Stereotactic surgical approach to hypothalamic hamartomas

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ABSTRACT – Hypothalamic hamartomas are often associated to a progressive epileptic encephalopathy. Non-invasive data indicates that destruction or isolation of the hamartoma may stop seizures. We present data on patients who underwent stereotactic radiofrequency with or without endoscopy. Epilepsy improved in 60% of patients with minimal morbidity. This approach was less succesful in large lesions. These results indicate that this approach should be considered in patients with small/medium lesions.

KEY WORDS: hypothalamic hamartoma, gelastic epilepsy, surgery

Hypothalamic hamartomas can be associated with precocious puberty and gelastic epilepsy. Over the past several years, the syndrome of hypothalamic hamartoma and gelastic seizures (HHGS) has been refined by a number of investigators [1-3]. Most characteristically, patients with HHGS syndrome present with gelastic seizures early in life followed by a progressive epileptic syndrome most typically with multifocal seizures or a secondary generalized epileptic encephalopathy. Patients often develop progressive behavioral and cognitive problems. Resistance to antiepileptic drugs, ketogenic diet and other, non-surgical treatments is common [4].

In 1997, we reported on three patients with this syndrome and intractable epilepsy [5]. This study conclusively demonstrated that gelastic seizures were associated with intrinsic epileptogenesis from the hypothalamic hamartoma, as confirmed by ictal SPECT and stereotactic depth EEG recordings. Recent experience from other centers confirms that in most patients, the generator of ictal and interictal activity is localized to the hypothalamic hamartoma [6]. Our early experience also suggested that radiofrequency lesioning of the hamartoma

in one patient had a favorable outcome on seizures, cognition and behavior. This and recent reports have propelled the development of surgical approaches to these lesions, that include the traditional pterional method, disconnection, gamma knife radiation, and trancallosal resection, which are discussed in this volume by others.

Because of the higher morbidity associated with traditional procedures, we have developed a minimally invasive surgical approach to these patients, with relatively low morbidity and good results. In this study, we present our experience using stereotactic and combined endoscopic radiofrequency lesioning to treat this catastrophic epilepsy syndrome.

Patients and methods

Twelve patients with hypothalamic hamartomas and medically intractable gelastic seizures were evaluated and underwent surgery at the University of Alabama's Birmingham Epilepsy Center between 1995 and 2001. Presurgical evaluation included routine EEG, extended EEG video monitoring with scalp and sphenoidal elec-

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trodes and neuropsychological studies.

Magnetic resonance imaging studies were performed in all patients. This included T2-weighted, T1-weighted, and three-dimensional volume sequences. All patients underwent interictal and ictal SPECT with HMPAO. Details of the MRI and ictal SPECT methodology have been reported in detail previously. Qualitative and quantitative analysis of SPECT images were carried out according to previously published methods.

Surgical technique

Patients #1 through #8 underwent stereotactic depth EEG electrode implantation studies and subsequently underwent radiofrequency lesioning. Patients #9 to #12 underwent endoscopic surgery, with acute intraoperative depth EEG followed by radiofrequency lesioning, and in some patients, endoscopically guided, partial resection. For the first eight patients, the procedure consisted of a two-stage investigation. In Stage I, a stereotactic frame-based MRI was obtained, and under sedation, stereotactic, depth EEG electrode placement was performed using the frontal approach into the hamartoma. The number of contact electrodes varied between 3-5 depending on the size of the hamartoma and surgical planning. We used custom-made, platinum electrodes with a 0.5 mm recording surface and 0.5 mm intercontact distance. All patients but one underwent implantation of one electrode. The remaining patient was implanted with two depth electrodes due to the size of the lesion. Prolonged EEG video monitoring was obtained until seizures were recorded (mean: 3 days). Electrical stimulation was carried out at the bedside to reproduce typical ictal events. Once confirmation and recording of ictal activity were obtained, the patient was taken back to the operating room for Stage II surgery. During Stage II, a stereotactic MRI frame was again placed under local anesthesia with mild sedation. The patient was taken to the OR and, if an adult, was kept awake. If a child, the patient was under general anesthesia. A stereotactic, radiofrequency, thermocoagulation probe was placed using the same coordinates as for the depth electrode placement. Prior to thermocoagulation, the electrode was stimulated to reproduce typical seizures. Following stimulation, stereotactic thermocoagulation was carried out by heating the probe to 78°C for one minute. The probe was then removed, followed by the frame, and the patient was taken to the NICU for 24 hours' observation. An MRI was obtained at 24 hours following lesioning.

For patients #9 to #12, image-guided endoscopy through the third ventricle was used to visualize placement of the radiofrequency probe and/or remove portions of the hamartoma via microinstrumentation. Under direct visualization, a 3-contact depth EEG electrode was placed in the hamartoma for EEG recording. Following satisfactory intraoperative EEG recordings, patients underwent endoscopically-guided partial resection and radiofrequency ablation of the hamartoma. The patients were then taken back to the NICU for recovery, and an MRI was obtained 24 hours post-operatively. Patients were discharged home at 36-48 hours post-operatively if stable. Post-operative follow-up was obtained at one month, and thereafter every three months. Medication adjustments were done according to the patient's clinical status.

Seizure outcome was classified using a modified Engel's outcome scale. Class I patients were seizure-free, class II were those with a 90% or more improvement in seizure frequency and Class III were those with a 50-90% reduction in seizures. Class IV was reserved for those without improvement.

Results

Clinical features

Clinical features were consistent with the typical HHGS syndrome. The age at time of surgery, gender, clinical features and surgical follow-up are presented in *table 1*.

Surgical results

Stereotactic radiofrequency technique

Patients #1 through #8 received stereotactic radiofrequency lesioning preceded by chronic depth EEG electrode recordings. At follow-up, (mean 33 months), three patients were in Class I, two patients were in each Class II and III, and one patient was in Class IV. Complications in this group included transient third-nerve palsy in one patient.

Endoscopic technique

Four patients underwent endoscopic visualization of the hamartoma, with a combination of both radiofrequency and partial resection. Two patients are Class I, one patient is Class II, and one patient is Class III outcome. Complications included brain stem infarction and death in one and transient memory loss in another patient. Overall, eight patients (67%) were either Class I or II, with the remaining patients (33%) Class III or IV.

Major improvements in social disposition have been reported by the families. This is interestingly independent of seizure status. Improvements in attention span and concentration have also been reported by most patients. In patient 5, who had evidence of autistic behavior, there has been a dramatic change, with ancillary language development and new learning skills. Improvements in the behavioral and cognitive domains have contributed to an improved quality of life for the patients and their families.

Endocrinological abnormalities were only observed in one patient (< 10%), following a second radiofrequency lesioning. This patient developed increased appetite, with hyperinsulinemia. Although her weight was above the

Table 1. Clinical and surgical results

Pt	Age	Elect stim	1st Surgery	Hamartoma Size	# Surg	Procedure	Complications	F/U (Mos)	Sz reduction
2	17	-	12/95	large	3	RF	none	72	50%
4	6	+	7/99	large	2	RF	none	36	25%
9	10	+	5/00	large	2	RF, Endo Res	none	36	80%
10	31	NA	4/01	large	1	Endo Res	none	24	100%
11	18	NA	4/01	large	1	Endo res	brainstem infarct/death	24	50%
1	30	+	6/95	med	1	RF	none	70	90%
3	16	+	2/99	med	1	RF	none	49	90%
8	14	+	3/00	med	2	RF	none	36	90%
7	19	±	12/99	med	2	RF	Trans 3rd N palsy	38	50%
5	2	+	7/99	small	1	RF	none	40	100%
6	30	±	12/99	small	2	RF, endo RF	trans memory loss	37	50%
12	15	NA	8/01	small	1	Endo RF	none	18	100%

RF: Radiofrequency

95th percentile, the parents also had a history of marked obesity in the family. No other endocrinological abnormalities were reported. In particular, no appetite, weight loss, or changes in temperature were reported by the family of patients.

Discussion

Growing interest in the treatment of hypothalamic hamartoma has led to the surgical and radiosurgical (gamma knife) treatment of these lesions. Each approach has its advantages and disadvantages and each needs to be evaluated on both the success rate and the complication rate [7-11]. These approaches are discussed in detail in this volume.

Surgical removal of hypothalamic hamartomas has been sporadically reported in the literature since 1969 [12]. Resection through subfrontal, transylvian, subtemporal, or supratemporal pterygial regions have been reported or suggested in the literature. A number of complications have occurred, including thalamocapsular infarctions with hemiplegia, transient third nerve palsies, diabetes insipidus, hyperphagia, and other complications [13]. More severe complications, including death, have occurred in a number of patients in the US, Europe and Japan, but these have not been reported in the literature (Kuzniecky, personal communication). The dismal out-

comes led to major resistance to surgical intervention until recently.

In our first series that included eight patients, we used the stereotactic approach for depth EEG electrodes for recordings, prior to radiofrequency lesioning. The advantages of this approach include EEG confirmation of interictal and ictal activity, since there are patients that appear to have either more than one epileptogenic area on scalp EEG or more than one seizure type. The other major advantage in the early days of surgery for HH, was the possibility of confirmation of seizure onset by induction through direct electrical stimulation. Radiofrequency lesioning was performed in a second stage with electrical stimulation prior to lesioning. Again the advantage of this approach is the relatively low morbidity of stereotactic implantation as no patient in our series developed a single complication from either the hamartoma depth EEG implantation or the radiofrequency probe placement. This has been reported by other groups as well [14].

However, the limiting factors of our approach are twofold. Firstly, even with stereotactic computerized planning, there is a small possibility of missing the target by a few millimeters. We encountered this problem in two patients who had relatively small hamartomas and fibrotic tissue. In these patients, the tip of the radiofrequency probe was not in the optimal position for lesioning. Secondly, without intraoperative MRI, electrode placement is blind. In most cases this problem can be overcome by electrical stimu-
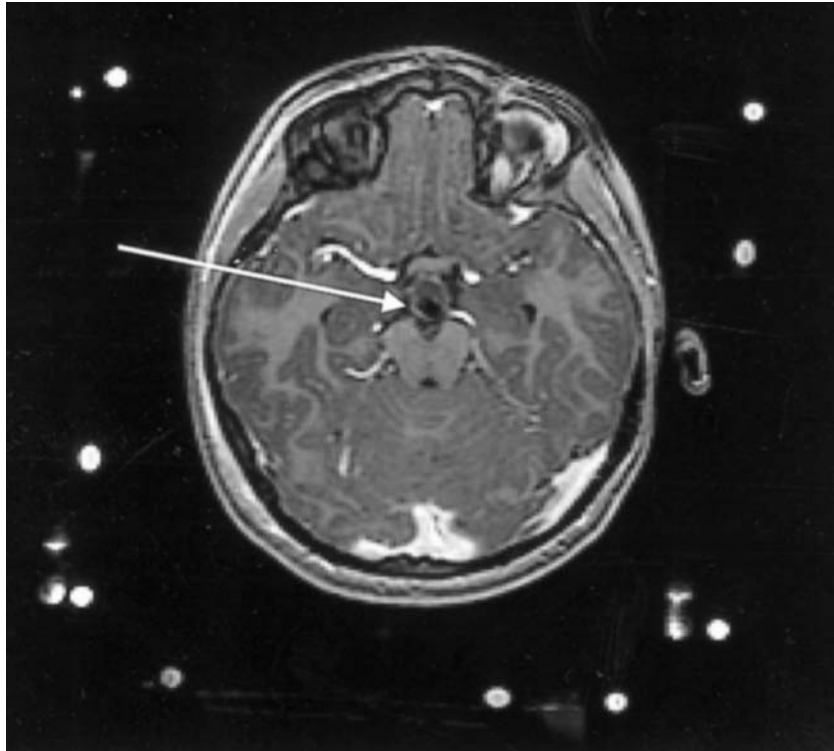
Figure 1. *MRI frame-based image.* *Stereotactic implantation of the hamartoma with a depth electrode for EEG recordings. Note electrode in the hamartoma (arrow).*
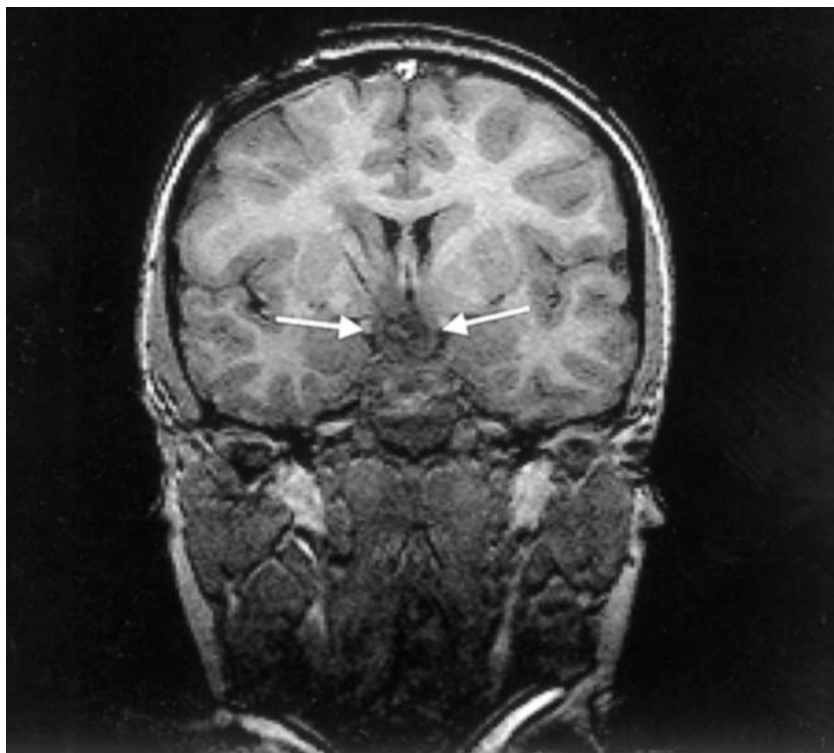

Figure 2. *Coronal T-1W MRI.* *This MRI was obtained 24 hours after radiofrequency thermocoagulation. Note the area of hypointensity within the hamartoma with mild edema (arrows). Tract through the frontal lobe is observed.*

Figure 3. *Saggital T1-W MRI in a 2 year-old child following radiofrequency lesioning.* Note the ring area in the center of the hamartoma (arrow) corresponding to area of radiofrequency lesioning.

lation and reproduction of seizures. However, this is not possible in patients under general anesthesia.

The above technical problem is what led us to change our purely stereotactic radiofrequency approach and use a combination of endoscopy for direct visualization, and radiofrequency ablation for destruction of the HH. This approach used in the last four patients, resulted in direct visualization of the target with a higher rate of lesion destruction. This approach is slightly more invasive than the purely stereotactic approach, but the relative advantages of direct visualization of HH is, in our experience, invaluable and a relatively worthy consideration.

The main weakness of the stereotactic approach is that the seizure-free rate is lower than with other, open approaches. This is certainly true in patients with large lesions, as it is unlikely that a small probe will destroy a large hamartoma. However, for medium or small size hamartomas, the stereotactic approach may be appropriate since destruction of the lesion can be achieved while the operative risks and post-operative complication rates are much lower than with any of the open cranial procedures [7].

The outcome of any of the treatments proposed for HH should be the halting and reversal of the progression of the underlying condition and its symptoms, i.e. epilepsy, cognitive impairment and behavioral disturbances. The stereotactic approach has inherently lower morbidity compared to open approaches, but at the same time has a lower seizure-free rate since it is clear that in some patients, complete isolation, resection or destruction of the hamartoma is necessary for seizure-freedom. The ultimate therapeutic approach for patients with HH, whether it is open surgery, stereotactic surgery or gamma knife surgery [9, 15], will depend on the balance between the long-term results of any of the methods discussed in this supplement and the morbidity and operative risks associated with the procedures *(figures 1, 2 and 3)*. □

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