Malignant Posterior Reversible Encephalopathy Syndrome—An Exacting Challenge for Neurocritical Care Physicians

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Abstract

We report a case of malignant posterior reversible encephalopathy syndrome (PRES) in a 62-year-old Caucasian female with a complex medical history and comorbidities admitted for bowel resection and lysis of iatrogenic bowel adhesions and enterocutaneous fistulas. Postoperatively, the patient developed sudden bilateral visual loss with no other neurologic deficits. Computed tomography scan showed very severe PRES-like changes, confirmed on magnetic resonance imaging (MRI). Systolic blood pressure remained around 170 mm HG. The patient was obtunded and remained unresponsive after MRI, with minimal response and a deteriorating clinical condition. The patient was given hyperosmolar therapy with a mannitol bolus. She recovered well with near resolution of imaging findings.

Keywords

malignant PRES, posterior reversible encephalopathy syndrome, cerebral edema, parenchymal hemorrhage, hyperosmolar therapy

Background

Posterior reversible encephalopathy syndrome (PRES) is characterized by altered mental status, hypertension, headache, seizures, vision loss, vomiting, and focal neurologic deficits along with characteristic brain white matter findings on magnetic resonance imaging (MRI).¹ It is typically triggered by elevations in blood pressure (BP) due to various predisposing conditions including several medications. Typical MRI findings range from bilateral parieto-occipital signal changes. However, in severe cases, Fluid-attenuated inversion recovery (FLAIR) signal changes can involve the cerebellum and frontal lobes. The clinical syndrome and the radiological findings are helpful in the diagnosis. A complete resolution and reversibility of all the symptoms and the imaging and radiological findings is one of the defining criteria of PRES.

Many atypical variants of PRES have been described, with a rare case of death due to PRES.^{2,3} Malignant PRES is an atypical variant of PRES which, although it has no set diagnostic criteria, Akins et al have described it as “imaging studies in line with PRES; Glasgow Coma Scale less than 8; and continued deterioration despite standard management of raised intracranial pressure.”¹ We present a rare case of malignant PRES with a near-fatal outcome that was prevented by timely neurocritical intervention.

Case Presentation

A 62-year-old morbidly obese Caucasian female with hyperlipidemia and a complex medical history had in the year 2009 developed *Clostridium difficile* colitis that required a total colectomy with end ileostomy and rectosigmoid pouch. She did well for a few years until 6 weeks prior to this admission, when she started complaining of abdominal pain with abdominal fistula discharge. She was admitted for an elective surgery to address persistent and painful jejunal discharge. During bowel prep, she had lower abdominal pain, nausea, and non-bloody, nonbilious vomiting. Exploratory laparotomy and resection of abdominal wall abscess cavities was done in November 2015, which was complicated by the development of pulseless ventricular tachycardia shortly after the incision, necessitating chest compressions for 3 minutes with a return of spontaneous circulation. Surgery was aborted and redone on December 2015 with successful takedown of the enterocutaneous fistulas, lysis of adhesions, and small bowel resection.

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Figure 1. Computed tomography (CT) scan of the head done on 4th postoperative day showing the intraparenchymal hemorrhage in the occipital lobe.

The patient remained stable postoperatively until postoperative day 4, when she suddenly woke up with inability to see with either eye. An acute stroke call was placed. On evaluation, she was found to have National Institutes of Health Stroke Scale (NIHSS) of 5 for cortical blindness bilaterally, not being able to recall her name, and right upper extremity drift. Initially, pupils were reactive bilaterally. The patient was taken for a computed tomography (CT) of the head, which demonstrated a large area of parieto-occipital hypodensity extending into frontal lobes bilaterally, a picture depicting an unusual but severe form of PRES with an additional parieto-occipital cortical hypodensity and left occipital pole acute parenchymal hemorrhage (Figure 1). MRI brain on the 5th post operative day showed hyperintense changes extending from the occipital lobe to frontal lobe (Figure 2). Blood pressure was elevated to a maximum of 180 mm Hg. While there was never a sudden change in pressure of 40 mm Hg or more in any 2 consecutive reads, vitals were done every 4 hours. Post MRI, she became obtunded with anisocoria and an unreactive right pupil. Glasgow Coma Scale dropped down to 7. Due to unresponsiveness and worsened examination, a portable HCT was repeated, which showed progression of mass effect with crowding of cisterns. Intravenous (IV) mannitol bolus was infused. Empirically, additional 1000 mg Keppra (levetiracetam) IV and 1 mg of Ativan were given, though no convulsion was witnessed. She was emergently intubated. Empirically, the patient also received 1 g Solu-Medrol for 5 days, with the other differential being a demyelinating process. All antibiotics (vancomycin, zosyn, and micafungin) and IV feeding (total parenteral nutrition) were stopped. A lumbar puncture was discussed; however, due to the mass effect on imaging, it could not be done. Magnetic resonance imaging of the cervical spine was performed the next day and was completely normal. Bedside electroencephalogram was

Figure 2. (A-D) Series of magnetic resonance imaging (MRI) showed bilateral FLAIR changes extending from the occipital lobe to the frontal lobe.

done for 24 hours that did not reveal any electrographical seizures. She was not on any medications with reported association with PRES.

Repeat CT of the head the next day showed stable but extensive cortical edema. Hyperosmolar therapy improved pupillary reactivity. Blood pressure was brought down medically. Intracranial pressure was monitored and cerebral edema gradually receded in the ensuing days. Interestingly, she was found to have recurrent episodes of elevated BP to 180s systolic and 100s diastolic in spite of being on 2 anti-hypertensives. Eventually, BP became stable after the addition of clonidine to her regimen. The patient gradually showed signs of recovery and was extubated following transfer to floor. Her abdominal postoperative recovery was also reassuring. A week after this event, she was discharged to acute rehabilitation facility for significant generalized weakness, severe cortical blindness, and noticeable memory complaints.

The patient was seen 3 months postdischarge when she had marked recovery in vision, except residual decreased acuity in the right superior quadrant. She also complained of mild cognitive and balance problems but otherwise was living at home, self-ambulatory with some assistance from family. A repeat MRI of the brain at that time showed bilateral occipital encephalomalacia with complete resolution of FLAIR signal in other areas (Figure 3). The patient has provided her consent for this case to be reported and published.

Figure 3. Magnetic resonance imaging (MRI) showing frontal and occipital lobe hypodensity changes with hyperintense signals.

Discussion

Posterior reversible encephalopathy syndrome is a clinico-radiological syndrome, described in 1996 by Hinchey et al in a series of case reports as a “reversible posterior leukoencephalopathy syndrome”² seen in association with clinical features of headache, focal neurological deficits, vomiting, seizures, usually generalized tonic-clonic,³ and visual defects such as cortical blindness, homonymous hemianopia, visual hallucinations,^{3,4} along with the hallmark radiological signs of subcortical white matter lesions on MRI, most noticeable in the parietal and occipital lobes, in many cases bilateral such as in this particular case as seen in Figure 2.⁵ The clinical features in collusion with the classic MRI findings lead to a diagnosis of PRES in most of cases; thus, further investigations are rarely required, except to find out the causative factors of PRES.

Etiologies of PRES include immunotherapy⁶ and agents like rituximab,⁷ cisplatin, gemcitabine, bevacizumab,⁸ tacrolimus,⁹ and mycophenolate,¹⁰ some autoimmune conditions like Henoch-Schönlein purpura,⁵ thrombotic thrombocytopenic purpura,⁵ systemic lupus erythematosus and systemic sclerosis,¹¹ and obstetrical conditions in which most commonly described are with cases of eclampsia¹² and chronic hypertension and renal failure,¹³ HIV,¹⁴ among others. Posterior reversible encephalopathy syndrome may develop suddenly as in our case due to stressors induced during a surgical procedure, fluctuating BP, or in a patient with an extensive and complicated history.

Various hypotheses have been postulated regarding PRES, the most accepted being that it may be due to the development of cerebral vasogenic edema, due to increasing BP resulting in a failure of the autoregulation of the blood-brain barrier, causing fluid transudates and edema.² Another theory suggests a spasm of the cerebral vessels is the culprit, which occurs due to acute elevation in BP, causing decreased cerebral blood flow and cytotoxic edema.¹⁵

Posterior reversible encephalopathy syndrome has a few atypical presentations, such as our case, in which the female patient developed a “malignant” variant of PRES. Malignant PRES has no set criteria but has been defined by some

including Akins et al as, “imaging studies in line with PRES; Glasgow Coma Scale less than 8; and a continued patient deterioration despite standard management of the raised intracranial pressure.”¹¹ Usually, the cases of PRES described in medical literature have an associated trigger as listed above, but our case had no identifiable trigger, except that the presentation was of PRES as confirmed by her imaging studies and her refractory hypertension, which was uncontrolled even with administering 2 antihypertensive drugs and then finally controlled with clonidine. She had excellent recovery after the initiation of the supportive treatment.

A case of malignant PRES has been described recently by Martins and Marrone¹² of a patient receiving a renal transplant who developed vomiting, seizures, and malignant hypertension systolic BP in the ranges of 240 mm Hg. Computed tomography scan in that particular patient showed intraparenchymal hemorrhage, which was confirmed along with subarachnoid bleed. Our case fulfills this proposed definition of malignant PRES with evidence of an occipital bleed on her imaging studies in addition to fronto-parieto-occipital edema. In our patient, the imaging findings appear more malignant than the reported case of Martins et al.¹² Malignant PRES has better outcome if treatment is initiated early with neurointensive care reduction in intracranial pressure, stopping offending drugs/triggers, and reduction in BP.¹²

Alhilali et al¹⁶ have described hypertensive encephalopathy and findings of hemorrhage associated with increased fatal outcome and poor prognosis. In our patient, we believe timely intervention, especially intubation, IV mannitol bolus, and bolt placement, helped prevent an otherwise a highly fatal condition. Early diagnosis is of prime importance in *malignant PRES* and may reduce the long-term disability and have favorable neurological outcome.¹⁷ Also, PRES is a misnomer because it is not always reversible.¹⁸

Conclusion

Posterior reversible encephalopathy syndrome is a potentially reversible pathology having many etiologies. Sometimes PRES may develop with severe signs and symptoms and radiological findings without a known apparent trigger. It is important to identify PRES in a timely manner and initiate supportive treatment. Rarely, blood transfusions and complicated postoperative conditions may trigger malignant PRES. Hence, it is imperative for physicians to diagnose and intervene with hyperosmolar therapy to reduce intracranial pressure, maintain a tightly controlled BP and if needed, manage with anticonvulsant therapy for seizures. With a comprehensive plan of care in mind, patient outcome can be drastically improved. Delayed diagnosis of PRES can lead to long-term disability and poor neurological outcomes.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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