# Treatment Options for Hypothalamic Hamartomas—No Laughing Matter

**Surgical Management of Hypothalamic Hamartomas with Epilepsy: The Stereoendoscopic Approach.** Procaccini E, Dorfmuller G, Fohlen M, Bulteau C, Delalande O. *Neurosurgery* 2006 Oct;59(4 Suppl 2):ONS336–ONS346. OBJECTIVE: Hypothalamic hamartomas (HHs) require surgical treatment in patients presenting with refractory epilepsy. METHODS: The authors report on a single-center series of 33 patients (24 males, 9 females) who underwent surgery between January 1997 and April 2004. They experienced several types of seizure (gelastic, tonic, partial, atonic, generalized tonic-clonic, dacrystic, infantile spasm, mental retardation, and behavioral and endocrinological abnormalities). Forty-nine interventions were carried out. Every patient, with the exception of the first, underwent hamartoma disconnection (pterional approach, six patients; endoscopy, 15 patients; both, 11 patients). The endoscopic approach was carried out with a frameless stereotactic system to enhance feasibility and efficacy of the disconnecting procedure. RESULTS: Surgery-related neurological complications occurred in two patients, both after a pterional microsurgical approach. Furthermore, two patients experienced panhypopituitarism and one patient experienced transitory central insipid diabetes. All patients but one showed recovery or considerable improvement of their epilepsy (Engel Class 1, 48.5%; Engel Class 2, 3%; Engel Class 3, 45.5%; mean follow-up duration, 1 year 7 months). CONCLUSIONS: According to the proposed classification of sessile HH into four types, the best candidates for endoscopic disconnection are Type 2 and Type 3 HHs. In the present series, 90% of patients affected by Type 2 HH became seizure-free and the remaining 10% improved; of those with Type 3 HH at presentation, 35.3% recovered and 60% improved. Neuropsychological and endocrinological test results showed improvement in many patients. Data from our series demonstrate that frameless stereotactic endoscopic disconnection should be considered as the treatment of choice in the presence of favorable anatomic conditions.

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## COMMENTARY

Hypothalamic hamartomas represent one of the least common causes of medically intractable epilepsy, yet it can hardly be considered an orphan disease. Worldwide interest in this unusual form of cortical dysplasia, particularly within the neurosurgical community, has blossomed over the last 5 years as a result of a newfound understanding of the pathophysiology of the epileptogenesis and more importantly, on the success of a variety of elegant and sophisticated high-tech surgical approaches to treating the disease.

Hypothalamic hamartomas are nonneoplastic overgrowths of normal appearing tissue comprised of disorganized neurons and glia that are lacking the enlarged "balloon cells" characteristic of focal cortical dysplasia (1). Most occur sporadically, although 10% are associated with Pallister-Hall syndrome (1). Based on the anatomic relationship between the hamartoma and the hypothalamus, they can be divided into two main subtypes—pedunculated and sessile. The pedunculated lesions do not arise within the hypothalamus but attach with a narrow base and project outside the ventricle. These lesions are less often associated with seizures and more likely present with precocious puberty. Neuropsychological compromise is less frequent. Precocious puberty can be treated medically with gonadotrophin-releasing hormone (GnRH) agonists and require surgery only when resistant. Although hamartomatous cells stain for GnRH, it is unclear if they release GnRH or transforming growth factor-$\alpha$, which is trophic for release of GnRH from normal hypothalamus (1). In contrast, the sessile lesions lie within the hypothalamus and often cause seizures and variable degrees of mental retardation and aggressive behavior, particularly if the seizures are not well controlled. Seizures consist of gelastic attacks, which can evolve into drop attacks, tonic, tonic–clonic, and secondarily generalized seizures. Whole-cell recordings from these hamartomas have shown that most cells are small GABAergic inhibitory neurons that exhibit intrinsic pacemaker-like behavior (2). Precocious puberty also occurs with sessile lesions.

Initially, the etiology of the seizures associated with hypothalamic hamartomas was unclear. However, based on ictal perfusion studies and depth electrode recordings, it became clear that the seizures arose from intrinsic epileptogenicity of the hypothalamic hamartoma itself (3,4). Although the first surgical excision was performed as early as 1969 (5), even later attempts to remove these lesions from below with a subtemporal, subfrontal, or pterional approach met with high complication rates. More success was obtained removing the lesions from above using a transcallosal, interforniceal approach, first popularized by Rosenfeld (6). Using this approach, rates of seizure-freedom are as high as 54% with 90% having a 90% reduction in seizure frequency (7). Permanent morbidity rates, however, are not insignificant with 8% diabetes insipidus, 8% memory impairment, 4% hemianopsia, and 19% hyperphagia (7).

Less invasive methods of eradicating the hypothalamic hamartomas include radiofrequency thermoablation (8), interstitial brachytherapy (9), and stereotactic radiosurgery (10). The latter technique reports seizure-free rates of 37% after a delay of 6–12 months with 60% having a dramatic reduction in seizures and no permanent complications (10). However, the adverse effects of radiation may take several years to manifest. Although promising, this modality may be useful only for smaller lesions, which also have the best surgical outcome.

The stereoendoscopic technique described by Procaccini et al. introduces yet another treatment option for consideration. The authors have modified the Rosenfeld transcallosal approach and made it less invasive by using an endoscope passed through the foramen of Monro. In addition, drawing on the theoretical basis for the functional hemispherectomy, the authors argue that a disconnection of the hamartoma from the hypothalamus should be sufficient to eliminate seizures and a complete resection is not required. However, based on the anatomy of the lesion, the endoscopic approach alone is only applicable in 50% of their cases, whereas the remaining patients required an additional pterional craniotomy to disconnect those parts of the hamartoma that could not be reached from above. Overall a 49% seizure-free rate was reported with 97% showing improvement, although multiple surgeries were required for several patients. In their study, complications were associated only with the open pterional procedure (27%) and not with the stereoendoscopic approach. However, a more recent presentation revealed a complication rate of 10% for the stereoendoscopic approach (11).

How is the referring physician to decide between these seemingly similar treatment options? As with most surgical lesions, the easy ones are easy and the hard ones are hard, regardless of the surgical approach. Clearly, the small lesions within the third ventricle can be effectively managed using either modality, with a similar outcome with respect to seizure-freedom and complications. Currently, the choice of surgical procedure will depend on the abilities and confidence of the treating surgeon. The approaches that are most technically demanding can be difficult to proliferate to other centers. Radiosurgery is less "operator dependent" and may be a reasonable treatment in lower volume centers. Whether late complications arise from radiosurgery remains unknown and will require additional follow-up studies to determine. Minimally invasive endoscopic approaches have been shown to offer real advantages over open surgery in minimizing morbidity and are becoming the standard of care in the treatment of diseases, such as colloid cysts, pituitary adenomas, and noncommunicating hydrocephalus. As endoscopic microinstrumentation continues to improve, this modality will play an increasing role in the treatment of hy-

pothalamic hamartomas, perhaps in combination with endoscopic approaches from below, either through an eyebrow incision or an extended transsphenoidal route. Indeed, at a recent medical meeting, the authors, previously espousing the open transcallosal approach, presented data in favor of the minimally invasive endoscopic approach (12).

Although it has been said that "laughter is the best medicine," it appears that medicine is finally besting laughter.

*by Theodore H. Schwartz, MD, FACS*

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