ORIGINAL ARTICLE

Ophthalmic Manifestations of Posterior Reversible Encephalopathy Syndrome

Nicole Lifson^a, Andrew Pasquale^b, George Salloum^a, and Samuel Alpert^a

^aDepartment of Ophthalmology, State University of New York Upstate Medical Center, Syracuse, New York, USA; ^bDepartment of Ophthalmology, State University of New York at Buffalo, Buffalo, New York, USA

ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a condition of neurotoxicity that presents with a sudden onset of symptoms including headache, altered mental status, seizures, and visual disturbances. Monitoring visual symptoms in PRES is critical as visual deficits are found in nearly 40% of patients. This paper aims to identify the visual symptoms associated with PRES and determine visual outcomes following treatment. While the symptoms of PRES are alarming, the disease is typically reversible once the cause is eliminated. Our findings suggest that those who present with ocular complaints can be reassured that their symptoms will improve, if not completely resolve.

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a syndrome of neurotoxicity that typically involves headaches, confusion, seizures, and occasionally, loss of vision. Neuroimaging is one of the most important diagnostic features of the disease and typically indicates vasogenic oedema localized to the posterior occipital and parietal lobes, but other areas of the brain can be affected.¹ There is little consensus on the pathophysiology of PRES, but it is suspected to be related either to inadequate cerebral autoregulation or endothelial dysfunction. This causes cerebral hyperperfusion, which eventually leads to extravasation of fluid and blood in the posterior aspect of the brain.¹ PRES has been diagnosed in ages ranging from 4 to 90, with the diagnosis more commonly made in middle-aged adults, with the average age between 39 and 47 years.² Many patients diagnosed with PRES have comorbid conditions including hypertension, vascular and autoimmune diseases, eclampsia, organ transplant, immunosuppressive therapy, and chronic renal disease.¹

What makes PRES difficult to diagnose is its non-specific clinical presentation. Presenting signs ranging from mild confusion to patients being completely comatose, and 60–75% of patients develop tonic-clonic seizures, while the remainder often have non-convulsive seizures. Patients may present with visual

disturbances including decreased visual acuity, visual field deficits, cortical blindness or hallucinations, while others may have no visual deficits at all.^{3,4} While the symptoms of PRES are alarming, the disease is typically reversible once the cause is eliminated. Singer et al. identified 84% of cancer patients diagnosed with PRES to have complete resolution of their neurological symptoms within 7.5 days of symptoms onset.⁵

While there have been numerous studies illustrating the overall prognosis for patients diagnosed with PRES, few specifically analyse the resolution of patients' visual complaints. Discussing and monitoring visual symptoms in patients with PRES is critical as visual deficits are typically found in 36–39% of patients.^{4,6} This paper aims to identify the visual symptoms associated with PRES and determine visual outcomes following treatment.

Methods

This retrospective study was reviewed by an accreted Institutional Review Board and granted exempt status according to federal regulations. Health Insurance Portability and Accountability Act compliance was adhered to throughout this study. Using the “SlicerDicer” function of our electronic medical record, EPIC, we identified 62

patients with a diagnosis of PRES at SUNY Upstate Medical University in Syracuse, NY between the dates 1 January 2013 and 31 December 2017. Charts were reviewed and of those identified, 41 patients met the inclusion criteria of having an imaging confirmed diagnosis of PRES. There were no exclusion criteria.

PRES was defined as altered mental status, seizures, and/or abnormal visual symptoms that were associated with computed tomography (CT) or magnetic resonance imaging (MRI) proven abnormalities consistent with findings of PRES, as indicated by the attending radiologist. MRI PRES was defined as primary subcortical lesions present on standard fluid-attenuated inversion recovery (FLAIR) sequences in the setting of acute neurologic symptoms without radiographic evidence of acute infarct or other processes including new brain metastases or emboli (Figure 1). CT PRES was defined as new hypodensities primarily in the subcortical white matter (Figure 2).

We collected data on age, gender, predisposing conditions, presenting signs and symptoms, visual symptoms, visual field and visual acuity. The main objective outcome variables of the study included

Figure 1. MRI head T2 FLAIR of patient 5 shows bilateral enhancing parietooccipital lesions consistent with PRES.

Figure 2. CT head of patient 3 at presentation exhibiting white matter hypodensities in the parietal and occipital lobes with sulcal effacement (white arrows).

Snellen best-corrected visual acuity in distance reported at 20 feet and visual field testing to include confrontational bedside and formal Humphrey 24-2 Visual Fields. The main subjective outcome variables included patient identified visual changes.

Results

We identified 41 patients who met the inclusion criteria. The mean age at presentation was 48 years (ranging from 7 to 76 years old). Of those diagnosed with PRES, 85% ($n = 35$) were women. Comorbid conditions were common and included hypertension ($n = 27$ [65%]), renal disease ($n = 10$ [24%]), autoimmune disease ($n = 9$ [22%]) and malignancy ($n = 6$ [14%]). Of the patients with PRES, 11 (27%) had ocular complaints. Of the patients with presenting ocular complaints 10 (91%) of them had complete resolution of vision to their original baseline with an average time of 2.4 days and a median of 4 days (ranging from 1 to 10 days). One (9%) of the

patients with PRES did not have full resolution of their symptoms as they had residual intermittent binocular diplopia. Of the patients with ocular complaints, only three had follow-up brain imaging within 5 months of their initial diagnosis. Patients 2 and 6 had complete resolution of their MRI abnormalities, while patient 9 showed significant improvement with residual areas of cortical and subcortical signal changes along the anterior and posterior watershed zones (Table 1).

Of the patients who had ocular complaints, 64% were women ($n = 7$) and 100% ($n = 11$) had a history of hypertension. The ocular symptoms and physical exam findings included bilateral vision loss ($n = 7$ [64%]), unilateral vision loss ($n = 1$ [9%]), colour desaturation ($n = 1$ [9%]), diplopia ($n = 3$ [27%]), photopsias ($n = 1$ [9%]) and pain with extraocular muscle movements ($n = 1$ [9%]) (Table 1).

Not all patients with visual complaints had visual acuity or formal visual field testing. Of the 11 patients with ophthalmologic complaints, seven had their visual acuity formally assessed. Among these seven patients visual acuity ranged from 20/20 to light perception (Table 1). For the remaining four who did not have their visual acuity formally assessed, there was a subjective return to baseline within 1 day or less of symptom onset that did not warrant a further ophthalmology workup.

Discussion

PRES is a diagnosis that can have a varied clinical presentation ranging from a mild headache with confusion to generalized tonic-clonic seizures with bilateral loss of vision. What makes PRES a challenging diagnosis to make is its lack of consistent findings amongst patients, which is why CT or MRI is a critical diagnostic tool.

Of the patients diagnosed with PRES in our cohort, there was a predisposition to individuals who were female (85%), middle-aged (average age of 48 years), and previously diagnosed with hypertension (65%). Other studies report similar demographics; of those diagnosed with PRES 65–75% were female, the average age was between 45 and 52 years, and prior diagnosis of hypertension was found in 53–90% of patients.^{4,7,8} When treating patients with these demographics who present

Table 1. Patient demographics and findings.

Pt.	Sex	Age	Past medical history	Visual symptoms	Visual field	Visual acuity	Outcome
1	F	59	HTN, DM, HLP, obesity, MS, DVT	Diplopia	NA	20/40 OU	Full resolution
2	M	58	HTN, DM, HLP, obesity, OSA, COPD	OU vision loss	OS superior loss	20/50 OD, 20/200 OS	Full resolution
3	F	31	HTN, OSA	OS photopsias	NA	20/20 OU	Full resolution
4	M	27	HTN, CKD, PE, endocarditis, IVDU	OU vision loss	Full OU	20/20 OU	Full resolution
5	F	58	HTN	Diplopia, colour desaturation	NA	NA	Full resolution
6	M	50	HTN, HLP, CKD, glaucoma, anaemia	OU vision loss	NA	NA	Full resolution
7	M	37	HTN	OS vision loss, OS pain with EOMs	Full OU	20/20 OD, 20/40 OS	Full resolution
8	F	7	HTN	OU vision loss	Full OU	CF OU	Full resolution
9	F	62	HTN, COPD, anaemia	OU vision loss	Left lower quadrantanopia	NA	Full resolution
10	F	53	HTN, HLP, CAD, CVA	OU vision loss	NA	NA	Full resolution
11	F	62	HTN, epilepsy, recurrent PRES	OU vision loss, diplopia	OU diffuse depression	LP	Intermittent binocular diplopia

PT, patient; F, female; HTN, hypertension; DM, diabetes mellitus; HLP, hyperlipidaemia; MS, multiple sclerosis; DVT, deep vein thrombosis; NA, not assessed; OU, right and left eyes; M, male; OSA, obstructive sleep apnoea; COPD, chronic obstructive sleep apnoea; OS, left eye; OD, right eye; CKD, chronic kidney disease; PE, pulmonary embolism; IVDU, intravenous drug use; EOMs, extraocular muscle movements; CF, counting fingers; PRES, posterior reversible encephalopathy syndrome; LP, light perception; CAD, coronary artery disease; CVA, cerebrovascular accident.

with altered mentation, seizures and/or visual complaints, PRES should always be a consideration and further assessed with imaging of the brain.

Based on our study, only 27% of patients with a formal diagnosis of PRES had any sort of visual complaint, making vision a poor diagnostic criterion for the syndrome. Of the patients who presented with vision complaints, 91% regained full sight without any deficits. The remaining 9% was due to a single patient. Despite the fact that her symptoms did not fully resolve, they greatly improved. This patient originally presented with diplopia that progressed to light perception vision, which eventually improved to intermittent binocular diplopia and a return to patient's subjective "baseline" vision with a visual acuity of 20/20 without any visual field deficits (Table 1).

In our cohort the average time to recovery of visual symptoms was 2.4 days with a median of 4 days (ranging from 1 to 10 days). Other studies report a more protracted time to recovery of PRES-related symptoms with an average ranging between 3 and 8 days.^{9,10} Lai et al. presents a retrospective study of 23 patients diagnosed with PRES, 15 of which had visual impairments. The median time to full recovery of any PRES-related symptoms was 7 days. Visual abnormalities fully improved within 2 days in eight of the patients, while the remaining patients had residual visual deficits ranging between 3 days and 4 months.¹¹ The discrepancy in time to resolution of symptoms in our cohort could be attributed to our relatively small sample size.

The visual deficits from PRES usually fully recover^{12,13} but a few cases show a protracted course without full resolution. Stott et al. discusses a series of case reports of PRES. One 40-year-old male was diagnosed with PRES 6 days after being admitted to the hospital for acetaminophen overdose, which was complicated by hypertension and seizures. His visual symptoms began suddenly with bilateral no light perception vision and normal pupillary responses that eventually resolved over a 2-week period. Four months following hospital discharge, the patient had residual left inferior quadrantanopia with normal visual acuity, and MRI indicated minor residual right occipital

parenchymal damage.¹⁴ Despite partial recovery of this patient's visual symptoms, they significantly improved when compared to initial presentation, as also seen in patient 11 (Table 1).

Ferbert and Roth present a retrospective study of 25 patients with a diagnosis of PRES and the long-term prognosis of neurologic symptoms. They found that 23 of the patients had full resolution of their symptoms on average 7.5 days following diagnosis. Of the patients with non-resolving symptoms, one patient had died from septicemia and the other was a 67-year-old female who had residual symptoms vaguely described as "mild disturbed vision" 76 days after her diagnosis. Her presenting symptoms were not mentioned. Forty-three days after the inciting event the patient had an MRI that showed almost complete remission of white matter lesions, but new intracerebral bleeding in the posterior lobe, which may have contributed to her visual complaints.¹⁰ While there are case reports of non-resolving ocular symptoms in PRES, they are limited and tend to support the notion that symptoms will show significant improvement. Our study is unique in that it is the largest retrospective study of its kind specifically assessing visual outcomes in PRES.

The limitations of this study include lack of consistent or objective analysis of visual fields and visual acuity. 45% of the patients with ocular complaints did not have a formal ophthalmology consult with formal visual acuity testing or visual field analysis as there was prompt resolution of visual symptoms following initiation of treatment for PRES. Of those without formal visual acuity or visual field analysis, patients reported full resolution of their visual symptoms within 1 day or less following hospital admission. Of those without a formal consult, visual symptoms were based on more subjective measures, like patient-reported improvement of visual symptoms. These subjective findings make it more difficult to gauge severity of symptoms and subsequent improvement. In addition, our sample size ($n = 41$) was relatively small.

While visual symptoms occur in a minority of patients, they can be quite alarming. Our findings support the notion that patients with visual symptoms from PRES often have complete recovery of their

visual function following treatment. For those whose deficits remain, their vision is expected to greatly improve when compared to their initial presentation.

Declaration of interest

The authors declare that there are no conflicts of interest. The authors alone are responsible for the writing and content of the article.

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