CASE REPORT

Posterior reversible leukoencephalopathy syndrome as a presenting manifestation of p-ANCA-associated vasculitis

Upasana Vrijlal Patel, Nirajkumar Jagjivan Patel

Department of Neurology,
Sir Ganga Ram Hospital,
New Delhi, Delhi, India

Correspondence to
Dr Upasana Vrijlal Patel,
oops_691985@yahoo.com

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SUMMARY

Rapidly progressing glomerulonephritis like microscopic polyangiitis and allergic granulomatous angiitis are among the common presentations of perinuclear antineutrophilic cytoplasmic antibody (p-ANCA) vasculitis. Involvement of central nervous system is rare in contrast to mononeuritis multiplex, which is a well-known neurological manifestation of this condition. We report a case presented with uraemic encephalopathy and posterior reversible encephalopathy syndrome (PRES)-related symptoms, which showed recovery after haemodialysis although PRES with seizures recurred later. As uraemic encephalopathy appears to be the underlying aetiology as per the temporal correlation of correction of uraemia and resolution of the symptoms of PRES, it becomes a rare case of uraemia-induced PRES as a presenting manifestation of p-ANCA-associated vasculitis along with necrotising crescentic glomerulonephritis.

BACKGROUND

This is a rare case of involvement of central nervous system (CNS), in the form of posterior reversible encephalopathy syndrome (PRES), as a presenting manifestation of perinuclear antineutrophilic cytoplasmic antibody (p-ANCA)-associated vasculitis, which brings together neurology, nephrology and rheumatology.

CASE PRESENTATION

A man in his fourth decade, without any comorbidities, presented with a history of headache for past 3–4 months, with previous plain CT of the head normal. He then developed loss of appetite, pain in the abdomen with vomiting for 10–12 days. One day before referring to our hospital, he developed sudden blackout in front of his eyes followed by involuntary left-facial twitching and a brief episode of unresponsiveness. He had such three episodes in 1 day. Even after recovery from seizure episodes, his vision remained impaired. He was found to have a blood pressure (BP) of 160/90 mm Hg on admission. On examination, he was conscious, coherent, responding verbally, following verbal commands, moving all four limbs, with only perception of light in both eyes, both pupils normal sized and reacting normally to light. Fundus examination revealed bilateral haemorrhagic spots.

INVESTIGATIONS

Renal failure was revealed by raised serum creatinine (24.48 mg/dL) and hyperkalaemia (serum potassium

of 6.7 mEq/L). Urine examination showed albuminuria and numerous red blood cells (RBC) and RBC cast. Ultrasound of the abdomen showed normal-sized kidneys.

MRI of the brain revealed areas of altered signal intensity in right posterior temporal, bilateral medial basal ganglionic area, inferior and parasagittal bilateral occipital regions in the subcortical region showing hyperintensity in T2-weighted and TIRM images, isointense on T1-weighted and no restricted diffusion, suggestive of PRES ([figure 1](#)). MR angiography of the brain was normal. Visual evoked potential (goggles) revealed light perception only in both eyes.

On further evaluation, p-ANCA was found to be positive in high titre with both ELISA and immunofluorescence methods, with normal levels of cytoplasmic ANCA (c-ANCA), ANA profile, C3, C4 and antglomerular basement membrane antibody.

Renal biopsy (taken after 3 sessions of haemodialysis) showed necrotising crescentic glomerulonephritis (100% circumferential fibrocellular crescents with glomerular tuft necrosis and interstitial inflammation; [figure 2](#)). Immunofluorescence staining was negative.

DIFFERENTIAL DIAGNOSIS

PRES is a clinical—neuroradiological entity, initially described by Hinchey *et al*¹ in 1996, as reversible posterior leukoencephalopathy syndrome. Salient clinical features include headache, visual disturbances, seizures, altered mental status; whereas radiological findings are that of vasogenic oedema, primarily in the posterior fossa and parietal and occipital lobes of the brain.

In the presence of classic clinical and radiological features, diagnosis of PRES is clear. The main concern which comes next is the aetiology behind it.

Apart from systemic hypertension (HTN)² as the most common aetiology of PRES, other causes include the use of immunosuppressant drugs (primarily cyclosporine and tacrolimus), nephrotic state, sepsis and connective tissue diseases.^{1 3 4} In 8–10%, autoimmune disease is the underlying cause⁵ namely systemic lupus erythematosus (SLE), systemic sclerosis, polyarteritis nodosa, granulomatous polyangiitis, thrombotic microangiopathy, Takayasu arteritis, Hashimoto encephalopathy and Crohn's disease.

Therefore, a thorough evaluation should be made to reveal the cause in case of absence of accelerated HTN on clinical examination and negative drug history.

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Figure 1 (A–F) MRI of the brain—TIRM images, showing areas of altered signal intensity in right-posterior temporal, bilateral medial basal ganglionic area, inferior and parasagittal bilateral occipital regions in the subcortical region showing hyperintensity (isointense on T1-weighted images and no restricted diffusion—images not displayed).

TREATMENT

The patient was initiated on haemodialysis and three sessions were given in initial 3 days. In view of necrotising crescentic glomerulonephritis with p-ANCA vasculitis, he was given intravenous pulse methylprednisolone therapy comprising 500 mg/day for a total of 3 days, followed by oral prednisolone 60 mg/day. Cyclophosphamide was not started in view of more fibrous crescents and hence less chances of reversibility of glomerulonephritis as per the renal biopsy findings.

OUTCOME AND FOLLOW-UP

His vision improved to 6/18 bilaterally during hospital course and was discharged on oral prednisolone, antihypertensive and

other supportive treatment, with advice for maintenance haemodialysis.

Two months later, the patient again presented with recurrent seizures with repeat MRI of the brain revealing features of PRES. The reason behind the event was related to two missed sessions of haemodialysis and the steroid dose being tapered. Symptoms resolved with intensive haemodialysis sessions and up-titration in the dose of steroids.

In view of chronic kidney disease—stage V (end-stage renal disease) with clinical inactive disease and negative p-ANCA 5 months after the initial event, the patient underwent renal allograft transplantation, after which he showed good clinical recovery.

Figure 2 Renal biopsy (methenamine silver stain (A) and H&E (B)) showing changes of necrotising crescentic glomerulonephritis with (100% circumferential, fibrocellular crescents with glomerular tuft necrosis and interstitial inflammation).

DISCUSSION

ANCAs represent a family of antibodies directed against constituents of the neutrophil azurophilic granules.^{6 7} Based on immunofluorescence patterns, there are two groups, the first being c-ANCA targeting proteinase-3, associated with around 95% specificity for granulomatous polyangiitis, and the second perinuclear ANCA (p-ANCA) directed at myeloperoxidase, less specifically associated with microscopic polyangiitis and Churg-Strauss syndrome.^{6 7} In contrast to mononeuritis multiplex which is commonly associated with small vessel vasculitis, CNS involvement is observed in 6–8% of patients, with cerebral infarctions, intracerebral haemorrhages and subarachnoid haemorrhages being the most frequent manifestations.⁸ PRES is a very rare CNS manifestation with this condition.

As per the search from the MEDLINE database from 1966 to 2007, SLE was found to be associated with PRES in 22 patients.⁴ PRES in the background of ANCA-associated pauci-immune glomerulonephritis is rarely encountered.⁹ The patient in our case presented with seizures, acute vision loss and acute renal failure with a high creatinine level of 24.48 mg/dL. Interestingly, his BP was not significantly high, but uraemia was most prominent. Fortunately, his symptoms resolved with dialysis and corticosteroids. While the patient was being closely monitored, he presented to the emergency room with recurrent seizures. This second presentation with elevated serum creatinine value further confirms the association of PRES with uraemia. The exact mechanism behind the occurrence of PRES is still unknown. However, multiple pathophysiological processes can result into the clinical and radiological findings consistent with PRES.¹⁰ Vasogenic oedema explains the radiological findings consistent with PRES because the lesions tend to disappear once the underlying disease is treated; however, cytotoxic oedema is also observed in a minority. In patients with poorly controlled HTN manifested as PRES, the mechanism involves hyperperfusion of the brain overwhelming the capability of cerebrovascular autoregulation to regulate blood flow, so the excess hydrostatic pressure causes increased flow of fluid out of the vasculature into the brain parenchyma. Increased capillary permeability caused by HTN-induced injury of the endothelial cells also results in increased fluid infiltration to the brain parenchyma.⁹ Dual mechanism namely vasogenic oedema due to increased capillary permeability and cytotoxic oedema due to direct toxicity to brain parenchyma is presumed to occur by elevated nitrogenous waste products in the plasma in case of uraemia. Some nitrogenous waste products, specifically guanidine compounds, can activate neuronal N-methyl D-aspartate receptors leading to ultimate excitotoxic cell death¹¹ which leads to the release of intracellular fluid into the extracellular space causing cytotoxic oedema. As dialysis removes the nitrogenous waste products in the plasma, vasogenic oedema due to uraemic encephalopathy can be reversed with dialysis alone, as demonstrated in the management of our patient. The clinical and radiological findings of PRES resolved immediately after haemodialysis decreased the creatinine level to 4.38 mg/dL. The temporal correlation of the correction of the deranged renal function and rapid resolution of the symptoms of PRES corroborate with the pathophysiological aetiology in this patient as uraemic encephalopathy, making this a rare case of uraemia-induced PRES as a first manifestation of p-ANCA-associated vasculitis.

MRI of the brain is superior to CT of the brain in the diagnosis of this condition. Fluid attenuated inversion recovery MRI is sensitive in detecting subcortical leukoencephalopathy, particularly the posterior fossa and the parietal and occipital lobe regions that are characteristic of PRES. Diffusion-weighted

imaging (DWI) MRI sequence can be of help in differentiating between ischaemic lesions (cytotoxic oedema) and lesions due to PRES (vasogenic oedema); ischaemic lesions would display hyperintensity on DWI while PRES lesions would display hypointensity.^{12 13} The treatment for PRES depends on the underlying cause; however, antiepileptic drugs should be used to control acute seizures. As was demonstrated in our patient, if uraemia is deemed to be significant in the explanation of PRES, then haemodialysis should be carried out to improve the patient's condition.

Learning points

- ▶ Central nervous system involvement in perinuclear antineutrophilic cytoplasmic antibody-positive vasculitis is rare in contrast to mononeuritis multiplex which is more commonly associated with it.
- ▶ Posterior reversible encephalopathy syndrome (PRES), though a rare presenting feature, should be thought of as a differential diagnosis when a patient presents with neurological symptoms such as headache, visual loss, altered mental status and seizures in the setting of uraemia.
- ▶ When suspected, this should prompt immediate investigation with brain imaging techniques because neurological deficits due to PRES itself are potentially reversible if the underlying cause is addressed in a timely manner.

Contributors UVP participated in the study concept and design, drafting/revising the manuscript for content, including medical writing for content, analysis and interpretation of the data (including analysis of brain images), supervision and coordination of study. NJP participated in drafting/revising the content (including the medical terminology) of the manuscript, study concept and design, analysis and interpretation of data.

Competing interests None.

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REFERENCES

- 1 Hinchey J, Chaves C, Appignani B, *et al.* A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334:494–500.
- 2 Vaughan CJ, Delanty N. Hypertensive emergencies. *Lancet* 2000;356:411–17.
- 3 El Karoui K, Le Quintrec M, Dekeyser E, *et al.* Posterior reversible encephalopathy syndrome in systemic lupus erythematosus. *Nephrol Dial Transplant* 2008;23:757–63.
- 4 Zhang Y, Liu J, Ding M, *et al.* Reversible posterior encephalopathy syndrome in systemic lupus erythematosus and lupus nephritis. *Intern Med* 2008;47:867–75.
- 5 McKinney AM, Short J, Truwit CL, *et al.* Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. *AJR Am J Roentgenol* 2007;189:904–12.
- 6 Mohan N, Kerr GS. Diagnosis of vasculitis. *Best Pract Res Clin Rheumatol* 2001;15:203–23.
- 7 Niles JL. Antineutrophil cytoplasmic antibodies in the classification of vasculitis. *Annu Rev Med* 1996;47:303–13.
- 8 Sehgal M, Swanson JW, DeRemee RA, *et al.* Neurologic manifestations of Churg-Strauss syndrome. *Mayo Clin Proc* 1995;70:337–41.
- 9 Yasutaka T, Akihisa M. Reversible posterior leukoencephalopathy syndrome in p-ANCA-associated vasculitis. *Intern Med* 2006;45:1169–71.
- 10 Gross WL. Immunopathogenesis of vasculitis. In: Kippel JH, Dieppe PA, eds. *Rheumatology*. 2nd edn. London: Mosby, 1998:19.1–8.
- 11 De Deyn PP, D'Hooge R, Van Bogaert PP, *et al.* Endogenous guanidine compounds as uremic neurotoxins. *Kidney Int Suppl* 2001;78:77–83.
- 12 Ay H, Buonanno FS, Schaefer PW, *et al.* Posterior leukoencephalopathy without severe hypertension. Utility of diffusion-weighted MRI. *Neurology* 1998;51:1369–76.
- 13 Kawano H, Kimura E, Ishizaki M, *et al.* Reversible posterior leukoencephalopathy syndrome in two patients with microscopic polyarteritis nodosa. *Rinsho Shinkeigaku* 2002;42:949–95.

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