Gamma knife surgery for hypothalamic hamartomas accompanied by medically intractable epilepsy and precocious puberty: experience in Mexico

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Object. Hypothalamic hamartoma is a nonneoplastic malformative mass of neurons and glia in the region of the hypothalamus. Because of its location, open surgery is associated with high morbidity and mortality rates. Gamma knife surgery (GKS) may be an efficient and safe treatment approach, which produces little morbidity. The authors describe the results of GKS in three patients with hypothalamic hamartomas.

Methods. All patients were male, aged 3, 12, and 15 years. The lesions were classified according to the Valdueza scale: one was Type IIb and two were Type IIa. The patients presented with gelastic seizures (15–20 per day), generalized epilepsy, behavioral abnormalities, and alterations of the sleep cycle. Precocious puberty was present in one patient. The Type IIb tumor had a volume of 1.8 cm³, and the Type IIa tumors were 597 mm³ and 530.1 mm³. The lesions received 12.5 Gy, 14 Gy, and 15 Gy, respectively, to the 50% isodose line. The patients were followed for 30 to 50 months. After 3 months, all patients showed improvement of their sleep, behavior, and epilepsy. At the present time, these patients are receiving low-dose antiepileptic agents and have achieved adequate social development and school integration.

Conclusions. Gamma knife surgery appears to be a good, safe, and effective option for the treatment of selected hypothalamic hamartomas. No morbidity or mortality was associated with these three cases.

Key Words • hypothalamic hamartoma • gamma knife surgery • epilepsy

Hypothalamic hamartomas are nonneoplastic malformations. They include heterotopic and hyperplastic tissue resembling gray matter. They usually originate in the region of the tuber cinereum and mammillary bodies, and they vary in size. Valdueza, et al., have published a very complete paper on the subject. Clinically, most patients with HHs suffer from precocious puberty, gelastic epilepsy, as well as other types of seizures and behavioral abnormalities. Gelastic epilepsy is common in association with these lesions and is unresponsive to pharmacotherapy. Many of the symptoms caused by HHs can be cured by microsurgical resection of the lesions; however, the morbidity and mortality rates resulting from surgery in this area are significant. Gamma knife surgery is less invasive and may be well adapted for this indication.

Clinical Material and Methods

Between March 1995 and December 2000, three boys underwent GKS for HHs in our neurosurgery unit. The patients were 3, 12, and 15 years old. Their symptoms included drug-resistant gelastic seizures (15–20/day while receiving triple doses of medication), generalized tonic-clonic attacks, behavioral abnormalities, alterations in the sleep–awake cycle, and, in one patient, precocious puberty. Electroencephalography results were abnormal in all three patients. No campimetric defects were detected.

According to the Valdueza classification, one lesion was Type IIb and two cases were Type IIa. In two cases, the diagnosis of HH was based on MR imaging examination (Fig. 1). The third patient had undergone surgery at another institution so there was histological confirmation of the diagnosis.

Coronal, sagittal, and axial plane MR images were obtained using a 1.5-tesla unit with T₁-, T₂-, inversion-recovery and T₁-Gd-enhanced sequences. Images were obtained while the youngest patient received a general anesthetic and the other two received a local anesthetic.

The total dose, number of isocenters, and treatment time were calculated using GammaPlan software (Elekta Instrument AB, Stockholm, Sweden). The prescription dose at the lesion margin was determined in relation to the risk of radiation damage to the nearby optic pathways and hypothalamus. The margin doses were 12.5 Gy, 14 Gy, and 15 Gy.
respectively. The dose was placed at the 50% isodose line. The volume of the Type IIb lesion was 1.8 cm³, and the other two lesions had volumes of 597 mm³ and 530.1 mm³, respectively. The follow-up period ranged from 30 to 50 months.

Results

All patients exhibited improvement post-GKS. After three months their sleep–wake cycle had improved, as well as their mental and behavioral problems.

In the first Type IIa case, the gelastic seizures disappeared almost completely after 12 months, and the tonic–clonic seizures have not recurred. The patient is still receiving topiramato (100 mg/24 hours).

In the other Type IIa case (the 3-year-old patient), the tonic–clonic seizures disappeared but the gelastic seizures continued at a rate of three per day. He receives no medication because of parental preference.

In the Type IIb case, the tonic–clonic seizures disappeared 8 months after treatment, and the gelastic seizures persisted with a frequency of one per month. The patient continues to receive valproic acid (600 mg/24 hours).

Follow up in all three patients has included clinical evaluation, MR imaging, and campimetry; if possible, every 6 months. No treatment-related complications have been observed to date.

Discussion

Although HHs are not actually tumors, the evolution of the disease is considered to be invariably unfavorable because of the occurrence of several types of seizures, the worsening of electroencephalographic features (progressively marked by generalized discharges), and mental impairment.6–10

The possibility of curing the associated epilepsy with surgical treatment limited to the HH has been suggested by authors of some studies. Unfortunately, according to the classification system proposed by Valdueza, et al.,11 epilepsy associated with HHs is observed only in Types IIa and IIb, which correspond to medium/large sessile HHs broadly attached to the tuber cinereum or mammillary body. Microsurgical resection in this critical area is associated with a high risk of oculomotor palsy, hemiparesis, and visual field deficits, and most epilepsy surgeons have therefore abandoned this approach.10

The unfavorable evolution of this disease, the possibility of curing it through resection without incurring major morbidity, and the high risk of the surgical procedure are the main reasons that led Régis and colleagues6–10 to investigate the potential efficacy of GKS in the treatment of this condition. The two main difficulties they found are the proximity with the optic tract and chiasm and the limitation of the upper part of the lesion, which is frequently indistinguishable from the surrounding hypothalamus.

According to Régis and colleagues,6 although it is not completely understood, a possible reason that GKS is efficacious in treating this disease entity is the possibility that GKS biomodulation can modify an epileptogenic cortex sufficiently to reduce or abolish the epilepsy, while maintaining the cortex’s ability to assume its functional role. In an experimental model, the cholinergic system demonstrated reduced activity, and excitatory amino acid levels were greatly reduced, despite preservation of the inhibitory gamma-aminobutyric acidergic system, as observed on the basis of stable levels of glutamate decarboxylase and gamma-aminobutyric acid.6

To obtain the desired effects, they proposed a margin dose of more than 17 Gy (and no less than 13 Gy); however, they warned that the close relationship of these lesions to the optic pathways makes optimal dose delivery difficult if not impossible in some patients.6,7

Conclusions

Our limited experience with this disease entity supports the findings of others. Patients experienced clinical improvement without any significant morbidity. A multicenter study is required to evaluate the advantages and risks of this treatment.

References

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