Long-term outcome after emergency resection of hypothalamic hamartomas for status gelasticus

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Object. Gelastic seizures are epileptic events characterized by bouts of laughter. They are rare and mostly associated with hypothalamic hamartomas (HHs). Status gelasticus, a rare form of status epilepticus, is defined as a prolonged cluster of gelastic seizures (>20–30 minutes) without necessarily involving loss of awareness between seizures. Emergency resection of the hamartoma is highly effective in these situations and should be considered as early as possible. The authors retrospectively reviewed their surgical cases to document the success, complications, and long-term follow-up after emergency resection of HHs for status gelasticus.

Methods. The authors report on a retrospective case series from a single tertiary care center. Three patients who presented with status gelasticus underwent emergency resection of HHs. Demographic details, seizure history, medical treatment, and postoperative follow-up data were evaluated. Long-term follow-up (minimum 2 years) data were obtained either from the last clinic visit notes or via telephone and e-mail contacts. The institutional review board at St. Joseph’s Hospital approved this study.

Results. In the last 7 years, of 157 patients who underwent HH resection, the resection was performed on an emergency basis for status gelasticus in 3 cases. At emergency surgery, these 3 patients ranged in age from 9 months to 3.5 years. All of the patients were boys. Delalande and Fohlen Type II, III, and IV lesions were present in the 3 patients. Surgical approaches for resection of HH included an orbitozygomatic, transcaldosal anterior interfornical approach and endoscopic resection. Status gelasticus was terminated following emergency surgery in all cases, and 1 patient was seizure free. Postsurgical complications included, in 1 case, a small right thalamic infarct with mild transient left hemiparesis, which completely resolved within 2 days. Within 2 years of their original surgery, 2 patients underwent further elective surgeries (endoscopic resection and radiosurgery for persistent symptomatic seizures). Follow-up since their most recent surgery ranged from 8 months to 2 years. Two patients were seizure free and 1 patient had greater than 50% reduction in seizures.

Conclusions. Status gelasticus associated with HHs can be successfully terminated by emergency resection of the HH. Long-term follow-up in the present series suggests good seizure freedom results or at least greater than 50% reduction in seizures, although repeat operations were necessary. (DOI: 10.3171/2010.12.FOCUS10249)

Key Words • hypothalamic hamartoma • gelastic seizure • status gelasticus • status epilepticus

Gelastic seizures are epileptic events characterized by bouts of laughter and were first described by Trousseau in 1877. The conscious state may not be impaired, although this is often difficult to assess, particularly in young children. Gelastic seizures have been related classically with HHs, which are rare congenital malformations of the inferior hypothalamus and tubercinenum. Status gelasticus has been defined as a prolonged cluster of gelastic seizures (that is, for more than 20–30 minutes, a duration similar to that of status epilepticus), but without necessarily involving loss of awareness between seizures. These extremely frequent to near-continuous gelastic seizures fully impair the patient and family. Gelastic seizures, especially status gelasticus, are characteristi-
were included in the study. Demographic details, seizure history, presurgical evaluation, medical and surgical management of status gelasticus, and postoperative and long-term follow-up data were evaluated. Management of status gelasticus and presurgical evaluation were conducted by a team that included dedicated pediatric neuroradiologists, pediatric neurosurgeons, pediatric epileptologists, pediatric endocrinologists, and neuropsychologists. The Delalande and Fohlen Classification was used to describe HH. The Delalande and Fohlen Classification consists of 4 lesion types: Type I has a horizontal implantation plane and may be laterIALIZED on 1 side (parahypothalamic), Type II has a vertical insertion plane and resides in an intraventricular location (intrahypothalamic), Type III is a combination of Types I and II, and Type IV includes all giant hamartomas.

In addition to the follow-up interview conducted by our neurologist and endocrinologist, long-term follow-up was maintained via telephone and email contacts. A self-reported questionnaire about change in seizure frequency was used by the patient and family members.

In the last 7 years, of the 157 patients in whom an HH was resected, 3 underwent emergency resections for status gelasticus. Age at time of emergency surgery ranged from 9 months to 3.5 years. All of the patients were boys. Delalande and Fohlen Type II, III, and IV lesions were present in the 3 patients. Emergency surgical approaches for resection of HH included orbitozygomatic, transcallosal anterior interforniceal approach, and endoscopic resection. Status gelasticus was terminated following emergency surgery in all 3 cases. Postsurgical complications included, in 1 case, a small right thalamic infarct with mild transient left hemiparesis, which completely resolved within 2 days. In the next 2 years, 2 patients underwent elective endoscopic resections and 1 underwent radiosurgery for symptomatic seizures associated with the HH. Long-term follow-up ranged from 8 months to 2 years. At last follow-up, 2 patients were seizure free and 1 patient had greater than 50% reduction in seizures. A summary of the 3 cases is shown in Table 1.

Case 1

**History and Examination.** This 2.5-year-old boy was transferred to our institution from another hospital via air ambulance for further management of status gelasticus. He was a developmentally normal child in whom gelastic seizures began at age 4 months. He had seizures that were typical and consisted of laughing, crying, and violent behavior in the form of slapping and extreme thirst—he would ask for water and drink ferociously. A Delalande and Fohlen Type II HH was subsequently diagnosed on brain MR imaging. His gelastic seizures were brief and lasted for 60–90 seconds. In the course of time, these seizures increased in frequency, and over the following 6-week period, a seizure occurred every 5 minutes. They even persisted during his sleep. Pharmacotherapy with levetiracetam, acetazolamide, and lorazepam failed to terminate these near-continuous gelastic seizures.

**Operation and Postoperative Course.** His status gelasticus was finally resolved after emergency resection of the HH. The surgical approach was the transcallosal anterior interhemispheric approach, which has been described in literature. Postoperatively, he had mild right-sided thalamic stroke with mild transient left hemiparesis that completely resolved within 2 days. The pre- and postoperative MR images confirmed a 67% disconnection and 58% resection. His seizure frequency was reduced by more than 90%.

Twelve months after surgery, he had brief episodes of gelastic seizures every 2 weeks. Levetiracetam therapy continued during that time. Eighteen months postsurgery, he had an episode of viral illness that increased the frequency of gelastic seizures to every week. He was further evaluated by our team and was deemed appropriate for further resection. He underwent endoscopic resection of the residual HH. No new postoperative complications were present. At the last clinical follow-up, which was about 3 years after the initial emergency resection and 12 months after his most recent resection, he was seizure free. He has had no further rage attacks or violent behavior.

**Case 2**

**History and Examination.** This 3.5-year-old boy was referred to our institution for further management of status gelasticus. He had mildly delayed milestones, achieving speech and walking status at 16 months of age. At 2 years of age, he talked in brief phrases and had infrequent rage attacks. He had 3 seizure types (gelastic, atonic, and atypical absence) that had started shortly after birth. At 20 months of age, the patient was diagnosed with refractory epilepsy related to a giant (Delalande and Fohlen Type IV) bilaterally attached HH. He had undergone 2

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**TABLE 1: Patient information and long term seizure outcome following emergency surgery for status gelasticus**

<table>
<thead>
<tr>
<th>Case No., Sex</th>
<th>Age at Seizure Onset (mos)</th>
<th>Seizure Type</th>
<th>Delalande &amp; Fohlen Class</th>
<th>1st Op</th>
<th>Emergency Op for Status Gelasticus</th>
<th>Immediate Complications</th>
<th>Subsequent Ops</th>
<th>Seizure Outcome at Last FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, M</td>
<td>4</td>
<td>gelastic</td>
<td>II</td>
<td>NA</td>
<td>TAIF</td>
<td>rt-sided thalamic stroke</td>
<td>endoscopic</td>
<td>seizure free</td>
</tr>
<tr>
<td>2, M</td>
<td>w/in 1st wk of birth</td>
<td>gelastic, atonic, atypical absence</td>
<td>IV</td>
<td>rt OZ, lt OZ</td>
<td>endoscopic</td>
<td>none</td>
<td>NA</td>
<td>seizure free</td>
</tr>
<tr>
<td>3, M</td>
<td>w/in 2nd wk of birth</td>
<td>gelastic, tonic, complex partial</td>
<td>III</td>
<td>NA</td>
<td>lt OZ</td>
<td>none</td>
<td>endoscopic; GKS</td>
<td>50–90% seizure reduction</td>
</tr>
</tbody>
</table>

* FU = follow-up; NA = not applicable; TAIF = transcallosal anterior interforniceal; OZ = orbitozygomatic approach.
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prior HH resections at another institution; both were orbitozygomatic resections, 1 from the right at 22 months of age, and the other from the left 9 months later. The second surgical procedure was complicated by the development of hydrocephalus requiring ventriculoperitoneal shunt placement. The first surgery resulted in complete cessation of the atonic seizures and marked reduction of the atypical absence seizures. The second operation stopped the residual atypical absence seizures, but the gelastic seizures persisted even after both operations and, in fact, worsened to status gelasticus. His gelastic seizures were described as strained, painful laughter often associated with flatulence for about 15 seconds (maximal 30 seconds) without loss of awareness. He was having gelastic seizures every 5–10 minutes. Four antiepileptic medications (clonazepam, acetazolamide, carbamazepine, and levetiracetam) were unable to terminate these near-continuous gelastic seizures. Twenty-four-hour video electroencephalographic monitoring captured numerous gelastic seizures (> 100).

**Operation and Postoperative Course.** He underwent endoscopic resection of the residual HH as described previously without any complications. Postoperatively, his status gelasticus was resolved. Follow-up MR imaging showed only a trace of residual HH tissue “floating” in the tuber cinereum. Eight months postoperatively, the patient remained seizure free while taking 1 antiepileptic drug, with significantly improved behavior and cognition.

**Case 3**

**History and Examination.** This 9-month-old boy was referred to our institution for further management of status gelasticus. He had severe developmental delay and was impaired cognitively. He had 3 seizure types (gelastic, tonic, and complex partial) that had started within the 2nd week of birth. The brief episodes of gelastic seizures were increasing in frequency to almost 1 every 10–12 minutes in the preceding 2 weeks. He had been diagnosed at 5 months of age with refractory epilepsy related to a Delalande and Fohlen Type III HH. He also had a prominent left frontotemporal arachnoid cyst. None of the antiepileptic medications had ever significantly helped his seizures.

**Operation and Gamma Knife Treatment.** The patient underwent emergency HH resection via a left orbitozygomatic approach as described previously and arachnoid cyst fenestration (2-stage procedure) (Fig. 1) His near-continuous gelastic seizures were reduced by greater than 50%. However, he continued to have at least 2–3 brief episodes daily. The patient was treated with 3 antiepileptic medications (levetiracetam, clonazepam, and carbamazepine). In the next 2 weeks, he had further endoscopic resection of the residual HH. Post surgery MR imaging brain confirmed a 48% disconnection and 67% resection. Complication after the endoscopic resection included a right internal capsule infarct that resulted in left-sided weakness. His gelastic seizures were resolved completely, and he remained seizure free while taking 2 antiepileptic medications (levetiracetam and clonazepam) for the next 2 months. Seven months after surgery, he started to have clusters of complex partial seizures every 2–3 weeks, which were not well controlled by 4 antiepileptic medications (levetiracetam, clonazepam, carbamazepine, and zonisamide). He was again evaluated by our team and underwent GKS at the age of 20 months. At the last clinic follow-up, almost 15 months after the emergency resection, his seizures were reduced by greater than 50%. His present seizures are complex partial seizures that consist of crying and then unresponsiveness for a few seconds.
At the time of this draft, the plan was to admit the patient to our epilepsy-monitoring unit for further presurgical evaluation.

Discussion

These cases illustrate the potential value of emergency resective lesional epilepsy surgery in patients with a form of status epilepticus (status gelasticus secondary to HHs). Gelastic (that is, laughing) seizures represent one of the hallmark features of the HH. They can be associated with little or no change in consciousness, particularly early in the clinical course. They are typical and automatic repetition of laughter without pleasure and appear to be forced pathological laughter. Patients with gelastic seizures that are associated with the intrahypothalamic form of HH usually present at an early age and are often the first seizure type. Tassinari et al.17 reported a mean age of onset of 2.8 years, with seizures occurring in more than one-third of patients. In addition, these seizures have been reported to occur on the 1st day of life, as illustrated in Case 2.16 The frequency of status gelasticus in patients with HH remains unknown. Our small series of patients would suggest that it tends to present in young patients. Recent electrophysiological studies have clearly demonstrated the intrinsic epileptogenicity of the HH and its direct association with induction of gelastic seizures.6,8,9 SPECT studies have demonstrated hyperperfusion within the hamartoma itself during gelastic seizures.2,4 The authors of 2 recent studies performed iodinated fluorodeoxyglucose-PET scanning in patients with intractable gelastic seizures associated with HHs.14,15 They demonstrated a large circumscribed hypermetabolic region within the location of the HH, representing localized intense epileptiform activity. Resection of the HH successfully terminated the status gelasticus in all of our cases despite their not remaining seizure free. This suggests that emergency surgical intervention is the best option for terminating intractable, near-continuous gelastic seizures and improving cognitive function. Complete and sustained seizure control with medications alone is achieved in fewer than 5% of patients with intractable HH and epilepsy. Medications are often described as lacking efficacy against gelastic seizures.7

In all 3 of our cases, multiple operations appeared to help the patients by reducing seizure frequency and improving overall cognitive and behavioral functioning. None of the antiepileptic drugs were able to terminate status gelasticus. A number of different surgical approaches have been developed and advocated for resection of the HH lesions. The surgeon should choose among these approaches based on the specific anatomical features of each HH lesion. No single approach is best suited for every patient, as evident in our illustrated cases. All 3 patients had different types of HH and underwent emergency resection in which 3 different surgical approaches successfully stopped the status gelasticus. In addition, the repeat surgical procedures, which resulted in seizure freedom in 2 patients, were distinctly different from the initial operation (or operations, as in Case 2). The reason multiple procedures were necessary was the difficulty or impossibility of safely removing the entire HH due to its location, attachment, and size in a single approach and procedure. In general, the aim is to completely remove the HH; if this is not possible, disconnection should be the goal, and, if necessary, repeat surgery (via a different approach) can be performed. The results in our 3 cases also illustrate the merit of different surgical approaches for emergency resection.

In summary, we present immediate and long-term outcomes following emergency surgery of HHs for status gelasticus. Status gelasticus can be successfully terminated by emergency resection of the HH. Long-term follow-up in our small series resulted in seizure freedom in 2 patients and greater than 50% reduction in seizures in 1 patient, although a “more complete” repeat resection was necessary.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Ng, Abla, Rekate. Acquisition of data: Pati, Rastogi. Analysis and interpretation of data: Pati, Rastogi. Drafting the article: Pati, Rastogi. Critically revising the article: Ng, Abla, Rekate. Reviewed final version of the manuscript and approved it for submission: Ng, Abla.

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References

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