**Case Report**

**Association between Posterior Reversible Encephalopathy Syndrome and Mycoplasma pneumoniae infection**

Archana Ramgopal, Aravind Thavamani, Abdulla Ghori

MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH

**ABSTRACT**

*Mycoplasma pneumoniae* is a microbe known to affect numerous organ systems, and in particular, can cause neurological manifestations. We describe an otherwise healthy child who presented with acute onset intractable headache with magnetic resonance imaging (MRI) findings consistent with posterior reversible encephalopathy syndrome (PRES), a neurological manifestation that presents with headache, vision changes, altered mental status, or seizures. Our patient did not have any of the common etiologies for PRES reported but tested positive for acute *M. pneumoniae* infection. The clinical course followed that expected in PRES with rapid resolution of symptoms and MRI findings in subsequent imaging. Literature review shows association between *Mycoplasma* infection with encephalitis and cerebellitis, but none with PRES in children. Evidence of recent mycoplasma infection in a healthy patient presenting with clinical/radiological findings consistent with PRES, especially in the absence of known predisposing factors, raises the question of *M. pneumoniae* infection being a trigger for PRES.

**KEYWORDS:** Headache, mycoplasma, PRES

**INTRODUCTION**

A 10-year-old otherwise healthy, overweight (BMI 90–94th percentile) African–American girl presented with intractable headache and vomiting for a week without altered mental status, cough, or any other symptoms. She had always remained normotensive. Her cell counts, renal/hepatic function, glucose, and lipid profile were normal at baseline. Her blood pressure (BP) on first day was 136/106 mm Hg in emergency room. She had worsening of her symptoms and was admitted on seventh day of her illness. She was alert but fatigued with dry mucus membranes. She was afebrile, and her BP was 120/88 mm Hg and heart rate was 98 beats per minute. Examination was otherwise unremarkable including a full neurological evaluation by neurologist, with no cerebellar signs. Ophthalmological evaluation showed normal visual acuity and intraocular pressure with no papilledema.

Investigations yielded normal values for blood counts, serum chemistry, liver function, CRP (C-reactive protein), ESR (erythrocyte sedimentation rate), thyroid function, and urinalysis. EBV (Epstein–Barr virus) and Lyme serology test results were negative.

Magnetic resonance imaging (MRI) of the brain on admission demonstrated diffuse T1 and T2 signal abnormality throughout the folia of the cerebellum bilaterally with no evidence of enhancement after contrast, consistent with posterior reversible encephalopathy syndrome (PRES), and mild hydrocephalus and periventricular edema. There was no diffusion restriction to suggest acute infarct, and no susceptibility artifact to suggest hemorrhage. Normal flow void present on T2-weighted images. MR venography (MRV) with contrast demonstrated congenital hypoplasia of transverse and sigmoid sinus with a small jugular bulb. There was no evidence of venous thrombosis.

**Address for correspondence:** Dr. Abdulla Ghor, MetroHealth Medical Center, Case Western Reserve University, 2500 MetroHealth Drive, Cleveland, OH, 44109.

E-mail: aghori@metrohealth.org

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She received supportive IV fluid therapy and one dose of parenteral hydralazine. During the 4 days in ICU, her headache and hypertension resolved. Serum mycoplasma IgM antibody resulted after discharge was positive at 2874 U/mL (positive >950 U/mL), suggestive of an acute infection. MRI a month later showed marked improvement of the hydrocephalus and cerebellar T1/T2 signal abnormality, with subtle persistent signal abnormality in the posterior superior aspect. MRI 6 months later showed complete resolution.

**Discussion**

PRES described in 1996 is also known as reversible posterior leukoencephalopathy, reversible posterior cerebral edema, and hypertensive encephalopathy.[1] The presentation includes headache, seizures, changes in mentation and vision, and typical transient MRI findings of subcortical white matter edema in T2-weighted images and fluid attenuation inversion recovery (FLAIR) images.[2] There are reports of irreversible neurological deficits in 12% cases.[3,4] Areas of the brain perfused by the posterior circulation are affected preferentially due to the protective effect of the pial and intracerebral vessels in anterior circulation with higher concentration of adrenergic nerves.

PRES has been described mostly with hypertension in the background of a variety of acute and chronic conditions. The pathophysiology was thought to be the result of endothelial damage secondary to hypertension. Alternative hypothesis postulates that hypertension could be a reaction to insufficient brain perfusion caused by endothelial dysfunction from systemic toxic effects.[5] However, 15%–20% of patients with PRES are normotensive or hypotensive.[6] Even among the hypertensive, <50% were above the limits of cerebral flow autoregulation of ≥140–150 mm Hg. When infection predisposes to PRES, the BP is reported as normal or minimally elevated and vasogenic edema in neuroimaging is inversely proportional to BP.[6]

The associated risk factors for PRES reported in children include renal failure, nephrotic syndrome, acute nephritis, hemolytic uremic syndrome, high-dose steroid therapy, autoimmune disorders, and patients with malignancy and transplantation on immunosuppressive therapies. PRES has also been reported with infection, sepsis, shock, hypomagnesemia, hypercalcemia, hypercholesterolemia, intravenous immunoglobulin, and Guillain–Barré syndrome.[7]

*Mycoplasma* is a prokaryotic microbe that has a complex pathogenesis and affects different organ systems. The proposed mechanisms of neurological manifestations are direct invasion, neurotoxin production, or immune-mediated mechanism.[8] When associated with cerebellitis, the abnormalities are typically seen in the cerebellar gray and white matter, with hyperintensities on T2 imaging, as in PRES. In addition, hypointensities in T1 are seen in cerebellitis. Thus, there are radiological similarities on MRI between PRES and cerebellitis. However, the absence of signs of cerebellar dysfunction and papilledema throughout the course of the illness makes cerebellitis less likely in our patient.

The classic clinical symptomatology, MRI findings and spontaneous resolution in eight days in this patient, are consistent with PRES which typically resolves in 2–8 days.[9] Mycoplasma infections are well known to resolve without specific therapy. Thus, in the absence of known reported triggers for PRES based on current literature, we postulate that *M. pneumoniae* infection may have triggered the onset of PRES in our patient.

Cases of PRES have been reported with fever as one of the symptoms. Although such patients had underlying renal conditions, it is unclear if their febrile illness could be an infection such as mycoplasma. Recurrent cases of PRES have been reported with uncontrolled hypertension, sickle cell disease or allo bone marrow transplant with infection, or atypical autoimmune disease and possible viral infection.[10] It is possible that one of the triggers for PRES in those situations could be mycoplasma infection without obvious respiratory symptoms and potentially missed. Literature on PRES in children is limited and lacks strict clinical criteria for diagnosis. There have been case reports of PRES with atypical manifestations as well. A review of PubMed literature showed association of *M. Pneumoniae* infection with cerebellitis and encephalitis in children, but not any reports of association with PRES. Therefore, it is necessary to evaluate for new triggers contributing to PRES, especially in cases with no known risk factors.

**Conclusions**

This case supports the theory that mycoplasma infection can present with reversible hypertension, headache, MRI findings suggestive of PRES with no other concurrent neurological symptoms, or sources of localized infection. This case also supports that PRES could develop in an otherwise normal child with no other underlying medical conditions. Whether mycoplasma infection acts as a trigger in those susceptible to PRES with baseline renal, autoimmune, or malignant conditions will be worth studying in a prospective manner. The range of etiologies and manifestations in PRES is likely getting wider than originally known.
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Conflicts of interest
There are no conflicts of interest.

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