American Journal of Clinical and Medical Case Reports

ISSN: 2771-4098

Case Report

Posterior Reversible Encephalopathy Syndrome (PRES) In ANCA-Negative Vasculitis Causing Rapidly Necrotizing Glomerulonephritis: Case Report and Review of the Literature

Strizzi CT[1,2], Urciuolo F[1,2], Baccaro R[1,2], Ambrogio M[1,2], D'Ambrosio V[1,2], Pesce F[3], Costanzi S[2] and Grandaliano G[1,2]*

[1]*Università Cattolica del Sacro Cuore, Roma, Italy*

[2]*UOC Nefrologia, Fondazione Policlinico Gemelli IRCCS, Roma, Italy*

[3]*UOSD Nefrologia, Gemelli Isola – Ospedale Isola Tiberina, Roma, Italy*

Abstract

Background: Posterior Reversible Encephalopathy Syndrome (PRES) is a rare neurological complication of renal disease. The diagnosis relies on the combination of typical clinical features (encephalopathy, headache and seizures) and risk factors (chronic kidney disease, autoimmune diseases, moderate to severe hypertension and exposure to cytotoxic drugs) supported by Magnetic Resonance Imaging (MRI) findings. Although it is usually a benign syndrome, a few cases of progressive cerebral edema and intra cerebral hemorrhage resulting in death have been reported. The occurrence of PRES is not uncommon in Anti-Neutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis (AAV) and has been described in several case series reports in AAV. Nevertheless, there is currently no definitive evidence of its frequency in ANCA-negative small vessel vasculitis, an autoimmune disorder with a different disease spectrum, whereas patients tend to be younger, with fewer extra renal symptoms, and at higher risk of End-Stage Renal Disease (ESRD) due to rapidly progressive Pauci-Immune Glomerulonephritis (PIGN).

Case presentation: An 18-year-old woman with a recent histological diagnosis of ANCA-negative small vessel vasculitis and rapidly progressive PIGN that led to ESRD, on hemodialysis treatment, presented with acute-onset neurological symptoms including stupor, headache and tonic-clonic seizures. Several risk factors for PRES were present as she underwent immunosuppressive therapy, in a background of uncontrolled hypertension and hemodialysis catheter-associated sepsis. At the time of onset, MRI showed vasogenic edema with a predominantly posterior disposition. Management revolved around gradual increase of antihypertensive therapy to maintain mean arterial pressure between 105 mmHg and 125 mmHg at all times, intravenous antibiotic therapy to achieve infection resolution, strict volume control maintenance to avoid volume overload and oral anti-epilectic was prescribed for seizure control. One month later, MRI control showed resolution of the areas of altered signals.

Conclusions: Management of PRES patients with neurological symptoms in the context of renal failure requiring hemodialysis treatment, moderate to severe hypertension and exposure to cytotoxic drugs, particularly in the presence of small vessel vasculitis, should undergo MRI to rule out PRES. The primary disease should be treated with targeted therapy, and risk factors should be corrected, along with blood pressure control. Although the patient had several risk factors for PRES, we cannot exclude a possible causal effect of the underlying diagnosis of ANCA-negative vasculitis. To our knowledge, this is the first case of PRES in a patient with ANCA-negative vasculitis.

Keywords: Posterior reversible encephalopathy syndrome; Negative small vessel vasculitis; Rapidly necrotizing glomerulonephritis; Neurological involvement in vasculitis

Introduction

Pauci-Immune Necrotizing Glomerulonephritis (PING) is a known cause of rapidly progressive glomerulonephritis. It is defined by the presence of focal glomerular necrosis, fibrosis and extra-capillary proliferation, in the absence significant glomerular immune deposits [1]. This autoimmune disease is etiologically related to small vessel vasculitis and it is usually associated with the presence of Anti Neutrophil Cytoplasmic Antibodies (ANCA), which can be detected by Immunofluorescence, Enzyme-Linked Immunosorbent Assay (ELISA), or immunodot tests. These antibodies are directed against Myeloperoxidase (MPO) and Proteinase 3 (PR3) enzymes in neutrophils and monocytes [2]. In a minority of PING cases, ANCA cannot be detected by Immunofluorescence, ELISA or immunodot tests. ANCA-negative PING has been the subject of a limited number of rather small retrospective studies. It has been suggested that pauci-immune small vessel vasculitis has a different disease spectrum in which circulating ANCA are not detectable [3]. Furthermore, it has been observed that patients with ANCA-negative vasculitis are typically younger, present fewer extrarenal symptoms and have a higher risk for End-Stage Renal Disease (ESRD) when compared to those with ANCA-positive disease [4]. Central Nervous System (CNS) involvement is not uncommon in Anti-Neutrophil Cytoplasmic Antibody (ANCA)-Associated Vasculitis (AAV) throughout the

Citation: Strizzi CT, Urciuolo F, Baccaro R, Ambrogio M, D'Ambrosio V, Pesce F, et al. Posterior Reversible Encephalopathy Syndrome (PRES) In ANCA-Negative Vasculitis Causing Rapidly Necrotizing Glomerulonephritis: Case Report and Review of the Literature. Am J Clin Case Rep. 2024;2(2):1014.

Publisher Name: Medtext Publications LLC

Manuscript compiled: Jun 03rd, 2024

***Corresponding author:** Camillo Tancredi Strizzi, Policlinico Universitario Fondazione Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 8-00168 Roma, Italy, Tel: +39-3319883029

disease course [4]. However, there is currently no definitive evidence of the frequency of CNS involvement in ANCA-negative small vessel vasculitis. Posterior Reversible Encephalopathy Syndrome (PRES) is a rare yet unique CNS complication of small vessel vasculitis and an uncommon entity in patients with ESRD [4-7]. It is a generally reversible, complex clinical-radiologic syndrome that manifests with various neurological symptoms such as headache, confusion, altered mental status, visual disturbances and tonic-clonic seizures and may presents as status epilecticus. PRES is pathogenetically characterized by the presence of vasogenic edema in the posterior regions of the brain in patients with autoimmune diseases, nephropathies, moderate to severe hypertension, pre-eclampsia/eclampsia, postpartum atypical hemolytic uremic syndrome and exposure to cytotoxic drugs [8-11]. Although PRES is usually benign, there have been reported cases of progressive cerebral edema and intra cerebral hemorrhage resulting in death [9]. This article presents the case of an 18-year-old woman with a histologically confirmed diagnosis of ANCA-negative small vessel vasculitis with rapidly progressive glomerulonephritis leading to ESRD. The patient developed PRES, which could not be attributed to a single trigger due to the presence of various possible triggers, consistent with its multifactorial etiology.

Case Presentation

An 18 year-old female was admitted to the hospital due to a sudden decline of renal function, generalized edema, hypertension, vomiting, asthenia and oligo-anuria. There were no underlying systemic diseases or history of medication use, and no abnormalities were found in her family history. Two months before admission, a complete blood test was conducted, which yielded normal results. Additionally, a skin biopsy was performed on a dermatitis lesion on the right thigh, revealing a subcutaneous infiltrate of lymphocytes, histiocytes and eosinophilic granulocytes associated with focal septal fibrosis. The patient reported turbinate hypertrophy with recurrent sinusitis, which was monitored by an ENT specialist. Upon arrival at the emergency room, the patient's blood pressure was 170/95 mmHg. Blood work revealed a hemoglobin level of 7.5 g/dL, a WBC count of 6.75/L × 109/L, a normal eosinophils count, platelets at 209/L × 109/L, a serum creatinine of 5.57 mg/dL, uric acid at 8.2 mg/dL, phosphate at 5.6 mg/dL, NT-pro BNP level of 32091 pg/ml. The patient's C-reactive protein level was 8.1 mg/L and there were no electrolyte disturbances. The urinalysis revealed microscopic hematuria with proteinuria of 0.74 g over 24 hours. Autoimmunity tests showed no abnormalities, including Anti Nuclear Antibodies (ANA), ANCA (both PR3 and MPO), anti-GBM, rheumatoid factor, lupus anticoagulant, anticardiolipin antibodies, immunoglobulins, anti-centromere, and anti-SCL70 and anti ds DNA, which were all within normal limits, as were complement levels. Protein electrophoresis was also normal. Abdominal ultrasonography revealed normal-sized kidneys with bilaterally preserved parenchyma and a slight increase in echogenicity, without dilatation or lithiasis. A renal biopsy was performed and the histologic report indicated ANCA-negative pauci-immune necrotizing glomerulonephritis with diffuse cicatricial glomerulosclerosis (Figure 1).

Intravenous (IV) methylprednisolone pulse therapy was administered at a dose of 500 mg/day for 3 days, followed by oral prednisone at a dose of 80 mg/day with gradual tapering. However due to progressive deterioration of renal function and lack of response to pharmacologic therapy, renal replacement therapy (hemodialysis) was initiated *via* temporary Central Venous Access (CVC) in the right internal jugular vein. On day 9, patient received an IV dose of

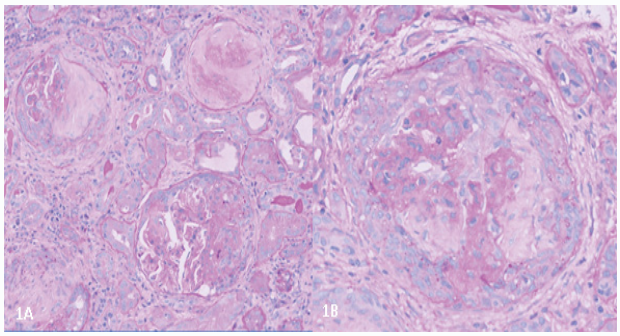

Figure 1: Pathology report on kidney biopsy. A. Light microscopy, global sclerosis of glomeruli (PAS). B. Light microscopy, tubular interstitium expanded with leucocyte infiltrate. Forty seven glomeruli were analyzed, of which thirty were scleral hyaline or in global sclerosis. One glomerulus showed a complete cellular crescent (fibrinoid necrosis and endocapillary proliferation) and the remaining glomeruli showed segmental sclerosis with the formation of complete cellular crescents. The expanded tubular interstitium compartment harbored a moderate inflammatory infiltrate of lymphomonocytic, plasma cellular, granulocytic and neutrophilic cells, which was associated focal inflammatory damage to the tubules and focal tubular atrophy. Protein casts and sporadic blood exudates were also observed. Intratubular abscesses were present, albeit rarely. Immunohistochemical staining for PLA2r and IgG4 yielded negative results. Immunofluorescence of a frozen sample revealed no significant positivity for IgA, IgG, IgM, kappa and lambda light chains, C1q and C3. Fibrinogen was slightly positive in areas of sclerosis, which was interpreted as non-specific.

Rituximab 375 mg/m^2, which was interrupted after thirty minutes of infusion due to the abrupt onset of an adverse drug reaction in the form of tremors. The patient was discharged on day 12 with a recommendation to continue hemodialysis, oral steroid therapy tapering (prednisone 50 mg/day) and antihypertensive therapy (amlodipine 5 mg/day).

After two weeks, the patient was readmitted to replace the temporary access for hemodialysis with a permanent tunneled CVC. Although the clinical condition was stable, purulent material was found at the catheter exit site. Blood tests revealed a WBC count of 14.32 /L × 109 /L (% neutrophils) a C-reactive protein level of 30.4 mg/mL and a procalcitonin level of 1.59 ng/Ml. Microbiological tests were performed. Swabs taken from the exit site and blood cultures from the peripheral venous blood and CVC were later tested positive for *Staphylococcus Aureus* Complex, defining the diagnosis of C-Related Blood Stream Infection (CRBSI).

Two days after the second admission, the patient was found lying on the floor of her room with amnesia. She reported experiencing only mild headache, nausea and a feeling of feverishness. The clinical examination revealed evidence of a tongue bite. Shortly after, a generalized tonic-clonic seizure occurred, whereupon she was administered intravenous midazolam and subsequently transferred to the intensive care unit for symptom management and possible need of mechanical ventilation. The electroencephalogram was within normal limits. A brain CT showed bilateral focal areas of hypodensity in the cerebellum and in the subcortical white matter in the frontal, parietal, temporal and occipital areas. The periaortic vessels and the main arterial vessels of the circle of Willis were deemed as patent. A first brain MRI was also performed (Figure 2A), revealing multiple areas of signal alterations in the subcortical white matter of both cerebral hemispheres, which were hyperintense in T2w and FLAIR and isointense in DWI. The most significant area affected the posterior part of the right temporal lobe and the subcortical white matter. In the

infratentorial area, two extensive regions with similar signal alterations were detected in T2w/FLAIR. These regions were characterized by a strong hyperintensity in DWI and signs of restriction in the ADC maps, which were indicative of cytotoxic edema. The findings of the lesions were indeed not clearly interpretable due to the different behavior of the infratentorial leukopathy. Four days later, a follow-up MRI (Figure 2B) was performed, revealing a marked decrease in the size and signal alteration of the previously identified foci and the regions with modified signal in the infratentorial area. The areas of altered intra parenchymal signal had reduced in size and changes were coexisting with vasogenic edema and cytotoxic edema. The absence of enhancement, the predominant posterior disposition, in conjunction with the improving radiological development, gave rise to the etiologic hypothesis of Posterior Reversible Encephalopathy Syndrome (PRES).

Supportive treatment was initiated, including a gradual increase in antihypertensive therapy to maintain mean arterial pressure of between 105 mmHg and 125 mmHg at all times (using amlodipine 10 mg/daily and ramipril 5 mg/daily). Additionally, intravenous oxacillin (3 g, four times daily) was administered as the previously performed blood cultures resulted positive for *Staphylococcus Aureus* Complex. The temporary hemodialysis CVC was replaced with a permanent tunneled CVC in the right internal jugular vein. Strict volume control was maintained to avoid exacerbating volume overload and amplify hypertension during long inter-dialytic gaps. Following neurological consultation, oral levetiracetam (250 mg twice daily) was prescribed for seizure control. The patient received maintenance immunosuppressive therapy for ANCA-negative vasculitis, which included continuing oral steroid therapy tapering and adding mycophenolate mofetil (1000 mg twice daily). On the 6th day since the second admission, the patient was transferred from the intensive care unit back to the ward, as her clinical condition had improved and no further seizures ensued. Negative new blood cultures were obtained and she was discharged on the 13th day after the second admission. One month later, a third MRI of the brain showed complete resolution of the areas of altered signals. In the susceptibility images the appearance of a punctuate deposit of paramagnetic material in the right occipital cortex (Figure 2C). This finding was inconsistent with the previous areas of altered signals and consistent with a micro-hemorrhagic result. Complete resolution of the previously described areas of altered supra- and infra-tentorial signals, in relation to the time course, was key to establishing the diagnosis of PRES with certainty.

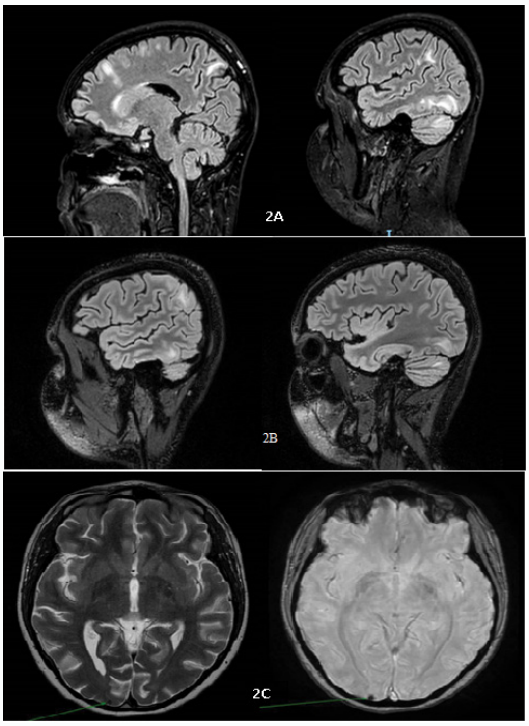

Figure 2: Magnetic Resonance Imaging. A. Foci of signal alterations (hyperintense in T2w and FLAIR sequences, isointense in DWI) in subcortical white matter of both cerebral hemispheres, posterior part of the right temporal lobe, infratentorial area, and compatible with vasogenic edema. Two extensive areas of characterized by a strong hyperintensity in DWI and signs of restriction in the ADC maps described as recent cytotoxic edema. B. Significant reduction in the size and signal change of the previously observed foci suggestive of posterior reversible encephalopathy syndrome. C. 1-month follow-up. Complete resolution of the areas of altered signals. Appearance of a punctuate deposit of paramagnetic material in the right occipital cortex consistent with a micro-hemorrhagic outcome of PRES (green arrow).

Discussion

During the course of the disease, Central Nervous System (CNS) involvement is not uncommon in small vessel vasculitis ranging from 22% to 54% in Granulomatosis with Polyangiitis (GPA) and 34% to 72% in Microscopic Poly Angiitis (MPA). It is important to note that a negative ANCA immunoassay, which occurs in up to half of pathologically diagnosed GPA and MPA, does not rule out vasculitis [12,13]. The potential for false negatives in ANCA tests, particularly in the early stages of the disease without systemic involvement, may be related to limited sensitivity. It is important to note that a negative ANCA test alone cannot rule out a diagnosis of vasculitis. Therefore, a biopsy of the affected organ is necessary for seronegative patients [14]. Existing literature suggests that small vessel vasculitis can affect the CNS in various ways, including inflammation, obstruction or increased permeability of small to medium-sized cerebral vessels due to systemic vasculitis. It can also be caused by infiltration or compression of granulomatous pathology from neighboring structures, or by the development of de novo granulomatous lesions in the CNS [15-17]. Extra-axial lesions involving the dura or pituitary gland are generally attributed to granulomatous inflammation, while pathologies of the parenchyma are caused by vasculitis and breakdown of the blood-brain barrier. Posterior Reversible Encephalopathy Syndrome (PRES) is a rare but unique CNS complication of small vessel vasculitis and an uncommon entity in patients with ESRD [18]. PRES was first described in 1996 by Hinchey et al [7]. Its clinic-radiological diagnosis is based on the combination of typical clinical features and risk factors supported by Magnetic Resonance Imaging (MRI) findings of the brain. PRES can occur at any age, from infants to the elderly, but it most commonly affects young or middle-aged adults, with an average age of 45 years and a female predominance [19-21]. Despite the lack of large prospective series, PRES has been observed in adults in up to 98% of patients with eclampsia, in 2.7% to 25% of patients after bone marrow transplantation, in 0.4% to 6% of patients after solid organ transplantation, and less frequently (0.4% to 0.8%) in end-stage renal disease or systemic lupus erythematosus [11].

The pathogenesis of PRES is not yet fully understood, but it seems to be associated with impaired cerebral auto regulation, dysregulation of the maintenance of normal blood flow despite changes in arterial pressure and endothelial dysfunction. These factors cause the breakdown of the blood-brain barrier, leading to extravasation from the vessels into the brain parenchyma. PRES is characterized by vasogenic edema, which has a debated pathogenesis regarding

whether hyperperfusion or hypoperfusion is the cause [18,22]. The most widely accepted hypothesis is that severe systemic hypertension overwhelms the self-regulatory capacity of the cerebral vasculature, particularly arterioles, resulting in hyperperfusion, arteriolar dilation, capillary bed injury and vasogenic edema. Sympathetic stimulation can increase the upper threshold of auto regulation. The fact that PRES occurs preferentially in the posterior part of the brain where there is a weak sympathetic innervations supports this hypothesis [7,18,23]. The other hypothesis suggests that cerebral vasoconstriction is the main cause, leading to capillary leakage, subsequent hypoperfusion, and ischemia and vasogenic edema. The debate surrounding the pathogenesis of PRES leaves doubt as to whether hypertension is the main culprit. Vasospasm and hypoperfusion may be triggered by endothelial cell failure, as occurs in autoimmune diseases (such as small-vessel vasculitis) and in post-transplant patients. The concept of hypoperfusion is also supported by the site of damage in PRES, which coincides with the watershed areas of the brain [22,24]. These observations suggest that a systemic process resulting in endothelial dysfunction leads to a cascade of events that culminate in cerebral vasoconstriction, hypoperfusion and ischemia.

PRES typically presents with an acute onset [4] and manifests with generalized symptoms potentially lasting several hours or days [11]. Encephalopathy develops in 28% to 94% of patients, ranging from mild cognitive impairment to stupor and coma [19]. Seizures affect up to 74% to 87% of patients [20] and typically occur within 48 hours of presentation. In a minority of cases (3% to 17%), seizures may evolve into status epilepticus. Up to 50% of affected patients develop dull and diffuse headaches with a gradual onset [21]. Visual disturbances are present in 39% of patients, including reduced visual acuity, diplopia, visual field deficits, cortical blindness, color vision abnormalities and visual hallucinations. Other focal deficits, such as weakness, sensory disturbance, or speech disturbance, may also be present.

Although Computed Tomography (CT) is often the initial form of imaging in acute neurologic syndromes, MRI is considered the gold standard for confirming the diagnosis of PRES and demonstrating its extent. This is because MRI provides better resolution, particularly of the structures in the posterior cranial fossa. Typical radiological features of PRES include vasogenic edema that affects the subcortical white matter and extends to the overlying cortex. The vasogenic edema is characterized by signal hyperintensity on T2w/FLAIR sequences and is typically found in a dominant bilateral parieto-occipital, holo-hemispheric watershed or a superior frontal sulcus patterns [24]. In some cases, the involvement of various brain regions has been described, including the temporal lobe, brainstem, basal ganglia, posterior limb of the internal capsule, cerebellum and periventricular regions, and spinal cord [11,24]. It is important to note that despite the original definition of the posterior phenomenon, all areas of the brain can potentially be affected [18]. It should be noted that up to 65% of patients undergoing MRI follow-up present micro-hemorrhages, which are likely due to reperfusion injury secondary to vasoconstriction or rupture of the pial vessel secondary to severe hypertension.

The development of PRES (Box 1) is associated with various conditions, with hypertension and the use of cytotoxic drugs being the two most prevalent instances in which this syndrome occurs in conjunction with ESRD and autoimmune diseases. In particular, the chimeric anti-CD20 monoclonal antibody rituximab which is increasingly used in the treatment of hematologic malignancies, rheumatoid arthritis, systemic lupus erythematosus, ANCA-associated vasculitis and membranous nephropathy, can cause direct cell injury, endothelin-mediated vasospasm and dysfunction given the expression of CD20 in activated endothelial cells, which may lead to PRES [25]. Furthermore, there is evidence of susceptibility within a few weeks of commencing hemodialysis treatment. During this time, patients adjust to fluctuations in mean arterial pressure through changes in their dry weight [18]. Those two instances were indeed present in the patient we reported.

The diagnosis of PRES is challenging, as its symptoms often overlap with those of other conditions, and requires clear communication between clinicians and radiologists [11]. It is imperative to review the patient's current status, medications, examination findings and blood pressure values during and outside hemodialysis session.

In our case report, we presented, to our knowledge, the first reported case of PRES in a patient with ANCA-negative vasculitis. The patient had several risk factors that could be associated with the development of PRES, including moderate to severe hypertension during and outside of hemodialysis sessions. A review of past hemodialysis session reports revealed multiple instances of BP values exceeding 180 mmHg/100 mmHg. Is it worth underlying that the patient had started hemodialysis treatment less than 20 days earlier and had recently been exposed to potent immunosuppressive drugs, including corticosteroid and rituximab, the latter with a short exposure time of thirty minutes due to the development of an adverse reaction in the form of tremors. In addition, the patient was experiencing a catheter-associated bloodstream infection at the onset of neurological symptoms, which occurred a few hours after hemodialysis session. Timely initiation of supportive treatment was crucial. This included upgrade of antihypertensive therapy, tapering of steroid therapy, intravenous antibiotic therapy for infection control and replacement of hemodialysis CVC with a new permanent tunneled one, oral antiepileptic therapy, strict volume control and avoidance of long inter-dialytic gaps. The combination of these maneuvers led to a significant improvement within a few days, resulting in complete resolution of the clinical manifestations and radiological features of PRES. However, micro-hemorrhage outcome in right occipital lobe was observed on MRI follow-up at 1 month, which is consistent with the existing literature [26].

Conclusion

Management of PRES patients with neurological symptoms in the context of renal failure requiring hemodialysis treatment, moderate to severe hypertension and exposure to cytotoxic drugs, particularly in the presence of small vessel vasculitis, should undergo MRI to rule out PRES. The primary disease should be treated with targeted therapy, and risk factors should be corrected, along with blood pressure control. Although the patient had several risk factors for PRES, we cannot exclude a possible causal effect of the underlying diagnosis of ANCA-negative vasculitis. To our knowledge, this is the first case of PRES in a patient with ANCA-negative vasculitis.

References

1. Ronsin C, Georges M, Chapelet-Debout A, Augusto JF, Audard V, Lebourg L, et al. ANCA-Negative Pauci-immune Necrotizing Glomerulonephritis: A Case Series and a New Clinical Classification. Am J Kidney Dis. 2022;79(1):56-68.e1.

2. Harris AA, Falk RJ, Jennette JC. Crescentic glomerulonephritis with a paucity of glomerular immunoglobulin localization. Am J Kidney Dis. 1998;32(1):179-84.

3. Lauren Floyd, Morris AD, Elsayed ME, Shetty A, Baksi A, Geetha D, et al. A Meta-Analysis and Cohort Study of Histopathologic and Clinical Outcomes in ANCA-

Box 1: Conditions associated with the development of PRES.

General conditions
- Hypertension*
- Sepsis*
- Solid organ transplantation
- Eclampsia and pre-eclampsia
- Renal failure*
- Malignancy (solid organ and hematological)
- Bone marrow transplantation
- Stem cell transplantation
- Hypomagnesaemia
- Hypercalcemia
- Hypercholesterolemia
- Late radiation-associated encephalopathy (SMART)
Autoimmune disorders
- Rheumatoid arthritis
- Chron's disease
- Systemic Lupus Erythematosus
- Scleroderma
- Vasculitis*
- Neuromyelitis spectrum disorder
Cytotoxic and immunosuppressive medications
- Hydroxydaunorubicin/Adriamycin
- Vinblastine/vincristine
- Gemcitabine
- Platinum-containing drugs: Cisplatin, Oxaliplatin and Carboplatin
- Bortezomib
- Cyclophosphamide
- Daunorubicin
- Interferon therapy
- Capecitabine, 5-fluorouracil
- Cytarabine
- Etoposide
- Corticosteroids*
- Rituximab*
- Ciclosporin
- Tacrolimus
- Sirolimus
- Mycophenolate mofetil
- Methotrexate
- Azathioprine
Toxins
- Scorpion poison
- LSD intoxication
- Ephedra overdose
- Alcohol intoxication
- Cocaine
Other medications
- Lithium
- Linezolid
- Intravenous contrast
- Intravenous immunoglobulins
- Tyrosine kinase inhibitors

*Conditions present in case report. Triplett JD, Kutlubaev MA, Kermode AG, Hardy T. Posterior Reversible Encephalopathy Syndrome (PRES): diagnosis and management. Pract Neurol. 2022;22(3):183-89.

Negative versus Positive Vasculitis. Kidney360. 2023;4(1):69-77.

4. Zheng Y, Zhang Y, Cai M, Lai N, Chen Z, Ding M. Central Nervous System Involvement in ANCA-Associated Vasculitis: What Neurologists Need to Know. Front Neurol. 2019;9:1166.

5. Fuentes AG, Komarla A, Gomez JI. Posterior reversible encephalopathy syndrome in a patient with ANCA-associated vasculitis. Rheumatol Int. 2012;32(8):2529-30.

6. Patel UV, Patel NJ. Posterior reversible leukoencephalopathy syndrome as a presenting manifestation of p-ANCA-associated vasculitis. BMJ Case Rep. 2014;2014:bcr2013202022.

7. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med 1996;334(8):494-500.

8. Lamy C, Oppenheim C, Mas JL. Posterior reversible encephalopathy syndrome. Handb Clin Neurol. 2014;121:1687-701.

9. Stott VL, Hurrell MA, Anderson TJ. Reversible posterior leukoencephalopathy syndrome: a misnomer reviewed. Intern Med J. 2005;35(2):83-90.

10. Bossuyt X, Cohen Tervaert JW, Arimura Y, Blockmans D, Flores-Suarez LF, Guillevin L, et al. Position paper: Revised 2017 international consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. Nat Rev Rheumatol. 2017;13(11):683-92.

11. Triplett JD, Kutlubaev MA, Kermode AG, Hardy T. Posterior reversible encephalopathy syndrome (PRES): diagnosis and management. Pract Neurol. 2022;22(3):183-9.

12. Eisenberger U, Fakhouri F, Vanhille P, Beaufils H, Mahr A, Guillevin L, et al. ANCA-negative pauci-immune renal vasculitis: histology and outcome. Nephrol Dial Transplant. 2005;20(7):1392-9.

13. Wiik AS. Autoantibodies in ANCA-associated vasculitis. Rheum Dis Clin North Am. 2010;36(3):479-89.

14. Kallenberg CG. Key advances in the clinical approach to ANCA-associated vasculitis. Nat Rev Rheumatol. 2014;10(8):484-93.

15. Holle JU, Gross WL. Neurological involvement in Wegener's granulomatosis. Curr Opin Rheumatol. 2011;23:7-11.

16. Drachman DA. Neurological Complications of Wegener's Granulomatosis. Arch Neurol. 1963;8(2):145-55.

17. Yokoseki A, Saji E, Arakawa M, Kosaka T, Hokari M, Toyoshima Y, et al. Hypertrophic pachymeningitis: significance of myeloperoxidase anti-neutrophil cytoplasmic antibody. Brain. 2014;137(Pt 2):520-36.

18. Canney M, Kelly D, Clarkson M. Posterior reversible encephalopathy syndrome in end-stage kidney disease: not strictly posterior or reversible. Am J Nephrol. 2015;41(3):177-82.

19. Lee VH, Wijdicks EFM, Manno EM, Rabinstein AA. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol. 2008;65(2):205-10.

20. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. Mayo Clin Proc. 2010;85(5):427-32.

21. Legriel S, Schraub O, Azoulay E, Hantson P, Magalhaes E, Coquet I, et al. Determinants of recovery from severe posterior reversible encephalopathy syndrome. PLoS One. 2012;7(9):e44534.

22. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: controversies surrounding pathophysiology of vasogenic edema. Am J Neuroradiol. 2008;29(6):1043-9.

23. Khurana K, Acharya S, Shukla S, Kumar S, Mishra P. Chronic Glomerulonephritis and Malignant Hypertension With PRES (Posterior Reversible Encephalopathy Syndrome) Presenting As Status Epilepticus: A Case Report. Cureus. 2023;15(8):e43902.

24. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. AJNR Am J Neuroradiol. 2007;28(7):1320-7.

25. Pathireddy S, Bose S, Baradhi K, Aeddula NR. Rare but not beyond care: a young female with altered mental status and seizures. Oxf Med Case Reports, 2019;8:omz072.

26. McKinney AM, Sarikaya B, Gustafson C, Truwit CL. Detection of microhemorrhage in posterior reversible encephalopathy syndrome using susceptibility-weightedimaging. AJNR Am J Neuroradiol. 2012;33(5):896-903.