

Gamma Knife Radiosurgery in Patients with a Hypothalamic Hamartoma Associated with Intractable Gelastic Epilepsy : Report of Three Cases

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Hypothalamic hamartoma(HH) is an unusual nonneoplastic developmental lesion associated with gelastic epilepsy and precocious puberty, mostly found in children. Although open surgery has been attempted when antiepileptic medication failed to control seizures, its deep location and surrounding vital structures often rendered surgery unsuccessful. We describe the outcome of gamma knife radiosurgery in three children with a HH associated with gelastic epilepsy and reviewed the literature for a possible therapeutic mechanism.

KEY WORDS : Hypothalamic hamartoma · Gelastic seizure · Gamma knife radiosurgery .

Introduction

Central nervous system hamartoma is a rare malformative lesion comprising of neurons, glia, and fiber bundles in ectopic position. Hypothalamic hamartoma(HH) locates in the posterior thalamus, the tuber cinerium, or the mamillary bodies, and has been reported to be associated with gelastic epilepsy which is characterized by brief episodes of clonic facial grimace with laughing sound. Gelastic epilepsy usually begins during early childhood and is accompanied by progressive mental deterioration³⁾. The patients with a HH also may present with precocious puberty. Among the classifications proposed for HH, topographical classification by Valdueza et al.¹⁷⁾, grouping HH into pedunculated (type Ia, Ib) and sessile (type IIa, IIb) based on its contour and size, is useful for the management of the lesion because each type correlates with presenting symptoms and potential surgical risks.

Gelastic epilepsy is invariably resistant to antiepileptic medications when it is associated with HH, which have motivated surgical trial for the management of this condition. The surgical role in the treatment of HH accompanying gelastic epilepsy has been, however, controversial because of its potential risk of operative complications. It has been suggested that radiosurgery would be a good alternative to open surgery, which can

obtain epilepsy control without major complications. We present the outcome of three cases of HH treated with Gamma knife radiosurgery(GKRS).

Case Report

Case 1

A 12-year-old girl presented with medically intractable epilepsy. She was healthy at birth and met normal developmental milestones until she started to experience gelastic seizures at the age of 7 months. The initial features of seizure were sudden laughing and frightening, which have developed to multiple daily episodes of head version to right side with generalized clonic movement. Physical examination revealed delayed development and precocious puberty, and she was evaluated to have mental retardation (WAIS-R full scale IQ 77) on neuropsychological test. Scalp EEG disclosed suspicious polyspike discharges followed by spike and wave discharges on both fronto-cento-temporal areas during ictal state, and frequent spike or polyspike discharges from left fronto-central area during interictal state. Magnetic resonance imaging(MRI) revealed hypothalamic mass, 11mm in diameter, which was not enhanced in contrast study, suggestive of HH (Valdueza type IIa) (Fig. 1).

GKRS was performed considering expected high risk of

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surgical resection of the lesion ; the volume was 508.2mm³ and the margin dose of 18Gy was placed at the 50% isodose line (Fig. 2). Post-GKRS course was uneventful. The lesion on MRI per-formed after 5 months remained unchanged. She exhibited gradual decrease of epileptic activity after 6 months of GKRS. After a follow-up period of 18 months, she was free of seizures except sparse episodes of brief aura without medication. After 42 months, she was completely free of any seizure activity.

Case 2

A 5-year-old boy suffered from gelastic seizures since the age of 27 months. At the time of his visit, gelastic seizures lasting 10 seconds occurred 10 to 16 times a day even with antiepileptic medication. He was born as a healthy baby without perinatal problem and showed normal development until the first seizure occurred. On physical examination, the features of precocious puberty were observed. HH was diagnosed with brain MRI, which revealed a hypothalamic nonenhanced mass compressing

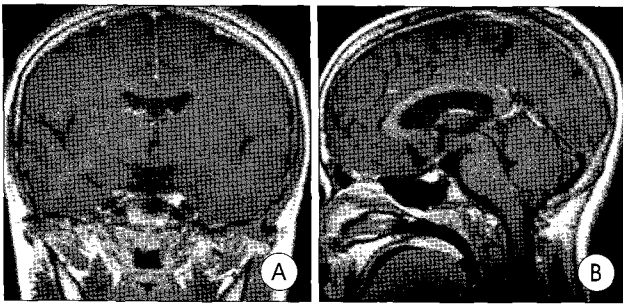


Fig. 1. Brain magnetic resonance images demonstrate a non-enhanced hypothalamic mass measuring 11mm in diameter in T1-weighted coronal (A) and sagittal (B) view. The mass is adherent to tuber cinerium and minimally compresses surrounding structures.

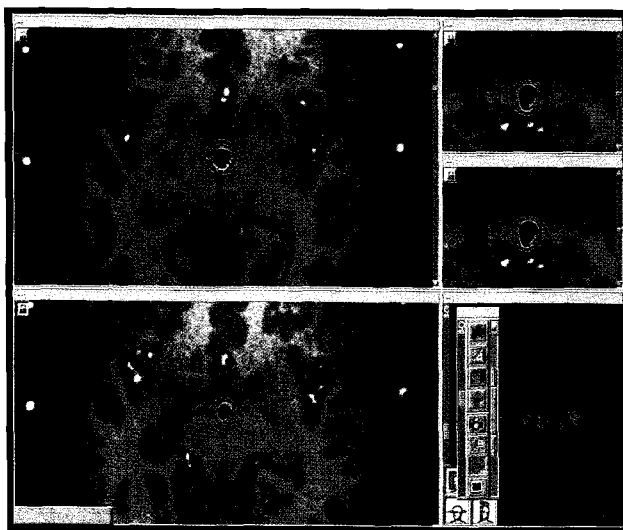


Fig. 2. The image for gamma knife radiosurgery planning for case 1. Margin dose of 18Gy is applied at 50% isodose line in total volume of 508.2mm³.

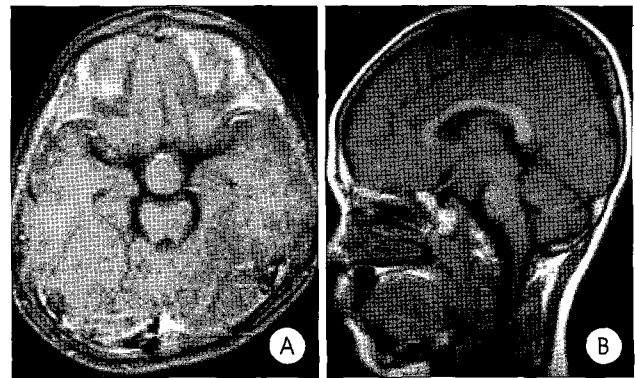


Fig. 3. Brain magnetic resonance images demonstrate a non-enhanced hypothalamic mass measuring 18mm in diameter in T1-weighted axial (A) and sagittal (B) view. The mass is adherent to optic chiasm.

surrounding structures (Valdueza type IIb) (Fig. 3). GKRS was performed to a maximal diameter of 18mm with target volume 2,100mm³; a shot in which margin dose of 17Gy was delivered to the 50% isodose area. At one month post-GKRS, the epileptic activity, speech and behavior were all observed to start improving. The patient demonstrated 60% reduction of gelastic seizures in frequency at one year after GKRS. On follow-up 30 months after GKRS, 50% reduction of seizure frequency was observed with reduced dose of medication.

Case 3

A 6-year-old girl had met normal development until she exhibited the first episode of gelastic seizure at the age of 6 months. While she exhibited seizure activities 5 times a day, the medication failed to abolish or reduce seizure. Physical examination revealed delayed development and precocious puberty. Brain MRI indicated a hypothalamic mass with evident compression of surrounding hypothalamic structures (Valdueza type IIb). She underwent GKRS to the mass lesion; the margin dose of 18Gy was placed at the 50% isodose line and the volume was 1,100mm³ with a maximal diameter of 16mm. She experienced gradual reduction of frequency of seizures, leading to 30% reduction at 21 months after GKRS.

Discussion

Surgical resection has been assumed to be a plausible therapeutic option for medically intractable gelastic epilepsy associated with HH, based on the neurophysiological evidence that the HH lesion itself has intrinsic epileptogenicity^{7,9}. Even though favorable outcomes using various surgical approaches have been reported by several studies^{8,11,15,17}, it has not been readily practiced due to the concern for potential morbidity and mortality that would be expected when deep seated lesions around hypothalamus and optic apparatus are surgically removed. Valdueza et al., moreover, described that sessile lesions

tends to produce epileptic symptoms more often than any other types, while sessile lesions may be more vulnerable to surgical complications than pedunculated ones because of their ambiguous border with surrounding hypothalamic structures¹⁷.

In the efforts to attain the control of intractable seizures without serious surgical complication, stereotactic radiofrequency thermocoagulation for HH lesions has been tried and the anecdotal reports are currently available in the literature. Some described excellent results without adverse effect^{5,7}, while others reported partial or delayed improvement of the epileptic activities with side effects including sensory change and hypothalamic dysfunction after radiofrequency lesioning^{10,12,15}.

Over the last few years, radiosurgery has been recognized as another alternative to surgical resection for controlling seizures of HH and several studies have been presented its outcome on gelastic epilepsy associated with HH^{1,2,4,6,9,13,16}. Majority of the studies, mostly using GKRS, have shown good results of near cessation or meaningful reduction of seizure along with occasional observation of additional behavioral and cognitive improvement^{2,4,6,13,16} except few reports of unfavorable outcome⁹. In a multicenter retrospective study which analyzed 10 cases of HH treated with GKRS^{12,13}, they demonstrated that there was a correlation between the dose delivered to the HH lesions and the efficacy of seizure control, and that the cessation of seizure may not be probable with margin dose below 13Gy. When they analyzed the results of 8 patients who had follow-up of more than 12 months, all exhibited clinical improvement : four became completely seizure-free, two experienced disappearance of generalization with rare partial seizures, and the other two showed modest improvement. Among 8 patients, total three patients had received doses below 13Gy and none of them experienced seizure cessation; five had radiation more than 17Gy, four of whom could become seizure-free after GKRS. They also suggested that sporadic failure of GKRS might be partly attributed to incomplete coverage of dose in the area close to optic pathways. The authors proposed the possible mechanism underlying the cessation of the seizure after GKRS in the patients with HH based on the evidence from an experimental model : GKRS may modify an epileptogenic cortex sufficiently to reduce or abolish the epilepsy, while remaining the functional role of the cortex¹⁴.

All three patients who underwent GKRS in our study showed abolishment or reduction of seizure activities without demonstrating any adverse effects. Although longer follow-up for visual and hormonal functions is necessary to determine overall therapeutic safety in these cases considering delayed adverse effects of the irradiation, the patients were all without major complications related to the radiosurgical procedures during the follow-up. A further study with more cases is needed to determine the clinical efficacy of GKRS on HH in epileptic control.

Conclusion

We concluded that GKRS appears to be a safe treatment modality for surgically inaccessible HH associated with intractable seizure. Considering the rarity of this condition, multicenter study using standardized therapeutic protocol would be required for evaluating the efficacy of GKRS in patients with HH associated gelastic epilepsy.

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