A Presentation of PRES with Rapid Cortical Enhancement Caused by Hypertension Secondary to Structural Renal Abnormalities

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Abstract

Posterior reversible encephalopathy syndrome (PRES) typically presents with acute onset headaches, seizures, altered mental status, and visual disturbances. Common etiologies include uncontrolled hypertension, preeclampsia, and vasculitis. While the above constellation of features is usually seen, PRES is a diagnosis of exclusion corroborated by magnetic resonance imaging (MRI) of the head, and atypical manifestations are known to occur. There is a paucity of PRES cases with clinical findings of ophthalmalgia and serial MRI findings of rapidly developing and resolving cortical enhancement. In this report we present a case where the presenting symptoms were subacute onset headache, papilledema, visual field loss, and ophthalmalgia. Unusual MRI findings included the rapid development of cortical and leptomeningeal enhancements found on MRI 10 days after a prior MRI showed no specific findings. Further investigation demonstrated anomalous renal artery anatomy with a concomitant right renal artery stenosis.

Introduction

PRES is a clinical syndrome associated with a broad spectrum of clinical features, including seizures, headaches, focal neurological deficits, encephalopathy, and visual disturbances. The most common findings are seizures in over 70% of cases of PRES, hypertension present in 60% of cases, headache in 50% of cases, and encephalopathy in 28% of cases. Less commonly, PRES is noted to present with visual disturbances in roughly 20% of presentations. PRES is more prevalent in females, accounting for 63.5% of documented cases (1). The mean age of onset for PRES is 45 years old. However, a wide range of ages can be affected and there is literature documenting cases in patients ranging from age 4 through 90. The diagnosis of PRES is typically made with T2 or FLAIR MRI studies showing focal regions of symmetric hyperintensities with occipito-parietal involvement in 98% of cases. Special care must be taken to exclude other diagnoses such as vasculitis, infection, white matter disease, and autoimmune pathologies (2). There are few recorded PRES cases where patients have presented with visual disturbances without changes in mental status, focal neurologic deficits, or seizures and rapid development and resolution of cortical enhancements on MRI. In this case discussion we present a patient whose PRES diagnosis included ophthalmalgia, papilledema, and anomalous renal anatomy with concomitant right renal artery stenosis as key findings on clinical investigation.

Case Presentation

J.D. is a 19-year-old female with a history of anxiety who presented to the Emergency Department (ED) with two weeks of progressive headaches and bilateral visual changes. One week prior the patient saw outpatient ophthalmology, where fundoscopic exam revealed papilledema and MRI (Figure 1A) was unremarkable. A diagnosis of pseudotumor cerebri was made and a 7-day course of prednisone and acetazolamide was started with mild improvement.

In the ED the patient complained of bilateral eye pain, nausea, and vomiting. Patient denied sexual activity or travel and noted episodic rashes extending from her face to her clavicle. Physical exam revealed right central vision loss and left peripheral vision loss. Vital signs were a temperature of 100.4° F, blood pressure 190/130, pulse 80, and respiratory rate 16. Complete blood count revealed leukocytosis, thrombocytosis, and erythrocytosis. Comprehensive metabolic panel showed hypokalemia and erythrocyte sedimentation rate and c-reactive protein were normal. Repeat MRI revealed multiple enhancing flair hyperintense lesions with leptomeningeal and cortical enhancements and multiple enhancements in the posteromedial occipital and left anterior frontal convexities (Figure 1B). Tests for syphilis, gonorrhea, bartonella, tuberculosis, HIV, Lyme disease, COVID, and a respiratory virus panel were negative. Urinalysis showed mild ketonuria. Because her hypertension classified the patient's condition as a hypertensive emergency

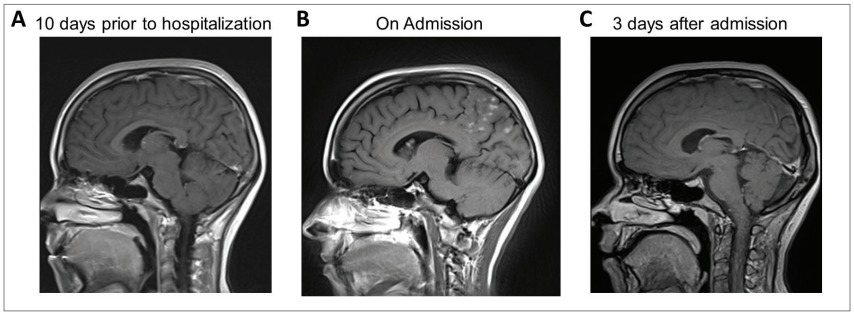

Figure 1. A comparison of T1 Sagittal FLAIR post-contrast MRIs of the brain taken (A) 10 days prior to patient presentation, (B) on presentation to the ED, and (C) on hospital day 3. Notice the diffuse hyper-intense lesions with periventricular and leptomeningeal involvement with resolution of enhancements on MRI conducted on hospital day 3.

with concurrent neurological symptoms, the patient was admitted. Overnight the patient's systolic blood pressure peaked at over 200 and was unresponsive to 5 mg nicardipine drip. The patient required a four-drug antihypertensive regimen of amlodipine 10 mg, lisinopril 10 mg, and hydralazine 25 mg daily in addition to the 5 mg nicardipine drip to maintain systolic blood pressure less than 140.

Day 2 blood tests for anti-neutrophilic cytoplasmic antibodies, anticardiolipin antibodies, anti-nuclear antibodies, anti-aquaporin 4 glycoprotein, and anti-myelin oligodendrocyte glycoprotein were negative, as were lumbar punctures for glucose, leukocytes, and oligoclonal bands. Abdominal computed tomography (CT) without contrast initially showed what was thought to be a potentially infarcted hypoattenuating left kidney (Figure 2A), however CT angiography showed right renal artery stenosis (RAS) with bilateral renal artery accessory poles. A diagnosis of RAS and PRES was made and the hypoattenuation of the left kidney in comparison to the right was understood to be due to delayed clearance of prior contrast administrations. The upper portion of the right kidney appeared bright due to right renal artery stenosis limiting blood flow and thus delaying clearance, while the lower lobe of the right kidney remained dark due to preserved blood flow via anomalous renal vasculature (Figure 2B). MRI of the brain conducted in hospital on day 3 showed resolution of contrast enhancement seen in previous MRI (Figure 1C). The patient was discharged on hospital day 3 with a course of prednisone and follow up appointments with nephrology and vascular surgery for renal angioplasty were scheduled.

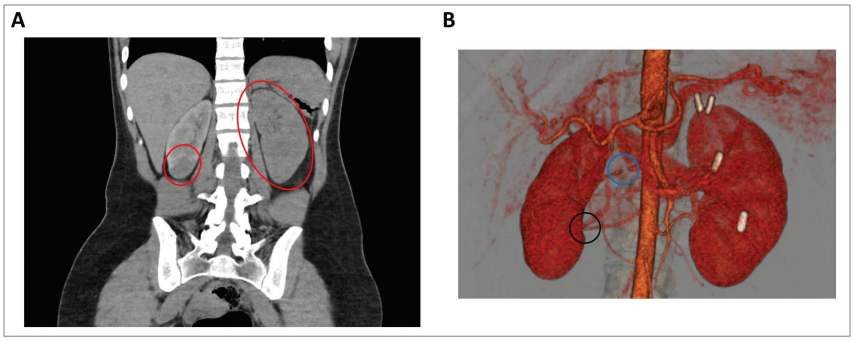

Figure 2. A) Non-contrast CT of the abdomen revealing swelling and hypo-attenuation in the left kidney and right lower pole of the right kidney, originally suspicious for infarctions, eventually determined to be due to delayed clearance of contrast from prior imaging studies by right kidney, secondary to right renal artery stenosis and right accessory renal arteries. Hypo-attenuated regions (circled in red) later understood to be areas with healthy renal function supplied by accessory renal vasculature while vasculature supplying hyper-attenuated regions is stenosed. B) CTA of the abdomen demonstrating two accessory right renal arteries (circled in black) extending into the right kidney's lower pole, with main right middle renal artery demonstrating high-grade stenosis (circled in blue). Compare to intact left renal artery on the other side.

Discussion

This case was an atypical PRES presentation with headache, hypertension secondary to RAS and accessory renal arteries bilaterally, visual changes, and papilledema without AMS or seizures — two notable exclusions for PRES. While PRES commonly presents with seizures and altered mental status changes, clinicians should elevate their suspicion of PRES in cases with emergent hypertension of unknown cause and neurological findings. A pertinent feature in this case was the findings of accessory renal arteries and renal artery stenosis, a remarkable finding in this otherwise healthy, young female patient with no prior contributing history. Physiologically, the previously undiagnosed renal artery abnormalities explained this patient's emergent hypertension, hypokalemia, and poor response to blood pressure medications on admission. The blood pressure changes in this patient were likely chronic, eventually leading to her papilledema, intracranial hypertension, and the development of PRES.

Workup in this case was initially conducted to surveil for etiologies that could lead to contrast enhancement such as central autoimmune demyelination, Neuromyelitis Optica, SLE, vasculitis, idiopathic intracranial hypertension, and stroke. It included CBC, CRP, glucose level, B12 level, ANA, RF APA, lupus anticoagulant, serum ACE, UA, ANCA, Mantoux test, quantINTERFERON, infectious disease panel, HIV serology, mycoplasma serology, NMO, MOG antibodies, lumbar puncture, and MRI in addition to history and physical examination. In this case, the driver of hypertension was found on abdominal CTA to be right renal artery stenosis, despite non-contrast CT of abdomen giving the appearance of left renal ischemic changes. Renal artery stenosis is believed to cause 1–10% of cases of hypertension in the United States, with unilateral involvement in 53–80% of cases, typically affecting older male patients above 45 years old due to atherosclerotic changes (3).

Following diagnosis of PRES, treatment focuses on resolving the underlying cause, most commonly hypertension, iatrogenic causes, eclampsia, and systemic factors (4). After the patient was stabilized, follow-up with vascular surgery was necessary for placement of a renal artery stent to normalize blood pressures. The patient was followed up closely by vascular surgery and nephrology. Pathophysiology behind PRES is thought to be related to alterations in cerebrovascular autoregulation leading to subsequent vasogenic edema. Autoimmune etiologies and concomitant vasculitides such as thrombotic thrombocytopenic purpura, primary sclerosing cholangitis, rheumatoid arthritis, polyarteritis nodosa, and systemic lupus erythematous are notable associations. PRES also has a strong association with preeclampsia, with up to 50% of patients subsequently developing PRES during the peripartum period.

Other relevant points in this case were the acute development of hyperintensities on MRI over a 10-day period, with the prior diagnosis of papilledema masking the recognition of the patient's hypertension being secondary to vascular abnormalities. While pseudotumor cerebri traditionally presents as a headache and bilateral visual symptoms worse in the morning in a female patient with elevated BMI, some surveillance should be conducted to rule out other causes of intracranial hypertension4. Key considerations to rule out include malignancy, vascular abnormalities, overproduction

or under-resorption of CSF, and etiologies causing acute and chronic hypertension (5). A workup of this patient's elevated blood pressures could have led to prompt diagnosis and treatment.

Conclusion

In summary, PRES is a diagnosis of exclusion supported with MRI findings that requires workup for etiologies driving vasogenic changes. Treatment focuses on resolving underlying causes. In this case rare presenting features were accessory renal artery poles, right renal artery stenosis, and symptoms of ophthalmalgia with multifocal hyperintensities found on MRI presenting in a young patient with no prior medical history. Workup for PRES is broad, including assessment for hypertensive, vascular, autoimmune, inflammatory, pregnancy-related, and iatrogenic causes.

Disclosures

The authors have nothing to disclose.

References

1. Buchhanolla P, Bir S, Angelette A, Lewis A, Kandregula S, Guthikonda B, et al. Determination of Prevalence of Posterior Reversible Encephalopathy Syndrome (PRES) and Its Association with Cerebral Infarction, and Outcome in the Nationwide Inpatient Sample, 2016–2018 (P16-10.002). Neurology [Internet]. 2022 May 3 [cited 2023 Jun 19];98(18 Supplement). Available from: https://n.neurology.org/content/98/18_Supplement/3555
2. Zelaya JE, Al-Khoury L. Posterior Reversible Encephalopathy Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Jun 19]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK554492/
3. Bokhari MR, Bokhari SRA. Renal Artery Stenosis. [Updated 2022 Sep 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430718/.
4. Rigi M, Almarzouqi SJ, Morgan ML, Lee AG. Papilledema: epidemiology, etiology, and clinical management. *Eye Brain*. 2015;7:47–57.
5. Triplett JD, Kutlubaev MA, Kermode AG, Hardy T. Posterior reversible encephalopathy syndrome (PRES): diagnosis and management. *Pract Neurol*. 2022 Jun;22(3):183–9.