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Pediatric posterior reversible encephalopathy syndrome presenting with isolated cerebellar edema and obstructive hydrocephalus

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Abstract

In this report, the authors describe the case of a teenage boy who presented with hypertensive emergency, posterior reversible encephalopathy syndrome, and hydrocephalus due to fourth ventricle outlet obstruction. Posterior reversible encephalopathy syndrome is a well-characterized but uncommon syndrome in children that is generally triggered by severe hypertension. The unusual clinical picture of this patient, who had isolated cerebellar edema leading to obstructive hydrocephalus, has been rarely described in children.

Keywords

pediatric; posterior reversible encephalopathy syndrome; obstructive hydrocephalus; hypertension; vascular disorders

In this report, we describe a case of a teenage boy who presented with hypertensive emergency, posterior reversible encephalopathy syndrome (PRES), and hydrocephalus due to fourth ventricle outlet obstruction secondary to localized cerebellar edema. Posterior reversible encephalopathy syndrome is a well-characterized but uncommon syndrome in children that is generally triggered by severe hypertension.⁴ The spectrum of presentation can be quite varied, from headache and altered vision to confusion and obtundation, potentially prompting admission to a pediatric ICU for close monitoring and treatment. Presenting symptoms can have significant overlap with other important clinical entities such as effects from a mass lesion or infection. Although this patient's form of PRES has been

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Disclosure

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documented in adults,³ it has been very rarely described to occur in children.⁸ This case illustrates how it is essential for pediatric intensivists and pediatric neurosurgeons to be aware of the spectrum of clinical presentation of PRES and to keep this disease on their differentials.

Case Report

History

A 13-year-old, 30-kg Somali boy with reportedly no significant medical history was transferred to our hospital's emergency department (ED) from another hospital. On the day of presentation, the child woke up in the morning with vomiting, subsequently took a shower, and went back to bed. He was discovered there, unresponsive, at around lunchtime and 911 was called. When Emergency Medical Services arrived the child was unresponsive, with a noninvasive blood pressure of 260/150 mm Hg. In the other hospital's ED an immediate head CT was obtained, which showed "third and lateral ventricles ... markedly dilated with mild transependymal flow of CSF suggesting acute hydrocephalus." In addition, there was "mild edema of the cerebellar hemispheres bilaterally" and the "inferior most posterior fossa has a some-what tight appearance...." (Fig. 1). Due to the hypertensive emergency and acute hydrocephalus, he was electively sedated and intubated for airway protection. He was also started on a nicardipine drip for blood pressure control. He was transported to our hospital's ED by helicopter.

Examination

On arrival, the patient's heart rate was 91 bpm, noninvasive blood pressure was 164/106 mm Hg (mean 118 mm Hg), with normal temperature and normal oxygen saturation on pulse oximetry. He was admitted to the pediatric ICU, where an arterial line was placed. An external ventricular drain (EVD) was placed by pediatric neurosurgery. Initial intracranial pressures were measured in the high teens. A CSF analysis revealed no bacteria on the Gram stain and 14 nucleated cells (neutrophils 65%, lymphocytes 27%, monocytes 8%), with normal glucose and protein levels (77 and 12 mg/dl, respectively). Initial laboratory studies were significant for a blood urea nitrogen (BUN) of 42 mg/dl, a creatinine (Cr) of 2.4 mg/dl, normal cardiac enzymes, and a urine analysis with a protein of 300 mg/dl and "moderate" blood.

Ophthalmological examination revealed "mild to moderate optic nerve head edema" bilaterally, with "extensive retinal hemorrhages in the peripapillary region extending along the arcades, in the macula and in the periphery; hemorrhages are located at all layers of the retina" consistent with a likely diagnosis of hypertensive retinopathy/choroidopathy. Additional workup included an electrocardiogram, which revealed sinus rhythm with left ventricular hypertrophy and a prolonged QT interval ($QT_c = 475$ msec), and an echo, which revealed normal segmental anatomy but "marked concentric left ventricular hypertrophy with moderate left atrial dilation" and no pericardial effusion.

Neuroimaging

After this initial workup the differential remained wide, and possibilities such as rhombencephalitis⁶ or cerebellitis were considered. Because the initial CSF analysis was unremarkable and the patient's hypertension did not dramatically improve with CSF diversion, further imaging was obtained. Brain MRI without contrast as well as a brain MR angiogram and an MR venogram were obtained on hospital Day 1, which revealed "extensive edema throughout the inferior two thirds of the cerebellum, with compression of the outlet of the fourth ventricle" as well as "obstructive hydrocephalus ... likely the result of the very extensive swelling within the cerebellum. There is no well-defined mass causing obstruction..." (Fig. 2). Also noted was "very extensive vasospasm involving the bilateral anterior, middle, and posterior cerebral arteries" with "a filling defect ... at the inferior most aspect of the superior sagittal sinus posteriorly" raising concern for possible thrombus. Due to this concern, the patient was started on enoxaparin. A follow-up MR angiogram of the circle of Willis obtained without contrast as well as an MR venogram obtained on hospital Day 3 revealed continued arterial vasospasm and a "persistent defect in the superior sagittal sinus as well as significant attenuation of the transverse sinuses bilaterally"—again causing concern for possible thrombus.

Treatment

The child was extubated on hospital Day 1 after his initial MRI. Due to the severe hypertension, his blood pressure was initially treated with a nicardipine drip (peak dose 4 mg/hr). Intravenous esmolol was added on hospital Day 2 (peak dose 125 µg/kg/min). He was subsequently transitioned to oral antihypertensive medications (valsartan and amlodipine). With insertion of the EVD and control of his blood pressure, his mental status returned to normal, obviating the need for a posterior fossa decompression and most consistent with a diagnosis of PRES.

Workup for the etiology of his hypertension included the following: plasma metanephrines, which were normal; C3 levels, which were normal; and a follow-up urine analysis, which revealed continued "moderate" blood but decreased protein levels of 30 mg/dl, with no significant sediment. Serum aldosterone levels were normal. Renal ultrasound with Doppler revealed normal-sized kidneys that were "echogenic ... with loss of corticomedullary differentiation" consistent with medical renal disease but with a normal arterial Doppler signal. The C-reactive protein on hospital Day 1 was measured at 45.6 mg/L. To evaluate for possible infectious causes, a lumbar puncture was performed because it was considered to be safer by the presence of the EVD, given initial concerns that there might not be full communication of CSF. Opening pressure was 26 cm H₂O. Results of serum testing for HIV, West Nile virus, and hepatitis B were negative, as were bacterial, fungal, and acid-fast bacilli CSF cultures. A blood smear was negative for malaria. Rheumatological testing for possible polyarteritis nodosa was also negative, with a normal finding for antinuclear antibody.

Due to the continued unclear etiology of the PRES and hydrocephalus, and the ongoing concerns for sinus thrombosis, combined renal and cerebral angiograms were obtained on hospital Day 6. The renal angiogram revealed "normal-appearing abdominal aorta" and

“normal size, single renal arteries supply[ing] both kidneys.” Cerebral angiography revealed “no evidence of vascular thrombus in the venous outflow system” as well as no cerebrovascular malformations or aneurysms; therefore the patient’s anticoagulation therapy was stopped. The EVD was removed on hospital Day 9. After transfer out of the pediatric ICU, a renal dimercaptosuccinic acid scan was also performed, results of which were normal.

Postoperative Course

The patient was discharged home on valsartan and amlodipine. The BUN/Cr level at discharge was 46/1.94 mg/dl. An outpatient renal biopsy subsequently demonstrated “extensive interstitial fibrosis and glomerulosclerosis” that was “suggestive of reflux/chronic pyelonephritis.” He continues to receive oral anti-hypertensive agents (losartan and amlodipine) and is followed by pediatric nephrology. His most recent follow-up appointment 11 months after hospital discharge revealed no hydrocephalus and resolution of the MRI changes in the cerebellum. Results of a follow-up ophthalmological examination were also normal, with no papilledema. The patient’s mother reported intermittent headaches and on-going new school issues, for which the child is receiving assistance.

Discussion

Posterior reversible encephalopathy syndrome is well documented in both adults and children and is characterized by a reversible, predominantly posterior (classically parietooccipital) leukoencephalopathy with clinical features on a spectrum ranging from headaches and visual changes to confusion/altered mental status and seizures. It is thought to be due to diffuse vasogenic edema in white matter tracts, most often secondary to severe acute hypertension.⁹ First characterized by Hinchey et al.⁴ in children, PRES has primarily been described in association with cancer chemotherapy,¹⁰ primary renal disease,⁵ and autoimmune disease. Occasionally PRES is severe enough to trigger ICU admission. Chen et al.² characterized a series of Taiwanese pediatric ICU patients with PRES, reporting that all were associated with severe hypertension and altered mental status changes. With appropriate treatment of their hypertension and seizures and/or withdrawal of offending medications, all patients had both clinical and radiological resolution of their PRES. All 7 patients that Chen et al. documented had typical distributions of parietotemporooccipital lesions on their initial MRI scans.

In contrast, there are relatively few case reports or case series in children documenting exclusively cerebellar involvement.^{4,5,7,8} In adults, PRES with primarily cerebellar involvement is documented, although it is not typical.^{1,3,7} In 2004, Cruz-Flores et al.³ documented 2 adult patients and identified 15 other previously published case reports. They found that PRES with brainstem/cerebellar involvement tended to happen to younger adult patients (in their 40s vs in their 50s or 60s) and that most had renal failure as a comorbidity of their illness.

Cerebellar involvement severe enough to cause obstructive hydrocephalus is even more rarely documented. A recent report by Kumar et al.⁷ presented 3 adult patients who experienced PRES and reversible obstructive hydrocephalus. In their review of the literature,

hypertension was present in 56% of adult patients, and 50% of the patients received an EVD. Ninety percent had cerebellar involvement, with the remaining 10% having brainstem involvement. With the exception of 1 patient who had sepsis, all patients had symptom resolution with treatment. All of the additional case reports they reviewed involved adults, with the exception of Lin et al.,⁸ who described an 11-year-old boy who presented with headaches and blurred vision. On imaging he had parenchymal edema and a radiographic lesion infiltrating the left cerebellum and vermis. His MRI also indicated cerebellar tonsillar herniation. This patient was acutely treated with intravenous antihypertensive medications and had an EVD placed, with eventual resolution of symptoms. It is speculated that the posterior circulation is somehow inherently vulnerable to the effects of severe hypertension, leading to intermittent endothelial disruption, and in turn leading to edema.¹¹ It is unclear why our patient's edema and pathology were localized to the cerebellar vasculature.

Conclusions

The occurrence of PRES with exclusively cerebellar pathology is very rare in children, but this entity can present in dramatic fashion with obstructive hydrocephalus, triggering concerns for a mass lesion or CNS infection. We have described a perplexing case of severe hypertension leading to left ventricular hypertrophy (suggesting that the hypertension had a chronic nature, which was confirmed by renal biopsy), PRES, and cerebellar edema, ultimately resulting in obstructive hydrocephalus and altered mental status necessitating placement of an EVD. With appropriate treatment of his hypertension, this child was able to recover from his PRES and return to normal without any need for permanent CSF diversion. Early recognition of the spectrum of this syndrome by both pediatric neurosurgeons and pediatric intensivists is critical to obtain the appropriate imaging and to provide the appropriate management.

Abbreviations used in this paper

BUN	blood urea nitrogen
Cr	creatinine
ED	emergency department
EVD	external ventricular drain
PRES	posterior reversible encephalopathy syndrome

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Fig. 1. Axial CT images obtained without contrast material demonstrating the patient's hydrocephalus (**left**) and tight posterior fossa (**right**).

Fig. 2. Magnetic resonance imaging, FLAIR sequence, demonstrating cerebellar edema; axial (**A**) and sagittal (**B**) views. Diffusion-weighted axial image (**C**) of cerebellum demonstrating edema but no infarction.