Management of hypothalamic hamartomas: progress due to alignment of the stars

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The February 2011 issue of Neurosurgical Focus is devoted to a discussion of the recent explosion of information regarding the management of a rather rare birth defect that can have devastating effects on children and adults. The actual prevalence of hypothalamic hamartoma (HH) cannot yet be estimated because the clinical presentation of patients is so variable, and until very recently the diagnosis was extremely difficult. Some patients are minimally symptomatic, and it must be presumed that there are many in this group as well as a significant number of asymptomatic patients in whom the diagnosis is not made.

Historical Perspective of HH

Before approximately 1990, little was known about HH. For the most part a diagnosis was made when imaging studies showed very large lesions thought to be brain tumors within and below the third ventricle. Surgical exploration and biopsy revealed that these masses were composed of normal neuronal elements and glia, and a clear interface between the mass and the native hypothalamus could not be established. The relationship between HH and both isosexual precocious puberty and epilepsy was known, but until the 1980s there were no reports of surgical management except for the abovementioned biopsy. 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 CT scanner was installed in the US in 1973. Typical of these reports was an early publication by Machado and colleagues from the Hospital for Sick Children in Toronto. They reported the case of a child with refractory epilepsy surgically treated via the pterional approach. The patient had an excellent outcome, including freedom from seizures and no postoperative morbidity. Interestingly, these authors noted that they found a mass lesion within the hypothalamus, and its consistency and color were indistinguishable from the native hypothalamus. They stated that the entire mass was removed without difficulty. How these authors decided where to stop the resection was unclear from the operative description; however, the take-home message was that seizures in the context of HH are definitely related to the lesion itself and can be treated or ameliorated by surgical removal of the mass.

There are 2 types of HH and they overlap significantly. Sessile HH lesions with broad-based attachments to the hypothalamus, especially within the third ventricle, are primarily associated with epilepsy and especially with gelastic seizures. On the other hand, HHs that cause isosexual precocious puberty are more likely to be pedunculated lesions that “hang” below the tuber cinereum. Surgical strategies for the latter were more understandable, and soon thereafter the successful treatment of precocious puberty by removing the lesions began to be reported.1,11,18 In the US, this form of treatment has fallen from favor with the development of effective hormonal management. In China, however, it remains the treatment of choice because of the difficulty in obtaining and affording the hormonal analogs.7

Development of Modern Approaches to the Surgical Management of HH

The past decade has seen a dramatic increase in the understanding and management of HH, especially in terms of intractable epilepsy. These advances relate to the synchronous development of the technology needed 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. By the turn of the millennium, three major technological advances blossomed. Once considered in the realm of science fiction, but by that time fully realized, these three advances were MR imaging, neuronavigation, and the Internet.

Before the mid-1980s, only very large HHs could be diagnosed. To do so usually required the injection of a dye used for myelography and careful observation of the basal cisterns. All but the largest of these lesions were missed. With the development of MR imaging technology, particularly with multiple sequences, HHs that were only a few millimeters in diameter could be diagnosed within the third ventricle in patients with signs of precocious puberty or gelastic epilepsy.
This new information, plus the knowledge gained from the few published case reports, led to the thought that surgical removal might be appropriate for selected patients with HH. Before that time the standard approach to the hypothalamus was via a pterional or orbitozygomatic approach. 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.

The group from Melbourne, Australia, including neurosurgeon Dr. Jeffrey Rosenfeld and epileptologist Dr. Simon Harvey, explored the possibility of attacking HHs from above by using a transcoccal interfermncal approach. In 2003 they reported on their first 12 cases utilizing this approach with encouraging results. A year later their series had increased to 45 cases. The personal history associated with this set of accomplishments is highlighted in the first article in this issue by Rosenfeld.

At the same time, many families affected by the rages of HH were desperate for information. Essentially all were told that, yes, the problems their loved ones faced were due to the HH but that nothing could be done surgically to help them. At this point, the Internet was available to facilitate international communication. Several families affected by HH established a website, which served to form a support group and announced new findings. This website discovered the advances of the Melbourne group, and its membership became aware that there was indeed hope for treatment. As a result, a significant number of patients were referred to Australia for treatment. The group there collected a large series of patients in a very short period, allowing validation of the surgical approach and its value in improving the quality of life of individuals affected by HH.

The final technological advance needed was the general availability of frameless stereotactic neurosurgery known as neuronavigation. A neurosurgeon removing 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 MR imaging 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.

Multiple strategies are now available for the surgical management of HH. It is possible to tailor the treatment plan for each affected individual. It is increasingly clear that multiple surgical approaches or approaches from various trajectories, supplemented with Gamma Knife treatment, may be needed to safely treat large HHs causing both the behavioral abnormalities, which are the rule rather than the exception, and the seizure disorder. Aside from open craniotomy for HH, several other approaches are of value. Regis and his colleagues from Marseille have shown that in selected patients good results can be expected from Gamma Knife therapy. Delalande and Fohlen have been continuing advocates for the resection of HHs within the third ventricle by using the endoscope to remove or disconnect the lesions. The idea that these lesions can be managed using the quicker and somewhat safer option of endoscopic removal was suggested to me by Dr. Jung Uhn Choi at a neuroendoscopy meeting in Naples in 2003. Although I do not use this approach exclusively, I have found that most HHs within the third ventricle are excellent candidates for this type of excision. Radiofrequency obliteration and stimulation of the mamillothalamic tract have also proved useful in the management of HHs associated with intractable epilepsy.

Within this collection of works, there is a general discussion by Wait et al. of the surgical strategies that have proved useful in the management of HHs at the Barrow Neurological Institute and a review by Pati et al. of patients who have needed subsequent surgery for this lesion. There is also a discussion of the dreaded complication related to the hypothalamus that has previously been associated with the resection of large craniopharyngiomas. That complication is the severe cyclical problems with sodium metabolism that can occur when dealing with giant HHs. This complication is frustrating, and the fact that it has only followed the resection of giant HHs has led us to consider staging the surgery for the largest of these lesions; see the article by Abila et al.

Conclusions

At a very few centers the concurrence of technology has resulted in the ability to treat a relatively large number of patients with HH. The result has been a rapid and dramatic increase in our knowledge base of this disorder and in the improvements in outcomes in these patients. A great deal of credit for this progress goes to the individuals and families who have refused to accept that there was no hope for improvement. They have shown profound courage in dealing with these difficult problems. For their stories and more information about this amazing community, I refer you to the following website: www.hopeforhh.org. (DOI: 10.3171/2011.2.FOCUSIntro)

References