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Case Report

Pediatric Astrocytoma Causing Intractable Epilepsy

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Abstract

Intractable epilepsy can stem from numerous causes, including brain tumors. Here we describe an unusual presentation of a child with medically refractory epilepsy and developmental delay. She was determined to be an atypical case for epilepsy surgery due to the presence of multifocal lesions on MRI and poorly localizable ictal and interictal EEG features. A surgical resection was performed on the largest lesion and pathological analysis was consistent with astrocytoma. Post-resection she has had a significant reduction in her seizures, with an improvement in her development. Patients with refractory epilepsy should be evaluated for potential epilepsy surgery. It is important to identify these patients early to limit the potential morbidity and mortality and improve their quality of life.

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INTRODUCTION

Brain tumors account for roughly 20% of all childhood malignancies, of which astrocytoma is the most common [1]. The presenting symptoms can range from headaches and visual disturbances to seizures. Here we report the case of a child with and astrocytoma who presented with medically refractory epilepsy.

CASE PRESENTATION

A 9 year old girl emigrated from Puerto Rico to New York and presented with medically refractory epilepsy. She initially developed seizures at 4 months of age, which her mother described as "turning pale followed by shaking." She was treated with anti-epileptic medications and remained seizure-free until 5 years of age, at which time she experienced developmental regression and began having the current type of seizures. These seizures were described as screaming with eye deviation and stiffness of the arms followed by generalized tonic clonic activity. These episodes lasted from 2-15 minutes in duration and occurred 10-15 times per week. Developmentally she functioned at a 2 year level and was essentially non-verbal. On exam she exhibited decreased strength in her right upper and lower extremities, with a hemiparetic gait. A routine electroencephalography (EEG) revealed mild intermittent slowing in the left temporal region during sleep and in addition had prolonged runs of generalized spike and wave complexes (Figure 1), with some seen maximally at the left temporal region. Independent left temporal spike and wave complexes were seen as well.

The patient remained refractory on multiple antiepileptic medications including phenobarbital, carbamazepine, oxcarbazepine, lamotrigine, phenytoin, valproic acid, levetiracetam and zonisamide. Magnetic resonance imaging (MRI) scans of the brain (Figure 2) revealed enhancing architectural distortion of the left temporal lobe and foci of dural enhancement. Within the frontal and temporal lobes, there were multiple enhancing T1 lesions (Figure 3). CT scan of the head showed densely calcified masses in the left temporal region. Possible differential diagnoses included low grade glioma, calcified parenchymal hemorrhage or chronic infection with calcifications. PET scan revealed significant hypometabolism in the frontal, temporal and parietal lobes greatest in the frontal and temporal lobes. In addition, asymmetries of metabolism between the two cerebral hemispheres with the pattern on the left, congruent with the interictal expression of partial epilepsy focus in the left temporal lobe. The differential diagnosis when PET was interpreted with CT and MRI was suggestive of a possible infectious process.

Long term video EEG monitoring captured episodes of head version to the right followed by brief extension of one or both arms with some possible dystonic posturing which would evolve into a generalized arm and leg hypermotor seizure. The seizures would start abruptly and would evolve into myoclonic activity. The corresponding EEG revealed generalized electrodecrement intermixed with muscle artifact which at times was preceded by generalized delta slowing. This was followed by generalized spike and wave discharges.

An ictal SPECT scan revealed mild to moderate hyperperfusion in the cortices of the right anterior temporal lobe. In addition, mild hyperperfusion was seen in the right thalamus suggesting a potential epileptogenic focus in the right temporal lobe. Evidence of hyperperfusion in the medial frontal and medial

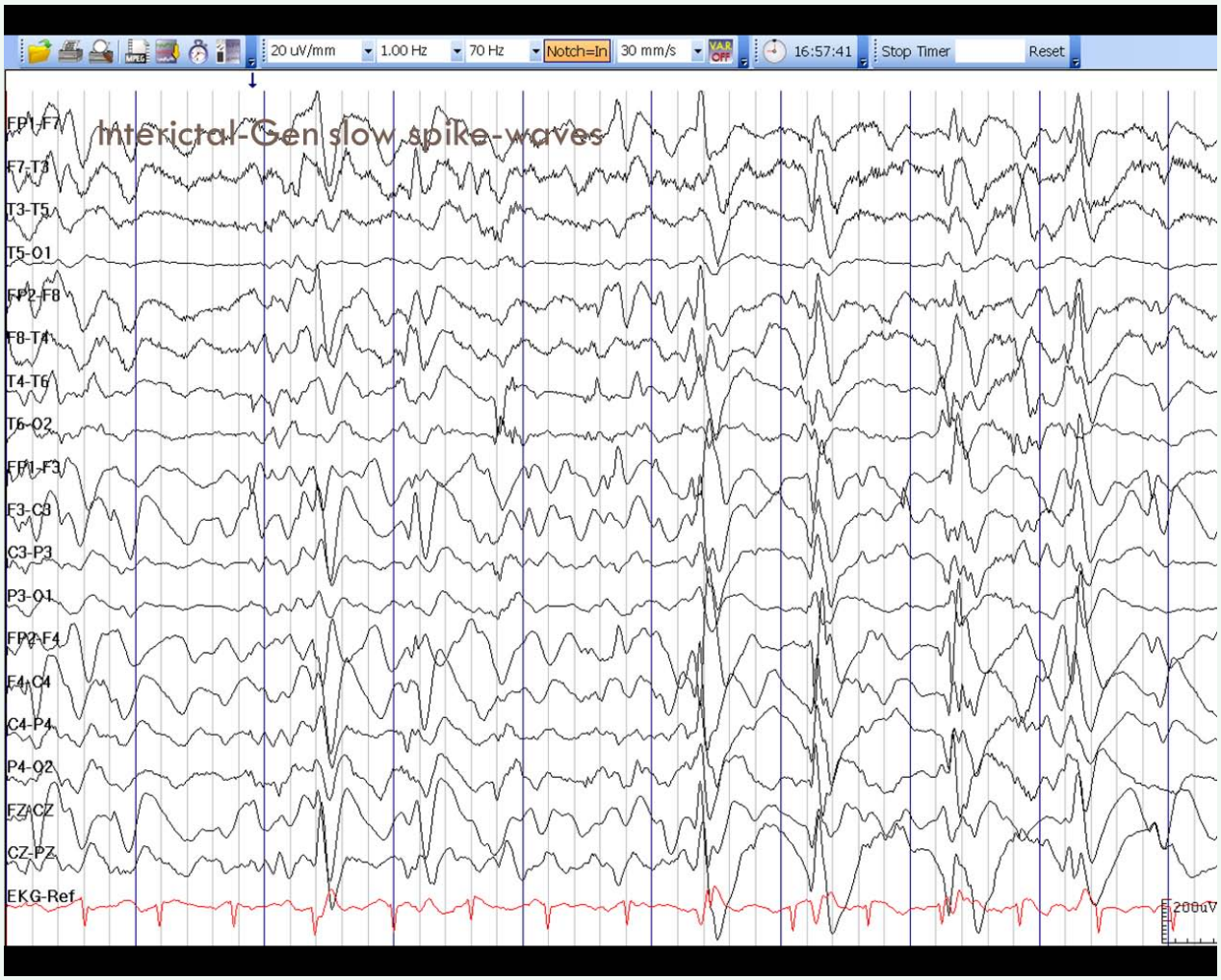

Figure 1 EEG revealing interictal bursts of generalized slow spike and wave complexes.

polar frontal cortices was also seen possibly representative of an area of deactivation. Hyperperfusion was also evident in the right posterior white matter.

Given the patient's migration from a tropical nation, infectious etiologies including tuberculosis, neurocysticercosis and toxoplasmosis were investigated. A thorough investigation, including cerebrospinal fluid and serum analysis did not yield evidence of an infectious etiology. The patient was presented in our institution's epilepsy-surgery conference. Due to the patient's refractory epilepsy, despite the frontal seizure semiology and inability to localize the onset of seizure on EEG, it was decided to proceed with a left temporal lobe resection of the largest enhancing mass. Pathological analysis of the mass revealed low grade astrocytoma in the background of focal cortical dysplasia.

DISCUSSION

Low grade astrocytomas are common brain neoplasms that primarily affect young adults [1]. They comprise a heterogeneous group of pediatric tumors including juvenile pilocytic astrocytomas (WHO grade I), low-grade diffuse astrocytomas, gangliogliomas, oligodendrogliomas and mixed oligo-astrocytomas (WHO grade II) [2]. They account for 30% to 40% of all primary central nervous system neoplasms in the pediatric population [3,4].

Astrocytomas, or any brain tumor for that matter, can present with a myriad of symptoms depending on their location. Initial symptoms are usually non-specific and are related to increased

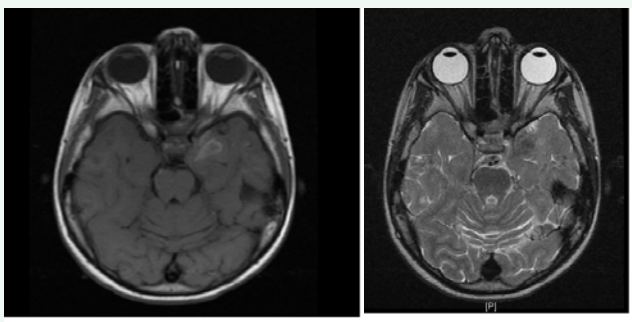

Figure 2 MRI of the brain (panel A axial, T1, panel B axial T2) revealed enhancing architectural distortion of the left temporal lobe and foci of dural enhancement.

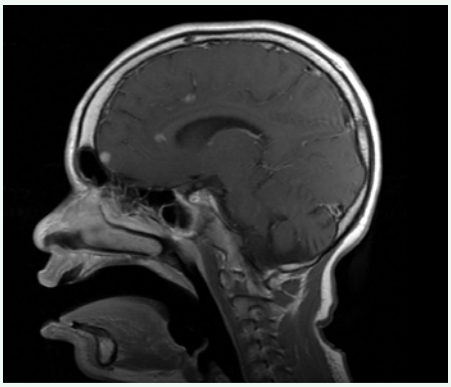

Figure 3 MRI of the brain (sagittal, TI sequence with contrast) revealing multiple scattered hyperintense lesions.

intracranial pressure. The classic triad of increased intracranial pressure consists of morning headaches, lethargy and vomiting. Seizures are present at diagnosis in roughly 30-50% of patients with supratentorial astrocytomas. Therefore the investigation of a patient with headaches and seizures is very important and should not be delayed [5]. Treatment of seizures should be initiated as they arise. Often these seizures can be refractory to treatment with conventional anti-epileptic medications. In such cases, management can be challenging and often requires multiple anti-epileptic medications to achieve a meaningful reduction of seizures frequency and/or severity. Any patient with epilepsy who does not respond to medical therapies should be evaluated for potential epilepsy surgery.

Although intracranial surgery involves inherent risks, the risks do not parallel the potential morbidity and mortality of uncontrolled seizures. Not only are refractory seizures linked to injury (both personal and public), but depression, anxiety and cognitive decline are also common. Mortality rates for patients with uncontrolled seizures far exceed those for age matched controls. Among patients with refractory epilepsy, Sudden Unexplained Death in Epilepsy (SUDEP) can reach a rate of 1 death per 500 patients per year. Retrospective and prospective trials have indicated that the morbidity and mortality associated with surgical treatment has been demonstrated to be less than that associated with the disorder, itself [6-8].

The work-up in patients for potential epilepsy surgery can be quite extensive. Neuroimaging should be obtained without delay. EEG and long term video EEG monitoring are the most useful tests in diagnosing and potentially localizing epilepsy. Brain MRI is the best structural imaging study, with preference to thin-cut coronal views perpendicular to the axis of the temporal horn. PET scanning demonstrates brain glucose metabolism rather than structure. The typical finding from an interictal scan is hypometabolism in the region of the epileptic focus. SPECT scans are also useful in the investigation of localization related epilepsies. SPECT scans measure blood perfusion within the brain and can be performed both ictally and interictally. Since cerebral blood flow is known to increase during seizures at the site of seizure onset, obtaining an ictal SPECT will reveal hyperperfusion to the epilpetogenic zone. This can often be useful in delineating the boundaries of a potential surgically resectable area of the brain tissue.

The optimal management plan for these tumors is controversial and ranges from observation to macroscopic excision, radiotherapy and chemotherapy. Treatment management is based on the tumor's characteristic indolent behavior. Therapy is directed towards local control, as these tumors only rarely metastasize outside the CNS [1,9]. Therefore surgery and radiotherapy are the initial treatments of choice. The incorporation of chemotherapy in the overall management of younger patients is also employed. Therefore, management of the pediatric patient with low grade astrocytomas should include the input from a multi-disciplinary team, including epileptologists, neuropsychologists, neurosurgeons, radiation oncologists and pediatric neuro-oncologists [3,10]. The five year survival rate of children with low-grade supratentorial astrocyomas is 71%; with the worst survival rates were in children less than 2 years of age and the best in those 10-14 years of age [4].

Our patient posed multiple treatment related questions. Typically, patients with focal abnormalities on EEG and MRI make ideal surgical candidates. However, our patient was an atypical case for epilepsy surgery because of a generalized pattern of abnormalities on interictal EEG as well as multifocal lesions present on MRI, and poorly localizable ictal and interictal EEG features. . Our epilepsy surgery panel determined that even though the patient's work up was non-localizing, removal of the largest lesion in the right temporal lobe would significantly reduce, if not resolve, her seizures as well as improve her developmental regression.

Our patient is now 2.5 years post tumor resection, and has had a dramatic improvement in her seizure frequency with a total of 6 seizures, of which 2-3 seizures occurred in the setting of a viral gastroenteritis. Her anti-seizure medications were weaned and she was maintained on levetiracetam and valproic acid. One of the most striking features of this case is that prior to the surgery, the patient was essentially non-verbal. In follow up she was assessed to be speaking in short sentences. Both her language and motor skills appeared to have improved post temporal lobe mass resection. In addition, to our knowledge, there have not been other cases reported in the literature in which a patient had multiple scattered lesions in the brain, with a predominantly generalized pattern of abnormality on EEG, and following resection of the largest lesion the patient had a dramatic near cessation of seizures.

CONCLUSION

Space occupying lesions, including brain tumors, should always be included on the differential list of patients with intractable epilepsy. Formal neuroimaging with a contrast-enhanced MRI should be obtained. Once a diagnosis has been established, a multi-disciplinary treatment team, including epileptologists, neuropsychologists, neurosurgeons, radiation oncologists and pediatric neuro-oncologists, should determine the best course of action for each individual patient.

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