Posterior Reversible Encephalopathy Syndrome in Thrombotic Thrombocytopenic Purpura

Sir,

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiologic syndrome, the presentation of which varies. The most common manifestation is seizures. A brain magnetic resonance imaging (MRI) done in these cases reveals the typical pattern of bilateral hyperintensities on fluid attenuation inverted recovery imaging, predominantly in the parieto-occipital region. The most commonly identified cause is hypertension, though it may occur in normotensive and even in hypotensive patients because of autoimmune diseases, renal failure, cytotoxic drugs, etc. Thrombotic thrombocytopenic purpura (TTP) is an uncommon cause that is rarely recognized.

TTP is rare, with an incidence of 1–13 cases per million individuals. Neurologic symptoms vary, though investigators have shown that close to 50% of TTP patients reveal PRES on imaging. Seizures appear to be the most common presentation in patients of TTP with PRES.

We describe the case of a normotensive patient presenting with seizures. Investigations revealed PRES due to previously undiagnosed TTP.

A 35-year-old male patient, on insulin for the past 8 years, presented to the Emergency Room with three episodes of generalized tonic clonic seizures, lasting about 10 min each. He had been discharged from another hospital 10 days prior, following disarticulation of the right index finger and toe due to digital gangrene.

Initial examination revealed a pulse of 68/minute, blood pressure of 130/80 mm Hg, respiratory rate of 22/minute, and post ictal confusion. His general random blood sugar was 244, with the arterial blood gas showing mild metabolic acidosis but no ketone bodies. He was shifted to the intensive therapy unit and started on antibiotics for possible aspiration pneumonia, insulin, and intravenous antiepileptics. His blood reports showed hemoglobin of 9.2 g/dL, thrombocytopenia of 77 × 10^9/L, with elevated blood urea and creatinine levels 83 and 2.8 g/dL, respectively. Serum ferritin was 2011 ng/mL. Urine analysis revealed 4+ albuminuria, RBC count 153/mm^3, WBC count of 42/mm^3, eosinophil count 5/mm^3, with granular casts. Serum Ca was 8.2 mg/dL, which when corrected for the albumin level of 2.2 g/dL was within normal limits. MRI brain found bilateral frontoparieto-occipital white matter T2 hyperintensities suggestive of PRES [Figure 1].

As the patient was normotensive, further evaluation for other causes of PRES such as test for antinuclear antibodies, antineutrophil cytoplasmic antibodies was done, which were all negative. The samples were sent to the laboratories and an elevated lactate dehydrogenase value of 904 U/L, elevated D-dimer levels of 1232 mg/dL, along with normal prothrombin time (12.1 s) and international normal range (1.0) values were found. A peripheral smear was requested, which revealed schistocytes and burr cells. The possibility of a thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS) spectrum disorder was considered, with acquired TTP being considered the most likely possibility, due to the absence of a family history, ruling out familial disease, or a recent history of diarrhea, ruling out acquired HUS.

Plasma exchange was initiated, with five cycles performed. The patient’s platelet count and renal function stabilized. The gangrene, which is initially thought to be related to diabetes mellitus, was attributed to thrombotic microangiopathy.
He was discharged with oral antiepileptics, insulin, and antihypertensives. On subsequent follow-up, clinical features had resolved.

The pathophysiology of PRES is still foggy. Some widely accepted hypotheses are: (1) breakdown of cerebral autoregulation of blood flow, leading to hyperperfusion with consequent vasogenic edema; (2) ischemic damage to the brain secondary to sudden variations in blood pressure, causing cytotoxic damage and edema; and (3) damage to the endothelial lining of the blood–brain barrier, causing transudation into the brain. The last hypothesis explains the syndrome in normotensive/hypotensive patients with immune disorders, renal failure, etc.

The differential diagnosis at presentation is broad, including various acute neurologic syndromes, such as stroke, cerebral venous thrombosis, encephalitis, and demyelinating disorders. Venous sinus thrombosis or intracranial hemorrhage can all present with headache, seizures, reduced consciousness, and focal neurologic deficits. If there is only focal neurologic deficit, PRES may be difficult to distinguish from simultaneous bilateral posterior cerebral artery infarction (top of basilar embolism/syndrome); the approach in both cases varies. In PRES, treatment of hypertension is recommended to reverse the pathological process, while in an ischemic stroke, treatment of mild-to-moderate hypertension is not recommended. Imaging can help differentiate between the two: the calcarine and paramedian occipital lobe structures are usually spared in PRES, while in patients with top of basilar syndrome there are often accompanying thalamic and midbrain infarcts.

Infective encephalitis or meningitis, particularly herpes simplex encephalitis must be considered, and rapid treatment with intravenous acyclovir and antibiotics may be lifesaving while a diagnosis is still being pursued. In central nervous system vasculitis, the presenting symptoms may be similar to PRES, but the MRI findings are usually more diffuse, and many of them are irreversible. Autoimmune encephalitis and metabolic encephalopathies—deranged serum glucose, sodium, uremia, and drug toxicities—can have similar progressive symptoms.

In our patient, the appearance of PRES is probably due to endothelial dysfunction secondary to TTP. This is in line with a study conducted by Burrus et al., who found no correlation between hypertension and PRES in their cohort of TTP patients. Neurologic symptoms are frequent in TTP and may mimic various conditions. Among their symptoms, PRES was the most common. It is important to note that kidney function is also often impaired in patients with PRES and TTP, and their prognosis is poor. However, on appropriate treatment, these lesions remain reversible.

In case of acute or subacute onset of neurologic symptoms in an appropriate clinical context—acute kidney disease, solid organ transplantation, pregnancy, and most importantly, hypertension—PRES must be considered. There are no clear-cut guidelines for the diagnosis of PRES, so a high degree of clinical suspicion must be maintained. An MRI must be ordered in these situations—characteristic posterior subcortical vasogenic edema will confirm the diagnosis. In normotensive patients particularly, disorders of the TTP-HUS spectrum must be considered as a cause, keeping the presenting complaints and laboratory findings in mind. The clinical and radiological signs of PRES are reversible most of the time, provided it is recognized and treated promptly and the symptoms are not too severe.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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