radiation with steep gradients providing a chance to achieve seizure freedom without hypothalamic or cranial nerve damage. Achievement of an excellent outcome following radiosurgery is related to the dose delivered. Régis *et al*[47] observed that four patients who received a peripheral dose of 18 Gy with the Gamma Knife became seizure free. Careful treatment planning and very tight dose distribution are essential to delivering similar doses without injuring the optic chiasm, optic tracts, pituitary stalk, fornices, mammillary bodies, and hypothalamic nuclei. The mean size of HH in a large series of radiosurgery was 19 mm in diameter, but radiosurgery can be accomplished in lesions smaller than 30 mm by using steep dose gradients around the target[47], while the size for ideal surgical candidate was reported less than 16 mm[48]. No serious complication has been reported with radiosurgery but temporary worsening of seizures can be seen as early as 2 mo after the procedure. Successful radiosurgical treatment of epileptogenic HHs was first reported in 1998 by Arita *et al*[22]. Régis *et al*[47] found a clear correlation between dose and efficacy; the marginal dose was > 17 Gy in all patients in whom seizure freedom was achieved and all patients who received < 13 Gy showed incomplete seizure control. Updated outcome of a large series (over 60 patients) by Régis *et al*[47] reported that thirty-one patients were evaluated for at least 3 years after radiosurgery; of these, satisfactory follow-up was available in 27. Only 10 (37%) of these 27 patients achieved seizure freedom; 6 others (22%) experienced a significant decrease in frequency of seizures[47]. The median prescribed marginal dose was 17 Gy (range 13-26 Gy). The authors judiciously used a beam blocking strategy to reduce the dose delivered to critical surrounding structures. However, in the other series in which doses ranging from 12 to 14 Gy were used, outcome of seizure control was variable[25,49].

Several other groups have reported their experience with GKS for treating intractable epilepsy related to HHs[25,50-56]. These studies demonstrate that GKS is an effective treatment modality for selected patients with HH-associated epilepsy. However, it is important to remember that, similar to the complications of microsurgical resection of the HH, radiosurgery can result in permanent neurological sequelae[57,58]. Also, there seems to be a dose-dependent response in which improved seizure control rates are attained with marginal doses > 16 Gy[59]. However, one of the main disadvantages is that clinical response can be very slow; the patient remains exposed to the risks of persistent seizures for up to 2 years after the radiosurgical procedure[60].

Stereotactic radiofrequency ablation

In 1999 Fukuda *et al*[61] reported on a single patient with HH treated by stereotactic radiofrequency thermocoagulation in the course of exploration with a depth electrode implanted within the lesion. Gelastic seizures ceased postoperatively and tonic seizures disappeared 4 mo later. Finally, this patient became seizure free within 14 mo. Kameyama *et al*[62] and Homma *et al*[63] reviewed results from 25 consecutive patients with HH and gelastic seizures who were treated with radiofrequency thermocoagulation. They divided HHs into 3 types based on coronal MRI findings: intrahypothalamic, parahypothalamic, and mixed type. Complete seizure freedom was seen in 19 (76%) of 25 patients over a mean follow-up of 2.3 years. Transient postoperative complications included hyperthermia, hyperphagia, hyponatremia, Horner syndrome, and short-term memory problems. Complications included low-grade fever (4 patients) and hyperphagia (2 patients) and occurred transiently as local hypothalamic symptoms. These transient symptoms resolved within

Table 1 Advantages and disadvantages between modalities

Treatment modality	Advantages	Disadvantages
Endoscopic surgery	Minimally invasive Low possibility to injure adjacent critical structures Critical tissue borders are readily apparent Relatively low complication even with Re-do surgery Relatively easy approach to the intrathird ventricular lesion	Multiple approaches for large HHs Dependent on surgeon's experience
Open surgery with craniotomy		
The standard pterional approach	The risk of endocrinological and hypothalamic damage may be lower than transcallosal approach	High complication rates Difficulties in completely excising the lesion which extended into third ventricle Inadequate exposure is usual Critical tissue borders are not readily apparent
Transcallosal interforniceal approach	Complete or nearly complete resection of HHs can be safely achieved *via* this approach Can be used alone to treat large HHs Injuries to the optic tract and cranial nerve were rare	Surgical trauma to the septal, forniceal, or mammillary body The risk of endocrinological and hypothalamic damage may be higher
Radiosurgery	Does not require invasive surgery Provide a chance to achieve seizure freedom without hypothalamic or cranial nerve damage	Delayed (4-6 mo) response Long-term seizure freedom are not clear Lesions smaller than 30 mm Dose-dependent response
Stereotactic radiofrequency ablation	Effective for a small hamartoma Immediate response	Effective for a small hamartoma Inexact volume of tissue ablation Multiple trajectories to treat larger hamartomas
Neuromodulation	No behavioral, endocrinological, or neurological side effects has been reported	No definite change in overall seizure frequency

HHs: Hypothalamic hamartomas.

1 wk after surgery after perifocal edema disappeared; no permanent complications were noted. All 10 patients who had behavior disturbances preoperatively showed complete resolution of their behavioral abnormalities following radiofrequency ablation.

This procedure seems to be effective for a small hamartoma but a long-term study of a large series will be necessary to con firm the efficacy and safety of this treatment[63-65]. The results with stereotactic radiofrequency ablation, unlike with stereotactic radiosurgery, can be seen immediately following the procedure. However, drawbacks of the technique include inexact volume of tissue ablation and the need for multiple trajectories to treat larger hamartomas, thereby adding to the risk of injury to the surrounding neurovascular structures compared with a single pass[25].

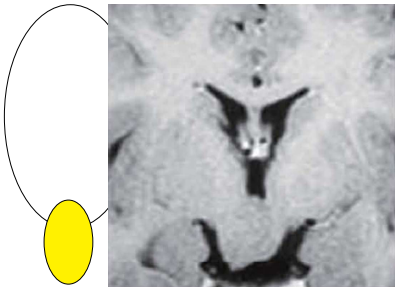
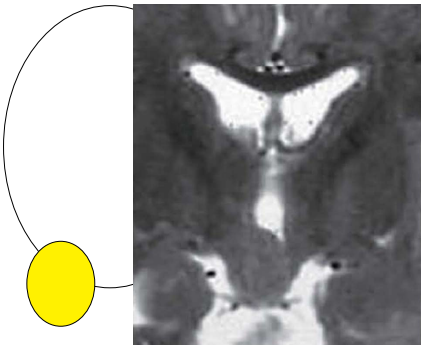
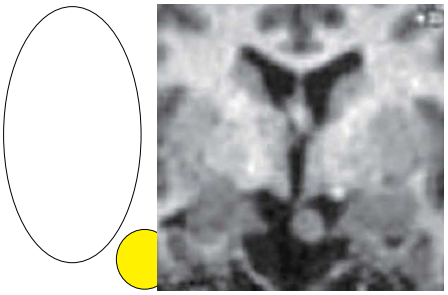
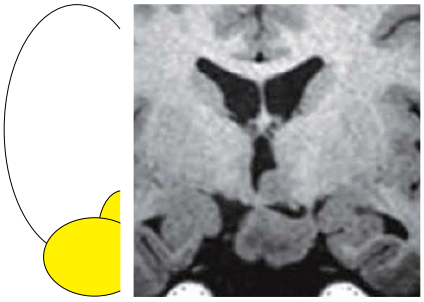
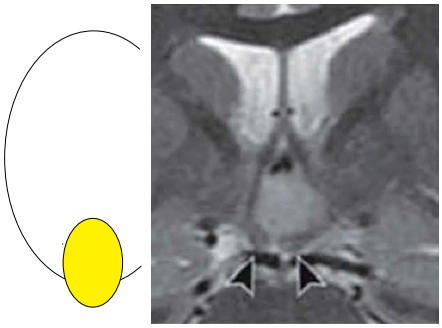
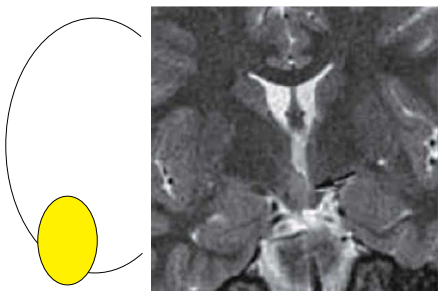
Neuromodulation

Deep brain stimulation and vagal nerve stimulation have tried to override epileptogenic activity from HHs[40,66-69]. No definite change in her overall seizure frequency (complex partial and gelastic seizures) as well as no behavioral, endocrinological, or neurological side effects has been reported. These palliative techniques are not effective in controlling gelastic seizures, and therefore have a very limited role in the treatment of patients with HH-associated gelastic seizures. Certainly, further work needs to be done to determine the role of these techniques in the treatment of epilepsy related to HHs.

Selection of the neurosurgical procedure to perform depends on the surgeon's preference and experience, but reasonable approaches can be selected according to the location, shape, and size of the HH. Possible treatment selections according to subdivided types of hypothalamic hamartoma are given in Figure 2, although treatment options can be different depending on the viewpoint of the surgeon[28].

No single approach is the best approach or is appropriate in all cases (Table 1). Adequate treatment requires individualization of the approach based on a patient's age and condition, on the anatomy of the HH, and on the surgeon's experience. It is becoming increasingly clear that a 1-stage approach to all HHs is probably inappropriate[36]. About 16% of patients required more than one procedure. By the nature and pathophysiology of HHs the complete disconnection from the surrounding structure and tracts which spread out its epileptogenic discharge to frontotemporal region will be enough to achieve the appropriate control of accompanying problems. If an HH can be disconnected completely from the hypothalamus, resection may not be necessary to eliminate seizures[4,30].

It is important to remember that a HH cannot be distinguished from normal hypothalamus under microsurgical view. Only the abnormal anatomy that it forms allows the surgeon to determine where to stop resection. Careful evaluation of the patient's preoperative MRI study and use of intraoperative stereotactic guidance

Type of hamartoma		Possible selection of treatment
Type Ⅰ midline		1 Radiosurgery 2 Endoscopic surgery 3 Stereotactic radiofrequency ablation
Type Ⅱ lateral Type ⅡA partially intraventricular		1 Radiosurgery 2 Endoscopic surgery 3 Stereotactic radiofrequency ablation
Type ⅡB totally extraventricular		1 Radiosurgery 2 Stereotaqctic radiolrequency ablation 3 Open craniotomy; pterional approach
Type ⅡC mixed		1 Endoscopic surgery + open craniotomy pterional 2 Staged radiosurgery
Type Ⅲ intraventricular Type ⅢA midline intraventricular		1 Endoscopic surgery 2 Open craniotomy; transcallosal approach
Type ⅢB lateral intraventricular		1 Endoscopic surgery 2 Open craniotomy; transcallosal approach

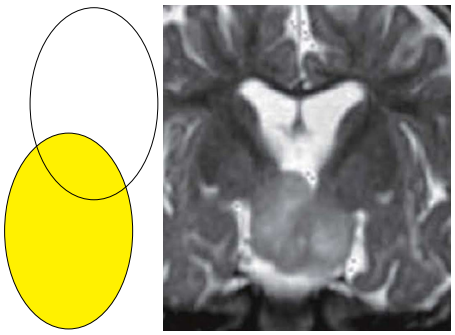


Figure 2 Possible treatments for subdivided types of hypothalamic hamartoma[28]. (Modification from Delalande *et al*[26]'s and Choi *et al*[27]'s classification).

help clarify the aforementioned limits of resection[36].

REFERENCES

1 **Gumpert J**, Hansotia P, Upton A. Gelastic epilepsy. *J Neurol Neurosurg Psychiatry* 1970; **33**: 479-483 [PMID: 5505675]
2 **Gascon GG**, Lombroso CT. Epileptic (gelastic) laughter. *Epilepsia* 1971; **12**: 63-76 [PMID: 5282883]
3 **Berkovic SF**, Arzimanoglou A, Kuzniecky R, Harvey AS, Palmini A, Andermann F. Hypothalamic hamartoma and seizures: a treatable epileptic encephalopathy. *Epilepsia* 2003; **44**: 969-973 [PMID: 12823582]
4 **Kuzniecky R**, Guthrie B, Mountz J, Bebin M, Faught E, Gilliam F, Liu HG. Intrinsic epileptogenesis of hypothalamic hamartomas in gelastic epilepsy. *Ann Neurol* 1997; **42**: 60-67 [PMID: 9225686 DOI: 10.1002/ana.410420111]
5 **Munari C**, Kahane P, Francione S, Hoffmann D, Tassi L, Cusmai R, Vigevano F, Pasquier B, Betti OO. Role of the hypothalamic hamartoma in the genesis of gelastic fits (a video-stereo-EEG study). *Electroencephalogr Clin Neurophysiol* 1995; **95**: 154-160 [PMID: 7555906]
6 **Likavec AM**, Dickerman RD, Heiss JD, Liow K. Retrospective analysis of surgical treatment outcomes for gelastic seizures: a review of the literature. *Seizure* 2000; **9**: 204-207 [PMID: 10775517 DOI: 10.1053/seiz.1999.0352]
7 **Kahane P**, Di Leo M, Hoffmann D, Munari C. Ictal bradycardia in a patient with a hypothalamic hamartoma: a stereo-EEG study. *Epilepsia* 1999; **40**: 522-527 [PMID: 10219284]
8 **Arroyo S**, Santamaría J, Sanmartí F, Lomena F, Catafau A, Casamitjana R, Setoain J, Tolosa E. Ictal laughter associated with paroxysmal hypothalamopituitary dysfunction. *Epilepsia* 1997; **38**: 114-117 [PMID: 9024192]
9 **Cerullo A**, Tinuper P, Provini F, Contin M, Rosati A, Marini C, Cortelli P. Autonomic and hormonal ictal changes in gelastic seizures from hypothalamic hamartomas. *Electroencephalogr Clin Neurophysiol* 1998; **107**: 317-322 [PMID: 9872433]
10 **Sturm JW**, Andermann F, Berkovic SF. "Pressure to laugh": an unusual epileptic symptom associated with small hypothalamic hamartomas. *Neurology* 2000; **54**: 971-973 [PMID: 10690995]
11 **Striano S**, Striano P, Cirillo S, Nocerino C, Bilo L, Meo R, Ruosi P, Boccella P, Briganti F. Small hypothalamic hamartomas and gelastic seizures. *Epileptic Disord* 2002; **4**: 129-133 [PMID: 12105075]
12 **Valdueza JM**, Cristante L, Dammann O, Bentele K, Vortmeyer A, Saeger W, Padberg B, Freitag J, Herrmann HD. Hypothalamic hamartomas: with special reference to gelastic epilepsy and surgery. *Neurosurgery* 1994; **34**: 949-958; discussion 958 [PMID: 8084405]
13 **Arita K**, Ikawa F, Kurisu K, Sumida M, Harada K, Uozumi T, Monden S, Yoshida J, Nishi Y. The relationship between magnetic resonance imaging findings and clinical manifestations of hypothalamic hamartoma. *J Neurosurg* 1999; **91**: 212-220 [PMID: 10433309 DOI: 10.3171/jns.1999.91.2.0212]
14 **Paillas JE**, Roger J, Toga M, Soulayrol R, Salamon G, Dravet C, Bureau M. [Hamartoma of the hypothalamus. Clinical, radiological and histological study. Results of excision]. *Rev Neurol* (Paris) 1969; **120**: 177-194 [PMID: 4981043]
15 **Rekate HL**. Management of hypothalamic hamartomas: progress due to alignment of the stars. *Neurosurg Focus* 2011; **30**: Introduction [PMID: 21370583]
16 **Breningstall GN**. Gelastic seizures, precocious puberty, and hypothalamic hamartoma. *Neurology* 1985; **35**: 1180-1183 [PMID: 4022351]
17 **Berkovic SF**, Andermann F, Melanson D, Ethier RE, Feindel W, Gloor P. Hypothalamic hamartomas and ictal laughter: evolution of a characteristic epileptic syndrome and diagnostic value of magnetic resonance imaging. *Ann Neurol* 1988; **23**: 429-439 [PMID: 3389755 DOI: 10.1002/ana.410230502]
18 **Cascino GD**, Andermann F, Berkovic SF, Kuzniecky RI, Sharbrough FW, Keene DL, Bladin PF, Kelly PJ, Olivier A, Feindel W. Gelastic seizures and hypothalamic hamartomas: evaluation of patients undergoing chronic intracranial EEG monitoring and outcome of surgical treatment. *Neurology* 1993; **43**: 747-750 [PMID: 8469334]
19 **Palmini A**, Chandler C, Andermann F, Costa Da Costa J, Paglioli-Neto E, Polkey C, Rosenblatt B, Montes J, Martínez JV, Farmer JP, Sinclair B, Aronyk K, Paglioli E, Coutinho L, Raupp S, Portuguez M. Resection of the lesion in patients with hypothalamic hamartomas and catastrophic epilepsy. *Neurology* 2002; **58**: 1338-1347 [PMID: 12011278]
20 **Nishio S**, Morioka T, Fukui M, Goto Y. Surgical treatment of intractable seizures due to hypothalamic hamartoma. *Epilepsia* 1994; **35**: 514-519 [PMID: 8026396]
21 **Rosenfeld JV**, Harvey AS, Wrennall J, Zacharin M, Berkovic SF. Transcallosal resection of hypothalamic hamartomas, with control of seizures, in children with gelastic epilepsy. *Neurosurgery* 2001; **48**: 108-118 [PMID: 11152336]
22 **Arita K**, Kurisu K, Iida K, Hanaya R, Akimitsu T, Hibino S, Pant B, Hamasaki M, Shinagawa S. Subsidence of seizure induced by stereotactic radiation in a patient with hypothalamic hamartoma. Case report. *J Neurosurg* 1998; **89**: 645-648 [PMID: 9761061 DOI: 10.3171/jns.1998.89.4.0645]
23 **Régis J**, Bartolomei F, Hayashi M, Roberts D, Chauvel P, Peragut JC. The role of gamma knife surgery in the treatment of severe epilepsies. *Epileptic Disord* 2000; **2**: 113-122 [PMID: 10954243]
24 **Régis J**, Bartolomei F, de Toffol B, Genton P, Kobayashi T, Mori Y, Takakura K, Hori T, Inoue H, Schröttner O, Pendl G, Wolf A, Arita K, Chauvel P. Gamma knife surgery for epilepsy related to hypothalamic hamartomas. *Neurosurgery* 2000; **47**: 1343-1351; discussion 1351-1352 [PMID: 11126905]
25 **Shim KW**, Chang JH, Park YG, Kim HD, Choi JU, Kim DS. Treatment modality for intractable epilepsy in hypothalamic hamartomatous lesions. *Neurosurgery* 2008; **62**: 847-856; discussion 856 [PMID: 18496191 DOI: 10.1227/01.neu.0000318170.82719.7c]
26 **Delalande O**, Fohlen M. Disconnecting surgical treatment of hypothalamic hamartoma in children and adults with refractory epilepsy and proposal of a new classification. *Neurol Med Chir* (Tokyo) 2003; **43**: 61-68 [PMID: 12627881]
27 **Choi JU**, Yang KH, Kim TG, Chang JH, Chang JW, Lee BI, Kim

DS. Endoscopic disconnection for hypothalamic hamartoma with intractable seizure. Report of four cases. *J Neurosurg* 2004; **100**: 506-511 [PMID: 15287464 DOI: 10.3171/ped.2004.100.5.0506]
28 **Choi JU**, Kim DS. Treatment modalities for intractable epilepsy in hypothalamic hamartoma. *Adv Tech Stand Neurosurg* 2012; **39**: 117-130 [PMID: 23250839 DOI: 10.1007/978-3-7091-1360-8_5]
29 **Boyko OB**, Curnes JT, Oakes WJ, Burger PC. Hamartomas of the tuber cinereum: CT, MR, and pathologic findings. *AJNR Am J Neuroradiol* 1991; **12**: 309-314 [PMID: 1902033]
30 **Rekate HL**, Feiz-Erfan I, Ng YT, Gonzalez LF, Kerrigan JF. Endoscopic surgery for hypothalamic hamartomas causing medically refractory gelastic epilepsy. *Childs Nerv Syst* 2006; **22**: 874-880 [PMID: 16770620 DOI: 10.1007/s00381-006-0125-4]
31 **Ng YT**, Rekate HL, Prenger EC, Wang NC, Chung SS, Feiz-Erfan I, Johnsonbaugh RE, Varland MR, Kerrigan JF. Endoscopic resection of hypothalamic hamartomas for refractory symptomatic epilepsy. *Neurology* 2008; **70**: 1543-1548 [PMID: 18427070]
32 **Pati S**, Abla AA, Rekate HL, Ng YT. Repeat surgery for hypothalamic hamartoma in refractory epilepsy. *Neurosurg Focus* 2011; **30**: E3 [PMID: 21374831]
33 **Procaccini E**, Dorfmüller G, Fohlen M, Bulteau C, Delalande O. Surgical management of hypothalamic hamartomas with epilepsy: the stereoendoscopic approach. *Neurosurgery* 2006; **59**: ONS336-ONS344; discussion ONS344-ONS346 [PMID: 17041502 DOI: 10.1227/01.NEU.0000233900.06146.72]
34 **Ito E**, Fujii M, Hayashi Y, Zhengang J, Nagatani T, Saito K, Kishida Y, Mori K, Wakabayashi T. Magnetically guided 3-dimensional virtual neuronavigation for neuroendoscopic surgery: technique and clinical experience. *Neurosurgery* 2010; **66**: 342-353; discussion 353 [PMID: 20489524 DOI: 10.1227/01.NEU.0000369659.19479.AF]
35 **Lekovic GP**, Gonzalez LF, Feiz-Erfan I, Rekate HL. Endoscopic resection of hypothalamic hamartoma using a novel variable aspiration tissue resector. *Neurosurgery* 2006; **58**: ONS166-ONS169; discussion ONS166-ONS169 [PMID: 16543875 DOI: 10.1227/01.NEU.0000193512.87279.69]
36 **Wait SD**, Abla AA, Killory BD, Nakaji P, Rekate HL. Surgical approaches to hypothalamic hamartomas. *Neurosurg Focus* 2011; **30**: E2 [PMID: 21374830]
37 **De Ribaupierre S**, Delalande O. Hemispherotomy and other disconnective techniques. *Neurosurg Focus* 2008; **25**: E14 [PMID: 18759615 DOI: 10.3171/FOC/2008/25/9/E14]
38 **Rosenfeld JV**, Freeman JL, Harvey AS. Operative technique: the anterior transcallosal transseptal interforniceal approach to the third ventricle and resection of hypothalamic hamartomas. *J Clin Neurosci* 2004; **11**: 738-744 [PMID: 15337137 DOI: 10.1016/j.jocn.2004.03.008]
39 **Freeman JL**, Harvey AS, Rosenfeld JV, Wrennall JA, Bailey CA, Berkovic SF. Generalized epilepsy in hypothalamic hamartoma: evolution and postoperative resolution. *Neurology* 2003; **60**: 762-767 [PMID: 12629230]
40 **Feiz-Erfan I**, Horn EM, Rekate HL, Spetzler RF, Ng YT, Rosenfeld JV, Kerrigan JF. Surgical strategies for approaching hypothalamic hamartomas causing gelastic seizures in the pediatric population: transventricular compared with skull base approaches. *J Neurosurg* 2005; **103**: 325-332 [PMID: 16270684 DOI: 10.3171/ped.2005.103.4.0325]
41 **Luo S**, Li C, Ma Z, Zhang Y, Jia G, Cheng Y. Microsurgical treatment for hypothalamic hamartoma in children with precocious puberty. *Surg Neurol* 2002; **57**: 356-362; discussion 362 [PMID: 12128318]
42 **Harvey AS**, Freeman JL, Berkovic SF, Rosenfeld JV. Transcallosal resection of hypothalamic hamartomas in patients with intractable epilepsy. *Epileptic Disord* 2003; **5**: 257-265 [PMID: 14975795]
43 **Ng YT**, Rekate HL, Prenger EC, Chung SS, Feiz-Erfan I, Wang NC, Varland MR, Kerrigan JF. Transcallosal resection of hypothalamic hamartoma for intractable epilepsy. *Epilepsia* 2006; **47**: 1192-1202 [PMID: 16886983 DOI: 10.1111/j.1528-1167.2006.00516.x]
44 **Lemole GM**, Henn JS, Zabramski JM, Spetzler RF. Modifications to the orbitozygomatic approach. Technical note. *J Neurosurg* 2003; **99**: 924-930 [PMID: 14609176 DOI: 10.3171/jns.2003.99.5.0924]
45 **Zabramski JM**, Kiriş T, Sankhla SK, Cabiol J, Spetzler RF. Orbitozygomatic craniotomy. Technical note. *J Neurosurg* 1998; **89**: 336-341 [PMID: 9688133 DOI: 10.3171/jns.1998.89.2.0336]
46 **Wethe JV**, Prigatano GP, Gray J, Chapple K, Rekate HL, Kerrigan JF. Cognitive functioning before and after surgical resection for hypothalamic hamartoma and epilepsy. *Neurology* 2013; **81**: 1044-1050 [PMID: 23946307 DOI: 10.1212/WNL.0b013e3182a4a3e3]
47 **Régis J**, Scavarda D, Tamura M, Nagayi M, Villeneuve N, Bartolomei F, Brue T, Dafonseca D, Chauvel P. Epilepsy related to hypothalamic hamartomas: surgical management with special reference to gamma knife surgery. *Childs Nerv Syst* 2006; **22**: 881-895 [PMID: 16807727 DOI: 10.1007/s00381-006-0139-y]
48 **Li CD**, Luo SQ, Tang J, Jia G, Ma ZY, Zhang YQ. Classification of hypothalamic hamartoma and prognostic factors for surgical outcome. *Acta Neurol Scand* 2014; **130**: 18-26 [PMID: 24382157 DOI: 10.1111/ane.12209]
49 **Schulze-Bonhage A**, Homberg V, Trippel M, Keimer R, Elger CE, Warnke PC, Ostertag C. Interstitial radiosurgery in the treatment of gelastic epilepsy due to hypothalamic hamartomas. *Neurology* 2004; **62**: 644-647 [PMID: 14981188]
50 **Abla AA**, Shetter AG, Chang SW, Wait SD, Brachman DG, Ng YT, Rekate HL, Kerrigan JF. Gamma Knife surgery for hypothalamic hamartomas and epilepsy: patient selection and outcomes. *J Neurosurg* 2010; **113** Suppl: 207-214 [PMID: 21121803]
51 **Barajas MA**, Ramírez-Guzman MG, Rodríguez-Vázquez C, Toledo-Buenrostro V, Cuevas-Solórzano A, Rodríguez-Hernández G. Gamma knife surgery for hypothalamic hamartomas accompanied by medically intractable epilepsy and precocious puberty: experience in Mexico. *J Neurosurg* 2005; **102** Suppl: 53-55 [PMID: 15662781]
52 **Drees C**, Chapman K, Prenger E, Baxter L, Maganti R, Rekate H, Shetter A, Bobrowitz M, Kerrigan JF. Seizure outcome and complications following hypothalamic hamartoma treatment in adults: endoscopic, open, and Gamma Knife procedures. *J Neurosurg* 2012; **117**: 255-261 [PMID: 22680243 DOI: 10.3171/2012.5.JNS112256]
53 **Dunoyer C**, Ragheb J, Resnick T, Alvarez L, Jayakar P, Altman N, Wolf A, Duchowny M. The use of stereotactic radiosurgery to treat intractable childhood partial epilepsy. *Epilepsia* 2002; **43**: 292-300 [PMID: 11906515]
54 **Kida Y**, Yoshimoto M, Hasegawa T. [Radiosurgery of hypothalamic hamartomas]. *No Shinkei Geka* 2008; **36**: 225-232 [PMID: 18341011]
55 **Mathieu D**, Kondziolka D, Niranjan A, Flickinger J, Lunsford LD. Gamma knife radiosurgery for refractory epilepsy caused by hypothalamic hamartomas. *Stereotact Funct Neurosurg* 2006; **84**: 82-87 [PMID: 16790990 DOI: 10.1159/000094036]
56 **Unger F**, Schröttner O, Feichtinger M, Bone G, Haselsberger K, Sutter B. Stereotactic radiosurgery for hypothalamic hamartomas. *Acta Neurochir Suppl* 2002; **84**: 57-63 [PMID: 12379005]
57 **Régis J**, Arkha Y, Yomo S, Bartolomei F, Peragut JC, Chauvel P. [Radiosurgery for drug-resistant epilepsies: state of the art, results and perspectives]. *Neurochirurgie* 2008; **54**: 320-331 [PMID: 18417166 DOI: 10.1016/j.neuchi.2008.02.016]
58 **Romanelli P**, Muacevic A, Striano S. Radiosurgery for hypothalamic hamartomas. *Neurosurg Focus* 2008; **24**: E9 [PMID: 18447748 DOI: 10.3171/FOC/2008/24/5/E9]
59 **Quigg M**, Barbaro NM. Stereotactic radiosurgery for treatment of epilepsy. *Arch Neurol* 2008; **65**: 177-183 [PMID: 18268185 DOI: 10.1001/archneurol.2007.40]
60 **Mittal S**, Mittal M, Montes JL, Farmer JP, Andermann F. Hypothalamic hamartomas. Part 2. Surgical considerations and outcome. *Neurosurg Focus* 2013; **34**: E7 [PMID: 23724841 DOI: 10.3171/2013.3.FOCUS1356]
61 **Fukuda M**, Kameyama S, Wachi M, Tanaka R. Stereotaxy for hypothalamic hamartoma with intractable gelastic seizures: technical case report *Neurosurgery* 1999; **44**: 1347-1350 [PMID: 10371639]

62 **Kameyama S**, Murakami H, Masuda H, Sugiyama I. Minimally invasive magnetic resonance imaging-guided stereotactic radiofrequency thermocoagulation for epileptogenic hypothalamic hamartomas. *Neurosurgery* 2009; **65**: 438-449; discussion 449 [PMID: 19687687 DOI: 10.1227/01.NEU.0000348292.39252.B5]
63 **Homma J**, Kameyama S, Masuda H, Ueno T, Fujimoto A, Oishi M, Fukuda M. Stereotactic radiofrequency thermocoagulation for hypothalamic hamartoma with intractable gelastic seizures. *Epilepsy Res* 2007; **76**: 15-21 [PMID: 17643965 DOI: 10.1016/j.eplepsyres.2007.06.007]
64 **Fujimoto Y**, Kato A, Saitoh Y, Ninomiya H, Imai K, Hashimoto N, Kishima H, Maruno M, Yoshimine T. Open radiofrequency ablation for the management of intractable epilepsy associated with sessile hypothalamic hamartoma. *Minim Invasive Neurosurg* 2005; **48**: 132-135 [PMID: 16015488 DOI: 10.1055/s-2004-830267]
65 **Parrent AG**. Stereotactic radiofrequency ablation for the treatment of gelastic seizures associated with hypothalamic hamartoma. Case report. *J Neurosurg* 1999; **91**: 881-884 [PMID: 10541251 DOI: 10.3171/jns.1999.91.5.0881]
66 **Khan S**, Wright I, Javed S, Sharples P, Jardine P, Carter M, Gill SS. High frequency stimulation of the mamillothalamic tract for the treatment of resistant seizures associated with hypothalamic hamartoma. *Epilepsia* 2009; **50**: 1608-1611 [PMID: 19243422 DOI: 10.1111/j.1528-1167.2008.01995.x]
67 **Marras CE**, Rizzi M, Villani F, Messina G, Deleo F, Cordella R, Franzini A. Deep brain stimulation for the treatment of drug-refractory epilepsy in a patient with a hypothalamic hamartoma. Case report. *Neurosurg Focus* 2011; **30**: E4 [PMID: 21284450 DOI: 10.3171/2010.11.FOCUS10241]
68 **Murphy JV**, Wheless JW, Schmoll CM. Left vagal nerve stimulation in six patients with hypothalamic hamartomas. *Pediatr Neurol* 2000; **23**: 167-168 [PMID: 11020644]
69 **Brandberg G**, Raininko R, Eeg-Olofsson O. Hypothalamic hamartoma with gelastic seizures in Swedish children and adolescents. *Eur J Paediatr Neurol* 2004; **8**: 35-44 [PMID: 15023373 DOI: 10.1016/j.ejpn.2003.10.003]

P- Reviewer: Sarica FB **S- Editor**: Ji FF
L- Editor: A **E- Editor**: Liu SQ

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com