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CLINICAL VIGNETTE

A Case of Central-Variant Posterior Reversible Encephalopathy Syndrome (PRES)

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinic-radiographic entity that is often reversible. It has been associated with a wide array of clinical diagnoses, including hypertension, immunosuppression, renal disease, or medications. Increasing numbers of atypical presentations with radiographic distributions of the signature vasogenic edema associated with PRES are being reported. Prompt recognition and acquisition of imaging is important to ensure adequate treatment.

Case

A 71-year-old male presented with progressive weakness. He had hypertension, prostate cancer treated with radiation, complicated by urinary retention, and asymptomatic cerebellar punctate hemorrhage on imaging within the past year. He had recurrent problems with medical nonadherence, related to transportation difficulties to appointments and difficulties obtaining medications.

He reported generalized weakness and fatigue, as well as dyspnea on exertion for the two weeks prior to presentation. He also reported intermittent blurry vision, and on the day of presentation nausea without emesis or any associated pain. He presented to the ED where blood pressure of 230/111 was obtained. He was alert and oriented, with a nonfocal neurologic exam. He acknowledged running out of his medications for the past month.

His initial exam was also notable for lower extremity edema to mid-shin and elevated jugular venous pressure and presence of an S4. His pulmonary and abdominal exams were unremarkable. Initial labs included an elevated troponin, which peaked at 0.34, in the setting of submillimeter ST depressions in the inferior leads. His creatinine was elevated to 1.8 from baseline ~1.2. He was admitted to the intensive care unit for hypertensive emergency in the setting of non-ST-elevation myocardial injury and acute kidney injury and was initiated on both nitroglycerin drip and nicardipine drips.

Given his history of prior cerebellar hemorrhage and severe hypertension, a CT head was obtained. No acute hemorrhage was identified, but hypodensity in the pons and medial thalami raised concerned for possible cerebral edema. Subsequent MRI showed nearly confluent FLAIR and T2-weighted hyperintensity in the pons from the junction with the midbrain to the medullary pyramids (Figures 1 and 2) as well as the bilateral medial thalami, suggestive of central variant brainstem posterior reversible encephalopathy syndrome (PRES).

His hypertension was controlled with nicardipine and nitroglycerin drips, and within four days he was transitioned to oral medications and transferred out of the ICU for gentle diuresis. His kidney function recovered partially, with residual chronic kidney disease attributed to chronic poorly controlled hypertension. His NSTEMI in the setting of hypertensive emergency and PRES, prompted scheduling post discharge left heart catheterization. Repeat MRI six days later showed slight decrease in the T2 signal abnormalities, indicating some improvement. (Figure 3)

Discussion

PRES is a clinico-radiographic diagnosis, which can present with a wide variety of symptoms ranging from subacute headache to true encephalopathy and seizures (Table 1). It is related to a wide variety of systemic disorders as well as medications (Table 2). A high index of suspicion is needed to facilitate early imaging to make the diagnosis. MRI is optimal imaging for PRES, and is characterized by vasogenic edema most clearly seen as cortical and subcortical hyperintensity on T2/FLAIR sequences,[1,2] generally with sparing of the deeper white matter.

The underlying pathophysiology of the disease is incompletely understood. There are two leading theories: “hyper-perfusion” in the setting of uncontrolled hypertension, and endothelial dysfunction.[1,5,6] As blood pressure elevates, it surpasses the range of autoregulation leading to a state of “hyper-perfusion” causing endothelial dysfunction and vascular leakage, ultimately resulting in vasogenic edema. It is proposed that sympathetic innervation of arterioles allows for vasoconstriction and better protection against this hyper-perfusion.[1,6,7] The posterior circulation has notably less sympathetic innervation than the anterior circulation, which may explain why the posterior circulation is particularly susceptible.[1,3,5] This hyper-perfusion theory does not account for the subset of patients

diagnosed with PRES with normal blood pressures. The second theory is that PRES is driven by a state of endothelial dysfunction in the setting of systemic toxicity such as sepsis or eclampsia.[1,3,5] Immunosuppressive mediations might also act through this mechanism.[1] In this model, hypertension would be a result of the endothelial dysfunction, either driven by the cytokines from the underlying toxic process or as a result of vasoconstrictors released from the endothelium itself after it is damaged.[1]

Bartynski and Boardman described the most common imaging patterns in PRES, classifying into the three most common patterns.[8] Nearly all cases show parietal-occipital involvement, with other frequently involved areas including the frontal-temporal lobes, the cerebellum, and the brainstem and basal ganglia in 9-22% of cases depending on the case series.[8-10] The central or "brainstem" variant of PRES without concomitant parieto-occipital changes, seen in our patient, occurs in only about 4% of cases.[10] They reported, five patients with centra-variant PRES, with involvement of other basal ganglia or periventricular matter associated with a variety of causes. It has been difficult to directly correlate causes of PRES with specific imaging findings.[5] One study of 28 patients, found no association between hypertensive vs non-hypertensive causes and imaging findings.[4]

McKinney et al propose that the pathophysiology of central variant PRES is endothelial dysfunction primarily within small, perforating vessels supplying the brainstem, though why these regions are particularly susceptible in not yet known.[10] Additional proposals are that relatively more sympathetic innervation of the parieto-occipital cortex via the posterior communicating artery from the anterior circulation compared to the brainstem, allowing for the sparing.[11] Alternatively, there is decreased vascular leakage in distal portion of the vertebro-basilar system, which would spare the parieto-occipital region, [11,12] possibly because the vessels supplying the brainstem come off of larger vessels and are subjected to higher perfusion pressures at higher blood pressures.[5] One series noted approximately 40% of cases of central-variant PRES were not associated with chronic hypertension, and proposed vascular sensitivity to rapid increase in blood pressure.[12] Animal models have shown that mild elevations of blood pressure caused predominantly supratentorial edema, whereas severe elevations in blood pressure produced infratentorial edema in the brainstem and basal ganglia.[5,12]

The differential diagnosis for central-variant imaging findings includes infectious rhombic and thalamic encephalitis or demyelinating disorders.[2,10,11] These were considered by our neurologists, though ultimately were not consistent with the clinical picture. An LP was recommended for complete evaluation. Another case report of central-variant PRES suggests an albuminocytologic dissociation in CSF studies of these patients,[7] which may be related to the increased permeability of the small perforating vessels referred to previously as susceptible to this process. At this time, CSF analysis is not a major aspect of evaluation for PRES, but may be valuable in the future.

Conclusions

Our case showed imaging findings consistent with atypical variant PRES, in the setting of both chronic poorly-controlled hypertension and renal disease, both common associations with PRES. Repeat MRI showed some resolution. Because there are relatively few cases of brainstem-variant PRES, it is difficult to predict outcome compared to more classical presentations. However, it is becoming increasingly recognized and ready for further research. Physicians should be familiar with atypical presentations and maintain a high index of suspicion to allow for appropriate recognition and treatment.

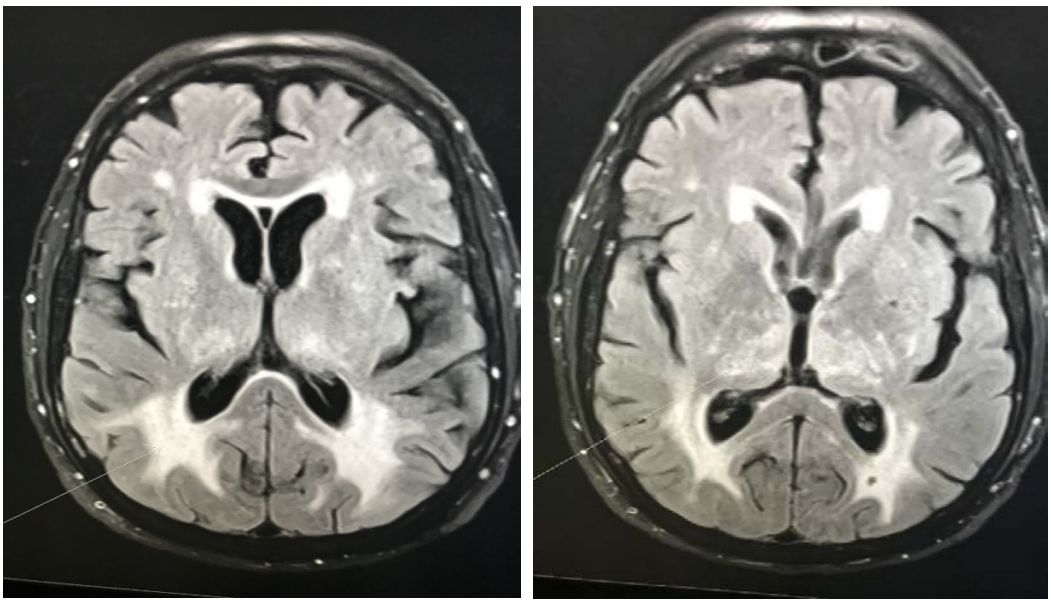

Figure 1. FLAIR signal abnormality involving posterior parieto-occipital white matter and the thalami (arrows).

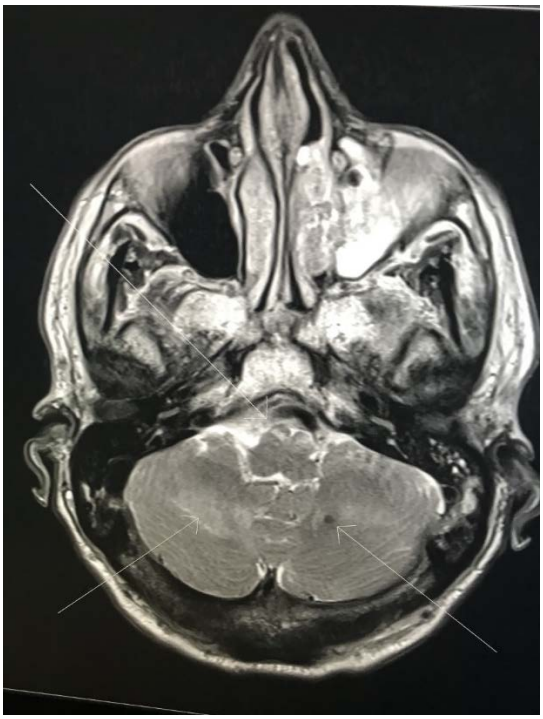

Figure 2. Edema in the right cerebellum (bottom left arrow) and ventral medulla (top left arrow). There is also a microbleed in the left cerebellum (right arrow).

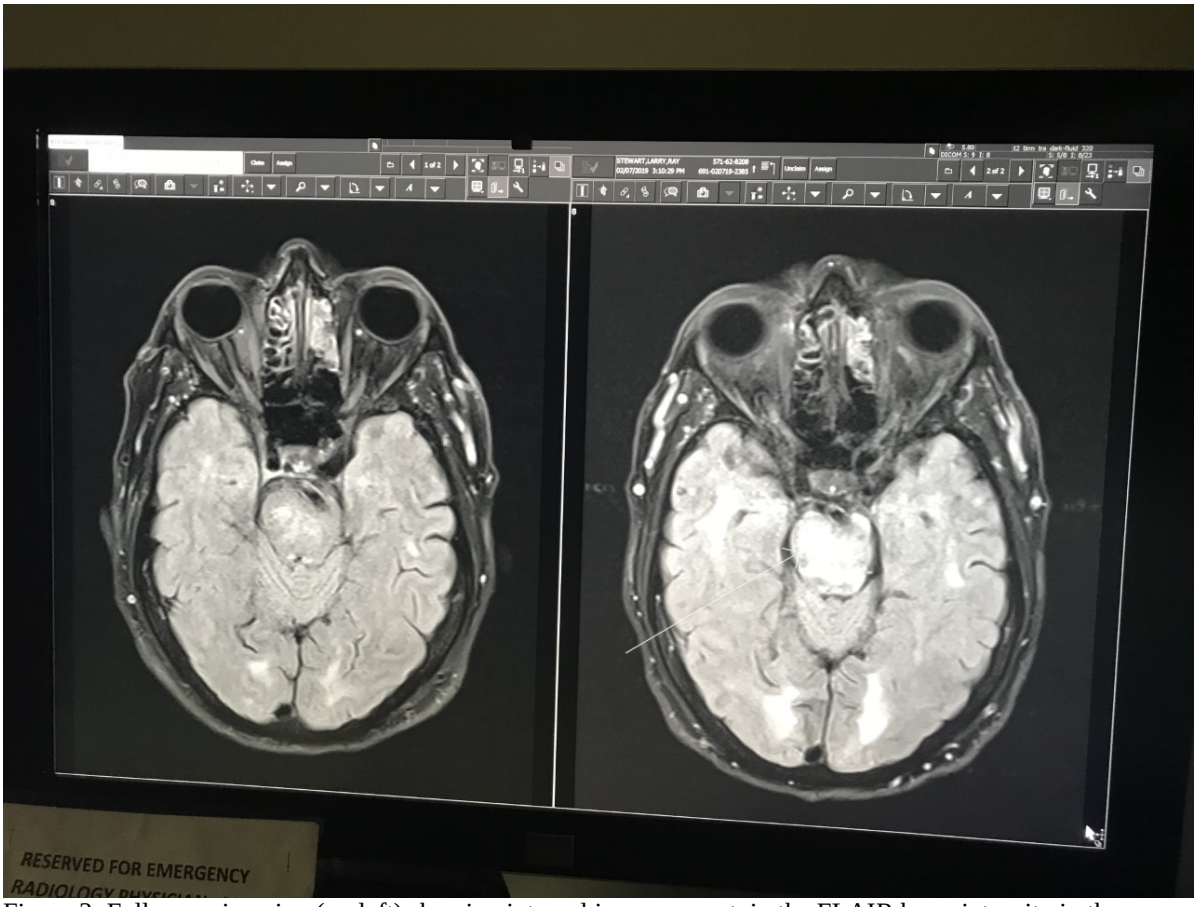

Figure 3: Follow up imaging (on left) showing interval improvement in the FLAIR hyperintensity in the pons and occipital white matter after one week.

Table 1: Incidence of neurologic symptoms associated with PRES, adapted from Fischer.[1]

Neurologic symptoms and incidence of association with PRES[1]	
Symptom	Incidence %
Encephalopathy	28-92
Alteration of consciousness	67-90
Arterial hypertension or blood pressure fluctuations	61-80
Seizures	70-74
Visual disturbance	20-67
Headache	26-53
Focal neurologic signs	5-15

Table 2: Conditions associated with PRE,[3,4]

Medical	**Medications**
Hypertension	Immunosuppressants, such as cyclosporine, tacrolimus, sirolimus
Autoimmune: systemic lupus erythematosus, polyarteritis nodosa, granulomatosis with polyangiitis, scleroderma	Chemotherapies, such as cyclophosphamide, cisplatin, gemcitabine, cytarabine
Thrombotic thrombocytopenic purpura	Bevacizumab, tyrosine kinase inhibitors
Hemolytic uremic syndrome	Venlafaxine
Eclampsia/preeclampsia	Alpha-interferon
Sepsis/shock	
Renal diseases (acute or chronic)	
Hypomagnesemia, hypocalcemia	
Guillain-Barre syndrome	

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