

HYPOTHALAMIC HAMARTOMAS

Transcallosal Resection of Hypothalamic Hamartomas, with Control of Seizures, in Children with Gelastic Epilepsy

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OBJECTIVE: Hypothalamic hamartomas (HHs) are associated with precocious puberty and gelastic epilepsy; the seizures are often refractory to antiepileptic medications and associated with delayed development and disturbed behavior. The current opinion is that surgery to treat intrahypothalamic lesions is formidable and that complete excision is not technically achievable. We report our experience with a transcallosal approach to the resection of HHs.

METHODS: Five children (age, 4–13 yr) with intractable epilepsy and HHs underwent preoperative clinical, electroencephalographic, and imaging evaluations. Two patients experienced only gelastic seizures, and three patients experienced mixed seizure disorders with drop attacks; all experienced multiple daily seizures. Patients were evaluated with respect to seizures, cognition, behavior, and endocrine status 9 to 37 months (mean, 24 mo) after surgery. The HHs were approached via a transcallosal-interforniceal route to the third ventricle and were resected using a microsurgical technique and frameless stereotaxy. **RESULTS:** Complete or nearly complete (>95%) excision of the HHs was achieved for all patients, with no adverse neurological, psychological, or visual sequelae. Two patients experienced mild transient diabetes insipidus after surgery. Two patients developed appetite stimulation, but no other significant endocrinological sequelae were observed. Three patients are seizure-free and two patients have experienced only occasional, brief, mild gelastic seizures after surgery, all with reduced antiepileptic medications. On the basis of parental reports and our own subjective observations, the children also exhibited marked improvements in behavior, school performance, and quality of life.

CONCLUSION: Complete or nearly complete resection of HHs can be safely achieved via a transcallosal approach, with the possibility of seizure freedom and neurobehavioral improvements.

Gamma Knife Surgery for Epilepsy Related to Hypothalamic Hamartomas

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

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OBJECTIVE: Drug-resistant epilepsy associated with hypothalamic hamartomas (HHs) can be cured by microsurgical resection of the lesions. Morbidity and mortality rates for microsurgery in this area are significant. Gamma knife surgery (GKS) is less invasive and seems to be well adapted for this indication.

METHODS: To evaluate the safety and efficacy of GKS to treat this uncommon pathological condition, we organized a multicenter retrospective study. Ten patients were treated in seven different centers. The follow-up periods were more than 12 months for eight patients, with a median follow-up period of 28 months (mean, 35 mo; range, 12–71 mo). All patients had severe drug-resistant epilepsy, including frequent gelastic and generalized tonic or tonicoclonic attacks. The median age was 13.5 years (range, 1–32 yr; mean, 14 yr) at the time of GKS. Three patients experienced precocious puberty. All patients had sessile HHs. The median marginal dose was 15.25 Gy (range, 12–20 Gy). Two patients were treated two times (at 19 and 49 mo) because of insufficient efficacy.

RESULTS: All patients exhibited improvement. Four patients were seizure-free, one experienced rare nocturnal seizures, one experienced some rare partial seizures but no more generalized attacks, and two exhibited only

improvement, with reductions in the frequency of seizures but persistence of some rare generalized seizures. Two patients, now seizure-free, were considered to exhibit insufficient improvement after the first GKS procedure and were treated a second time. A clear correlation between efficacy and dose was observed in this series. The marginal dose was more than 17 Gy for all patients in the successful group and less than 13 Gy for all patients in the "improved" group. No side effects were reported, except for poikilothermia in one patient. Behavior was clearly improved for two patients (with only slight improvements in their epilepsy). Complete coverage of the HHs did not seem to be mandatory, because the dosimetry spared a significant part of the lesions for two patients in the successful group.

CONCLUSION: We report the first series demonstrating that GKS can be a safe and effective treatment for epilepsy related to HHs. We advocate marginal doses greater than or equal to 17 Gy and partial dose-planning when necessary, for avoidance of critical surrounding structures.

COMMENTARY

A relatively uncommon structural substrate for epilepsy, hypothalamic hamartomas, are lesions comprised of neurons, glia, and myelinated fibers. These heterotopic lesions are associated with seizures, cognitive and behavioral impairment, and precocious puberty, although they may be asymptomatic. Gelastic seizures, in which patients display inappropriate and stereotyped laughter that is typically not accompanied by

mirth, are often associated with hypothalamic hamartomas, although patients with these lesions may experience other seizure types.

Epilepsy associated with hypothalamic hamartomas is commonly refractory to pharmacological management, and surgical attempts to treat this syndrome have been met with largely discouraging results. Various surgical techniques have been used to resect or ablate hypothalamic hamartomas, however reports of postoperative seizure control have been mixed, and morbidity has been concerning.

The two series presented here report two newer approaches to the surgical treatment of epilepsy associated with hypothalamic hamartomas. The article by Régis et al. provides preliminary evidence for the safe and effective use of gamma knife surgery for the syndrome. At a mean follow-up of 35 months, all eight patients exhibited improvement in seizure control, with four seizure free. No significant adverse effects were noted. The report by Rosenfeld et al. describes the use of a transcallosal-interforniceal microsurgical approach to treat five children with intraventricular hypothalamic hamartomas. All patients realized significant seizure control, with three being seizure free, at a mean follow-up time of 24 months. Neuroendocrine sequelae were relatively mild and transient.

These two preliminary reports provide encouraging results, although the number of patients treated in these series is small. Further experience in treating this relatively uncommon syndrome will be required in order to determine which technique is the most advantageous for patients in terms of long-term seizure control and complication rate.

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