Intralesional epileptiform activity in a fourth ventricular hamartoma associated with epileptic hemifacial spasm in a toddler: illustrative case

H. Westley Phillips, MD,1 Joanna E. Papadakis, BS,2 Brittany A. Borden, MD,3 Anna Pinto, MD,4 Melissa Tsuboyama, MD,4 Michelle Y. Chiu, MD,4 Joseph R. Madsen, MD,2 Rachit Patil, MD,5 and Scellig S. D. Stone, MD, PhD2

1Department of Neurosurgery, Stanford University School of Medicine, Palo Alto, California; Departments of 2Neurosurgery and 3Neurology, Boston Children’s Hospital, Harvard Medical School, Boston, Massachusetts; 4Department of Internal Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts; and 5Department of Neurology, The Warren and Alpert Medical School, Brown University, Providence, Rhode Island

BACKGROUND Focal epilepsy caused by a posterior fossa lesion is a rare phenomenon. In these cases, seizure onset typically occurs during the first few months of life, with episodes of epileptic hemifacial spasms and abnormal eye movements. Patients often present with drug-resistant epilepsy and often require resection for the best chance of seizure freedom.

OBSERVATIONS The authors present the case of a 19-month-old male with intractable epileptic hemifacial spasms and a dorsally exophytic right brainstem and middle cerebellar peduncle hamartoma, following 2 prior subtotal resections. The authors recommended a third suboccipital craniotomy with intraoperative electrocorticography, which revealed interictal spiking from an intralesional depth electrode. Near-total resection led to durable seizure freedom.

LESSONS Although posterior fossa lesions are rarely associated with epileptiform activity, this case demonstrates that pediatric patients with epileptic hemifacial spasms associated with a posterior fossa lesion may respond favorably to resection. Furthermore, this case demonstrates that intraleisional electrocorticography can detect epileptic activity in posterior fossa lesions, which may predict postoperative seizure outcomes.

Traditionally, subcortical and cerebellar structures were thought to exert neuromodulatory effects on epileptiform activity.1 While the majority of pediatric epilepsy cases suggest that epileptogenic foci may be restricted to the cerebral cortex, a minority of cases involving hypothalamic and cerebellar lesions suggest epilepsy can also originate from these areas.2-4 Epilepsy caused by cerebellar hamartomas of the floor of the fourth ventricle (HFFVs) is exceptionally rare.5-8 These lesions are usually benign and present in infancy with a similar clinical semiology, including epileptic hemifacial spasms, eyelid blinking, and partial seizures. 8 Patients generally respond poorly to antiseizure medications (ASMs) and may require resection for seizure control.5

Illustrative Case

A 19-month-old male presented with right hemifacial spasms and a dorsally exophytic right brainstem and middle cerebellar peduncle lesion (Fig. 1A–F). He had undergone 2 suboccipital craniotomies for excisional biopsy and partial resection at an outside institution at 15 months of age. Pathological analysis failed to reveal a diagnosis in the previous resections. A germline pathogenic CTNNB1 c.998dup (p.Y333*) was noted, which has been associated with a clinical syndrome of global developmental delay, microcephaly, and ocular abnormalities, but its significance in this patient was not well defined.9 Further genetic evaluation identified a 15q11.2 microdeletion, a known predictor of neurodevelopmental delay.10 The patient had a history of in utero illicit substance exposure, and his focal motor hemifacial spasms began around 6 weeks of age. These episodes occurred frequently for 30 seconds and clustered throughout the day, usually with preserved consciousness, evolving to rhythmic right-arm shaking.

At his neurological baseline, the patient experienced mild gross motor delays, dysphagia, and swallowing difficulties. In the month following seizure onset, the patient presented to an outside emergency...
department because of sustained seizure clustering and concern for status epilepticus, culminating in ASM initiation with phenobarbital and levetiracetam. He was later transitioned to oxcarbazepine due to medication failure. Magnetic resonance imaging (MRI) was performed and demonstrated the aforementioned posterior fossa lesion, prompting the recommendation for surgical intervention.

Following the 2 prior surgeries at another center, repeat MRI at 18 months of age demonstrated a 1.1 × 1.6 × 1.5–cm T2-hyperintense, nonenhancing, dorsally exophytic lesion arising in the right lateral aspect of the fourth ventricle with involvement of the right middle cerebellar peduncle and extension into the superficial aspect of the dorsal pons. Postoperative MR images (D–F) demonstrating near-total resection. Intraoperative microphotographs demonstrating the lesion (asterisks) preresection (G), a 10-contact intraliesional depth electrode (H), and near-total resection of the lesion (I).

FIG. 1. Preoperative sagittal (A), coronal (B), and axial (C) T1-weighted MR images demonstrating a 1.1 × 1.6 × 1.5–cm T2-hyperintense, nonenhancing, dorsally exophytic lesion arising in the right lateral aspect of the fourth ventricle with involvement of the right middle cerebellar peduncle and extension into the superficial aspect of the dorsal pons. Despite oxcarbazepine management, the patient's hemifacial spasms persisted, and neurological investigations suggested an epileptiform link. The initial electroencephalogram (EEG) at 15 months showed rare epileptiform discharges in the right temporal region, while subsequent EEGs following the previous surgeries suggested diffuse quasirhythmic slowing admixed with movement artifacts associated with the seizure events. Our multidisciplinary team recommended a third
suboccipital craniotomy with intraoperative electrocorticography to successfully resect the presumed epileptogenic lesion and obtain a tissue diagnosis.

A standard suboccipital craniotomy with C1 laminectomy was performed using image navigation and multimodal neuromonitoring. The fourth ventricle was entered rostral and dorsal to the obex, revealing the lesion as it arose from the right side of the brainstem and the right middle cerebellar peduncle (Fig. 1G).

A 1 × 4 strip of subdural electrodes was placed on the lesion from within the fourth ventricle. Contacts over the mesial aspect showed occasional epileptiform discharges (Fig. 2A). Another 1 × 4 subdural strip was placed on the nearby right cerebellar hemisphere; this

---

**FIG. 2.** Intraoperative electrocorticography tracings with accompanying photographs. A: First preresection recording: a 1 × 4 strip was placed over the cerebellar lesion, with C1–2 overlying the mesial aspect of the lesion and C4 over the right cerebellar hemisphere. Occasional high-amplitude sharp and slow waves were seen at C1. B: Second preresection recording: the 1 × 4 strip was then moved over the right cerebellar hemisphere, with C1 situated most rostrally and C4 situated most caudally. The recording was without epileptiform activity. C: Third preresection recording: a 10-contact depth electrode was carefully introduced into the lesion, with C1–5 in the lesion and C1 as the deepest contact. High-voltage sharp waves were seen with negative phase reversal at C3. Channels C1–2 and C6–10 have been hidden because of the presence of artifacts. D: Postresection recording: a 1 × 4 strip was placed in a similar orientation as the first preresection recording, with C1 near the cerebellum-brainstem interface, adjacent to the floor of the fourth ventricle, and C4 along the right cerebellar hemisphere. The recording was devoid of epileptiform activity. All tracings shown were taken after completing the process of artifact correction: low-frequency filter of 1 Hz, high-frequency filter of 70 Hz, notch filter off, sensitivity of 15 µV/mm, and time base of 30 mm/sec. > = floor of the fourth ventricle; * = cerebellar lesion; − = previous resection cavity; + = right cerebellar hemisphere.
area was devoid of interictal epileptiform activity (Fig. 2B). A depth electrode was carefully inserted into the lesion to ensure that the floor of the fourth ventricle and brainstem were not penetrated (Fig. 1H). Interictal spiking was observed in the middle contact of this electrode without involving peripheral contacts (Fig. 2C). The lesion was relatively hypovascular with a rubbery consistency. A clear margin was dissected on the superior and medial sides of the lesion, which was subsequently debulked.

Postresection electrocorticography was performed using a 1 x 4 subdural strip placed in the resection cavity, and no interictal spiking was recorded (Fig. 2D). Intraoperative MRI revealed minimal residual lesion in the superolateral corner of the resection. Additional tumor resection ensued. Notably, a thin rim of the lesion was adherent to the brainstem, and a near-total resection was subsequently performed, given the benign nature of the lesion and the desire to avoid injury to the brainstem, followed by a standard closure. A second intraoperative MRI study confirmed near-total resection without signs of ischemia or brainstem injury (Fig. 1D–F).

Postoperatively, the patient remained free of seizures and spasms at his preoperative baseline. He was discharged without complication on postoperative day 4. The pathology of the lesion was consistent with hamartoma, and the tissue was negative for BRAF p.V600E, clinically significant somatic mutations, and molecular evidence of malignant neoplasm. The patient was weaned from oxcarbazepine 3 months after surgery and has been seizure free for more than 1 year postoperatively, exhibiting additional motor and developmental gains.

Patient Informed Consent
The necessary parental informed consent was obtained in this study.

Discussion
Observations
We present the case of a 19-month-old male with an HFFV associated with epileptic hemifacial spasms. Traditionally, subcortical structures were not considered epileptogenic and instead were thought to play a neuromodulatory role in seizure activity.4 Although rare, several reports have documented an association among cerebellar lesions, epileptiform activity, and epileptic hemifacial spasm, resulting in the novel phenomenon of “cerebellar epilepsy.”5–7 Typically benign and appearing in infancy, these lesions respond poorly to ASMs and may warrant surgical management.5

In a small case series, Delande et al. described 2 cases of drug-resistant cerebellar epilepsy with hemifacial spasm.11 Resection during early childhood successfully resolved seizure activity in both cases. Similarly, a review of 31 patients with lesional cerebellar epilepsy found that over half of those with drug-resistant epilepsy responded well to resection of the posterior fossa lesion.5 Nonetheless, the optimal timing for surgery in this population is debated, with some reports favoring early intervention due to infantile onset, the risk of seizures impacting further brain development, and concerns regarding progression to status epilepticus.5,8,12

While the pathophysiology of cerebellar epilepsy is not fully defined, some theories propose that lesional interruption of the dentatothalamothalamic tract and compression of the facial nucleus may be involved.5,13–16 However, a growing number of reports propose that the seizure origin may be within the lesion itself.5,8,12,13 In a case by Gupta et al., intraoperative electrocorticography in an infant with a cerebellar gangliomatous hamartoma showed spikes from the left cerebellar cortex, which ceased along with symptoms after complete tumor removal.5 Several studies, including ours, have also observed both surface intraoperative epileptogenic activity and intralesional activity. During the resection of 2 HFFVs in 3-month-old and 3-year-old patients, Park et al. and Delande et al. obtained intraoperative intralesional recordings showing activity resembling electrical discharges originating from the lesion.11,12 In another case involving the resection of a mass in the left superior cerebellar peduncle of a 4-month-old infant, ictal activity was revealed from an intralesional electrode.13 Finally, in 2 resections of an HFFV in a 4-week-old infant, spike and sharp wave activity were recorded from the lesion using both a 1 x 4 strip in the first surgery and a single-needle electrode in the second.9

In our patient, interictal spiking was observed from an intralesional depth electrode, and sharp waves were seen along the mesial aspect of the hamartoma using a strip electrode. This is consistent with findings in similar cases of HFFV-associated epileptic hemifacial spasms, where no such activity was recorded from the nearby cerebellar cortex. Near-total resection in all cases, including ours, led to complete symptom resolution, allowing discontinuation of ASMs and highlighting the potential epileptogenic nature of these lesions. Although our patient had a CTNNB1 mutation, evidence linking this mutation to seizure activity is limited and was likely unrelated to their drug-resistant seizure presentation.9 Similarly, while some reports associate chromosomal microdeletions like 15q11.2 with epilepsy, this association is not considered common and is more strongly linked to neurodevelopmental disorders.10,17

Resection of posterior fossa lesions carries a high risk of morbidity given their proximity to eloquent cortical and subcortical structures, making gross-total resection challenging.18 Because of this, repeat resection is common due to the proximity of the brainstem.7,12 Similarly, in our case, near-total resection was required given the hamartoma’s adherence to the brainstem. Given the complete resolution of seizure activity following near-total resection, it is possible that the mass effect contributed to epileptogenesis in this patient. Conversely, intraoperative interictal activity suggests the seizure onset zone was located in the center of the lesion, which was removed en bloc.

Lessons
Although posterior fossa lesions rarely cause epileptic activity, we present the case of a 19-month-old male with an HFFV associated with hemifacial spasms. A third suboccipital craniotomy revealed intralesional interictal spiking and near-total resection led to complete symptom resolution, allowing the discontinuation of all ASMs. In line with other reports, this amelioration of symptoms, coupled with our observed intraoperative interictal spiking, supports the idea that posterior fossa lesions may be epileptogenic, and their resection can successfully eradicate target seizure activity. Despite this finding, we acknowledge that our report is limited in its ability to generalize to a broader population, given the overall rarity of this phenomenon. Therefore, further study into the underlying mechanisms causing intractable epilepsy in patients with posterior fossa lesions is warranted.

References


Disclosures
Dr. Tsuboyama reported consulting fees from the Neuroelectrics FDA study outside the submitted work

Author Contributions
Conception and design: Stone, Phillips, Borden, Pinto, Madsen, Patil. Acquisition of data: Stone, Phillips, Papadakis, Borden, Pinto, Tsuboyama. Analysis and interpretation of data: Stone, Phillips, Papadakis, Borden, Tsuboyama, Chiu. Drafting the article: Stone, Phillips, Papadakis, Borden. Critically revising the article: Stone, Phillips, Papadakis, Borden, Tsuboyama, Chiu, Madsen, Patil. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Stone. Administrative/technical/material support: Stone. Study supervision: Stone, Patil.

Correspondence
Scellig S. D. Stone: Boston Children’s Hospital, Harvard Medical School, Boston, MA. scellig.stone@childrens.harvard.edu.