Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

A Two-Case Series and Literature Review of Unusual Haemorrhagic Presentation of Posterior Reversible Encephalopathy Syndrome (PRES) in Systemic Lupus Erythematosus

Sourav Garai
All India Institute of Medical Sciences (AIIMS)
Ritasman Baisya
ritasman.rheumat@aiimskalyani.edu.in

All India Institute of Medical Sciences (AIIMS)
Sukdev Manna
All India Institute of Medical Sciences (AIIMS)
Soumya Bhowmik
All India Institute of Medical Sciences (AIIMS)
Sneha Dhali -
All India Institute of Medical Sciences
Swarnava Tarafdar
All India Institute of Medical Sciences

Short Report

Keywords: SLE, PRES, Hemorrhagic PRES, Lupus Nephritis

Posted Date: April 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9451770/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background - Posterior Reversible Encephalopathy Syndrome (PRES) is a clinical and radiographic condition characterised by reversible vasogenic oedema in the brain. This condition is mainly caused by severe hypertension in the presence of underlying risk factors such as organ transplantation, certain medications, and autoimmune diseases, including systemic lupus erythematosus (SLE). Hemorrhagic complications associated with PRES are rare, mostly occurring after transplantation and are even less common in patients with a background of SLE.

Case series – We reported two cases diagnosed as systemic lupus erythematosus (SLE) with multisystem involvement. They presented with acute onset generalised tonic-clonic seizures, severe headache, and hypertensive emergency in the background of biopsy-proven lupus nephritis. MRI of the brain revealed vasogenic edema involving the posterior aspect of the brain with hemorrhagic transformation. Both patients required prolonged intensive care admission with antihypertensives, immunosuppressives, and other supportive therapies. One of them (case 2) showed significant recovery, both clinically and radiologically. The other patient (case 1), although showing partial recovery in the initial phase, had ongoing sepsis and eventually succumbed.

Conclusion – Hemorrhagic conversion of PRES in the context of SLE is rarely reported. To date, fewer than ten case series have been documented with SLE-related hemorrhagic PRES, and these two cases emphasise the significance of this entity in the background of lupus. A detailed review highlights the comparative characteristics of our cases and those reported in the literature.

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a rare, acute-to-subacute neurological disorder characterised by headache, altered mental status, visual disturbances, and seizures, radiologically defined by reversible vasogenic oedema mainly in the parieto-occipital regions (1,2). While PRES can be triggered by various factors, autoimmune diseases account for nearly half of all cases, with systemic lupus erythematosus (SLE) being the most frequently associated rheumatological disorder (2). Despite this association, PRES remains an uncommon manifestation in SLE, occurring in less than 1% of patients (3). Conventionally, PRES is regarded as a benign, non-haemorrhagic condition; however, intracranial haemorrhage is increasingly recognised as an atypical and severe complication, occurring in roughly 15% to 17% of all PRES cases (4). The frequency of haemorrhagic PRES specifically within the SLE population is not definitively established, though some reviews note a haemorrhagic presentation in 8.6% to 16.7% of SLE-associated PRES cases (5,6).

Despite advancements in recognising PRES, it remains officially excluded from the 19 recognised neuropsychiatric SLE (NPSLE) syndromes, contributing to diagnostic ambiguity. Crucially, there is a significant gap in knowledge regarding the pathophysiology, risk factors, and optimal management of the atypical haemorrhagic variant of PRES in patients with SLE. This case series and review of the literature illustrate this critical knowledge gap, detailing atypical haemorrhagic presentations of PRES in

SLE to better define its clinical course and emphasise the urgent need for customised therapeutic strategies.

Case Vignette

Case 1

We had a 25 years old female, who was symptomatic since 2020, with intermittent low grade fever, was diagnosed in 2025 as a case of Systemic Lupus Erythematosus, with ascites, pleural effusion, lupus nephritis (Biopsy revealing Activity Index of 7/24, Chronicity Index of 5/12), with autoimmune hemolytic anemia with pancytopenia, with ANA 4+ (Speckled), 1+ for RNP, Smith and Nucleosome, with raised dsDNA and low complement. She presented with complaints of progressive anasarca, oliguria and shortness of breath for 15 days, and few episodes of generalised convulsive episodes with headache and blurring of vision for 1 day.

She was admitted in ICU, seizure was aborted with levetiracetam and infusion of Midazolam was started. Furosemide infusion was initiated in view of oliguria and labetalol infusion was started for her persistently elevated blood pressure. She underwent a MRI with a strong clinical suspicion of Posterior reversible encephalopathy syndrome, which revealed PRES changes in right parieto-occipital region and Haemorrhage in left occipital and right frontal region (Figure 1). In view of worsening renal function, oliguria, and volume overload state, she received 3 episodes of hemodialysis. Fundoscopic evaluation revealed grade 2 papilledema. Subsequently a brief period of hemodynamic stabilization was achieved and she was administered with Inj cyclophosphamide 700 mg following Inj methylprednisolone pulse in view of progressive renal damage.

However, her renal function had a downhill course and she developed refractory fluid overload state. She was intubated in view of respiratory distress and worsening sensorium. Her blood pressure further worsened, she was started on Labetalol infusion, and regular hemodialysis was started along with furosemide infusion in view of complete renal shutdown. She further grew pan-resistant *Klebsiella pneumoniae* in her urine, carbapenem-resistant *Acinetobacter baumanii* in her lung, and antibiotics were titrated as per limited available options. She also developed diffuse alveolar Haemorrhage with florid bloody aspirate from endotracheal tube and severe anemia, for which repeat pulse doses of Inj methylprednisolone and packed red blood cell transfusion was done. NCCT done during the latter half of her illness revealed resolution of Haemorrhage, However, her clinical status kept worsening with a very high disease activity and frank sepsis, and she ultimately succumbed to her illness.

Case 2

We had a 24-year-old woman who had been symptomatic since 2020, with intermittent low-grade fever, symmetrical inflammatory polyarthritis affecting both small and large joints, oral ulcers, and easy fatigability. She initially received symptomatic treatment at local hospitals and was later diagnosed with SLE with Sjogren's overlap in February 2023 at an external hospital, based on ANA-IIF showing 3+ and

ANA blot showing Ro52 2+, dsDNA 1+. During her illness, she developed pancytopenia and nephritis and was treated with monthly doses of Inj. Cyclophosphamide for 6 months in 2023, followed by maintenance therapy with Azathioprine. Due to significant proteinuria, Tacrolimus was added in October 2023. In April 2024, she was shifted to Mycophenolate Sodium because of worsening renal function, leading to the discontinuation of Tacrolimus and Azathioprine. In December 2024, she underwent a renal biopsy owing to worsening proteinuria, and a second cycle of monthly Inj. Cyclophosphamide for 6 doses was started due to high disease activity. The histopathological examination revealed Lupus Nephritis IV/V (ISN/RPS), with an activity index of 16/24, a chronicity index of 0/12, and IFTA of less than 10%. However, she was irregular with steroid tapering and experienced repeated infections. In June 2025, she was admitted with community-acquired pneumonia and spontaneous pneumothorax.

In hospital, her blood pressure showed an increasing trend, and she developed two episodes of generalised tonic-clonic seizures after a brief period of headache, followed by altered sensorium. She was managed in ICU with immediate control of seizures and gradual reduction of elevated blood pressure using Labetalol infusion over the next 3-4 days. A possibility of Posterior Reversible Encephalopathy Syndrome (PRES) was considered, and she underwent MRI. Imaging revealed PRES-related changes with haemorrhage in the left frontal and right parieto-occipital lobes (Figure 2). Renal artery Doppler excluded renal artery stenosis. She was managed conservatively, leading to the normalisation of hypertension. She regained consciousness with no residual deficits; there were no further seizures, and she was discharged in a haemodynamically stable condition within a week. Follow-up imaging showed resolution of the haemorrhage, correlating with her improved clinical status (Figure 3). Characteristics of both patients are depicted in Table 1

Discussion

We presented two cases of SLE with active nephritis, specifically crescentic glomerulonephritis, accompanied by severe renal hypertension. Both patients experienced haemorrhagic transformation of PRES, presenting as generalised seizures, headache, and hypertensive emergency. One of them experienced significant recovery, while the other succumbed due to sepsis following partial recovery.

Haemorrhagic PRES in the context of SLE is uncommon and may be triggered by various factors, including severe renal hypertension, crescentic glomerulonephritis, immunosuppressive therapy, and bacterial pneumonia (sepsis). We carried out a comprehensive literature review using the MeSH terms and relevant keywords such as ‘PRES’ OR ‘reversible encephalopathy’ AND ‘Intracranial haemorrhage’ OR ‘haemorrhagic transformation’ OR ‘haematoma’ OR ‘Micro-haemorrhages’ AND/OR ‘SLE’ OR ‘Lupus’ across databases and registers like MEDLINE (PubMed), Web of Science, and Scopus. The literature on haemorrhagic PRES in autoimmune diseases, including SLE, remains limited, mainly consisting of case reports or case series. (The comparative discussion of different case series on haemorrhagic PRES in SLE is provided in table 2)

Haemorrhage in PRES – Haemorrhage in PRES is a rare complication often observed after transplantation or immunosuppressive therapy, particularly with cyclosporine. (4) The prevalence of this condition varies across studies: Raman et al. (5) reported it in 9% of cases, Hefzy et al. (4) in 15%, Sharma et al. (6) in 19%, and Appiani et al. (7) in 30%. This variation in reported prevalence may be due to small sample sizes and the heterogeneity in the underlying aetiology and therapeutic approaches. Hefzy et al. (4) retrospectively studied 151 patients with PRES, and 23 of these had intracranial haemorrhage. The rate of haemorrhage was significantly higher in patients with allogenic bone marrow transplants (46.6%) compared to those with solid-organ transplants (11.7%), and this difference was statistically significant ($p = 0.02$). In their series, the autoimmune cause of PRES included 12 cases, two of which involved haemorrhagic complications. Both of these patients had severe hypertension at presentation. One patient experienced both a minor haemorrhage and a haematoma, resulting in a permanent neurological deficit.

Appiani et al (7) reported 10 cases of haemorrhagic PRES among 33 PRES cases in their retrospective study over 12 years. All of the haemorrhagic PRES cases occurred after transplantation, primarily following BMT. The study found that patients with brain bleeding were less likely to have been treated with corticosteroids and more likely to exhibit specific brain imaging abnormalities. Sharma et al. (6) reported that 19% of patients experienced haemorrhage related to PRES in their study, conducted from 2001 to 2008, which included 263 cases of PRES and 51 instances of haemorrhage. Autoimmune disease-associated PRES was observed in 10 cases (3.8%); however, haemorrhage occurred in only two of these cases. Furthermore, Haemorrhage occurred more frequently in patients with sepsis (28%) and eclampsia (25%), which differs from the observation reported by Hefzy et al (4) .

Imaging pattern - Sharma et al (6) reported on the imaging patterns of Haemorrhage in PRES , based on 51 cases. In 46 of these cases, intraparenchymal bleeding was observed, typically multifocal, punctate and located near areas of edema. Subarachnoid Haemorrhage (SAH) was present in 14 cases, with all instances sparing the basal cisterns. The SAH was mostly small and localized near the cerebral convexities. Hefzy et al.(4) reported that out of 23 cases of PRES with Haemorrhage, 16 presented with a single type of Haemorrhage, while the remaining cases showed combined types. The single Haemorrhage patterns included minute, sulcal, and focal hematomas. There was no significant difference in the type of Haemorrhage concerning the associated clinical condition or blood pressure status.

Haemorrhage in SLE-PRES - Ho Kyun Kim, et al (8) , presented a 29-year-old female with initial presentation of PRES, found to have class 4 lupus nephritis with high anti-dsDNA antibody and low complement level. She was treated with a methylprednisolone pulse, an injection of cyclophosphamide, followed by cyclosporine. She had recurrent attacks of PRES with minute petechial haemorrhagic spots. The authors postulated that the second attack of PRES might be triggered by cyclosporine therapy, which causes cytotoxic changes in the form of petechial haemorrhage. Chen et al. (9) reported a case of SLE with class 4 LN that was resistant to treatment with steroids and CYC. The patient experienced a hypertensive emergency accompanied by vasogenic oedema in the brain. An MRI angiogram revealed

focal vasoconstriction of the middle cerebral artery. During her hospital stay, her condition worsened, leading to haemorrhagic transformation, subarachnoid haemorrhage, and transtentorial herniation. Lai CC et al (10) reported four cases of SLE-PRES-related ICH in their case series. In two patients with PRES-related ICH, encephalomalacia was noted on follow-up MRI studies. Univariate logistic regression analyses showed that severe hypoalbuminemia (serum albumin < 20 gm/liter) and thrombocytopenia (platelet count < 30,000/mm^3) were both risk factors for PRES-related ICH. Maximal blood pressure at PRES, serum creatinine levels, and coagulation functions were not risk factors for PRES-related ICH.

Pathogenesis – The pathogenesis of intracerebral haemorrhage (ICH) related to PRES may be multifactorial. Appiani et al. (7) suggested that factors such as organ transplantation, immunosuppressive therapy, and pre-existing coagulation disorders can increase the risk of haemorrhagic conversion in PRES. Furthermore, there is ongoing debate about whether PRES and PRES-related ICH share the same pathophysiology or represent two distinct processes. While eclampsia and hypertension are well-known independent risk factors for ICH, literature also reports non-hypertensive risk factors for haemorrhagic PRES. In some case reports, the rate of haemorrhagic PRES associated with infection varied between 11.5% and 28%, which is comparable to the rates of ICH in PRES associated with eclampsia. (4,6) Clinical studies have found that therapeutic anticoagulation and coagulopathy are associated with ICH in PRES (11,12). Thrombocytopenia is linked to severe and often fatal ICH in these patients. (11) Additionally, ICH in PRES is related to increased vasogenic oedema, and a hypertensive crisis, especially when combined with hypoalbuminaemia or thrombocytopenia, may worsen PRES severity and ICH.

Clinical Outcome - PRES-related ICH can lead to permanent brain damage, bleeding disorders, significant morbidity, and generally poorer results. (11,13) Lai et al. (10) reported cases of encephalomalacia in two patients who suffered from haemorrhagic PRES, as seen on follow-up MRIs. Six patients experienced toxicity causing PRES with haemorrhage, with an average survival of 17 days (ranging from 1 to 64 days). One patient developed a hematoma within PRES oedema on day 4 and died from herniation and multi-organ dysfunction (MOD) on day 6. Another patient, who was in a coma due to deep thalamic-striatal minute haemorrhages related to PRES, ultimately died on day 64 from MOD. Additionally, Chen et al. (9) reported a case where PRES with haemorrhagic transformation and herniation resulted in the patient's death. In our case series, one patient had a better clinical and radiographic outcome. The other patient, with initial partial recovery, succumbed to sepsis.

Conclusion

Haemorrhagic posterior reversible encephalopathy syndrome (PRES) in systemic lupus erythematosus (SLE) is a serious neurological emergency that challenges the traditional view of PRES as a benign, fully reversible condition. This atypical form often occurs in the context of active lupus nephritis, severe hypertension, and aggressive cytotoxic therapy, closely resembling devastating primary neuropsychiatric SLE (NPSLE) events.

Declarations

Funding Statement:

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

Author Contribution

Conceptualisation: RB, SG, SB; Data curation: RB, SD, ST; Investigation: ST, SD; Methodology: RB, SG, SB; Supervision: RB, SM; Writing - Original Draft: RB,SG ; Writing - Review & Editing: RB, SB, SM

References

1. Fugate JE, Hawkes MA, Rabinstein AA. Posterior reversible encephalopathy syndrome: evolving insights in diagnosis, management, and outcomes. Lancet Neurol. 2025;24(9):789–800.
2. Anderson RC, Patel V, Sheikh-Bahaei N, Liu CSJ, Rajamohan AG, et al. Posterior reversible encephalopathy syndrome (PRES): pathophysiology and neuro-imaging. Front Neurol. 2020;11:463.
3. Chen B, Hong H, Wang J, Li X, Wang C, Xie T. Systemic lupus erythematosus with recurrent posterior reversible encephalopathy syndrome: a rare case report. Med (Baltim). 2025;104(29):e43428.
4. Hefzy HM, Bartynski WS, Boardman JF, Lacomis D. Haemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features. AJNR Am J Neuroradiol. 2009;30:1371–79.
5. Raman R, Devaramane R, Jagadish GM, Chowdaiah S. Various imaging manifestations of posterior reversible encephalopathy syndrome (PRES) on magnetic resonance imaging (MRI). Pol J Radiol. 2017;82:64.
6. Sharma A, Whitesell RT, Moran KJ. Imaging pattern of intracranial haemorrhage in the setting of posterior reversible encephalopathy syndrome. Neuroradiology. 2010;52(10):855–63.
7. Appiani F, Claverie CS, Klein FR. Posterior reversible leukoencephalopathy with haemorrhagic features: a case series. Cureus. 2023;15(11):e49587.
8. Kim HK, Lee HJ, Shin KM. Irreversible haemorrhagic complication of recurrent posterior reversible encephalopathy syndrome in a patient with systemic lupus erythematosus. J Korean Soc Magn Reson Med. 2013;17(2):144–9.
9. Chen HA, Lin YJ, Chen PC, Chen TY, Lin KC, et al. Systemic lupus erythematosus complicated with posterior reversible encephalopathy syndrome and intracranial vasculopathy. Int J Rheum Dis. 2010;13(4):e79–82.
10. Lai CC, Chen WS, Chang YS, et al. Clinical features and outcomes of posterior reversible encephalopathy syndrome in patients with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2013;65(11):1766–74. 10.1002/acr.22047.

11. Srichawla BS, Găman M-A, Can H, Kipkorir V, Garcia-Dominguez MA. Intracranial haemorrhage in posterior reversible encephalopathy syndrome: a systematic review and meta-analysis. Ann Med Surg (Lond). 2025;87(9):6023–32.
12. Aranas RM, Prabhakaran S, Lee VH. Posterior reversible encephalopathy syndrome associated with haemorrhage. Neurocrit Care. 2009;10(3):306–12.
13. Alshami A, Al-Bayati A, Douedi S, Hossain MA, Patel S, Asif A. Clinical characteristics and outcomes of patients admitted to hospitals for posterior reversible encephalopathy syndrome: a retrospective cohort study. BMC Neurol. 2021;21:107.
14. Ahmed AE, Al Zahib BM, Al-Rashidi AR, Almassloom AH, Althobaiti NS. Acute psychosis as the initial presentation of systemic lupus erythematosus complicated by posterior reversible encephalopathy syndrome with haemorrhage: a case report. Cureus. 2026;18(1):e102238.
15. Leroux G, Sellam J, Costedoat-Chalumeau N, Le Thi Huong D, Combes A, et al. Posterior reversible encephalopathy syndrome during systemic lupus erythematosus: four new cases and review of the literature. Lupus. 2008;17(2):139–47.
16. Gauiran VDT, Lladoc-Natividad TE, Rocha II, Manapat-Reyes BH. Seizure and acute vision loss in a Filipino lupus patient: a case of posterior reversible encephalopathy syndrome with intraparenchymal haemorrhage. Case Rep Med. 2018;2018:4238676.
17. Shaharir SS, Remli R, Marwan AA, Said MS, Kong NC. Posterior reversible encephalopathy syndrome in systemic lupus erythematosus: pooled analysis of the literature reviews and report of six new cases. Lupus. 2013;22(5):492–6.
18. Akins PT, Axelrod Y, Silverthorn JW, Guppy K, Banerjee A, Hawk MW. Management and outcomes of malignant posterior reversible encephalopathy syndrome. Clin Neurol Neurosurg. 2014;125:52–7.

Tables

Tables are available in the Supplementary Files section.

Figures

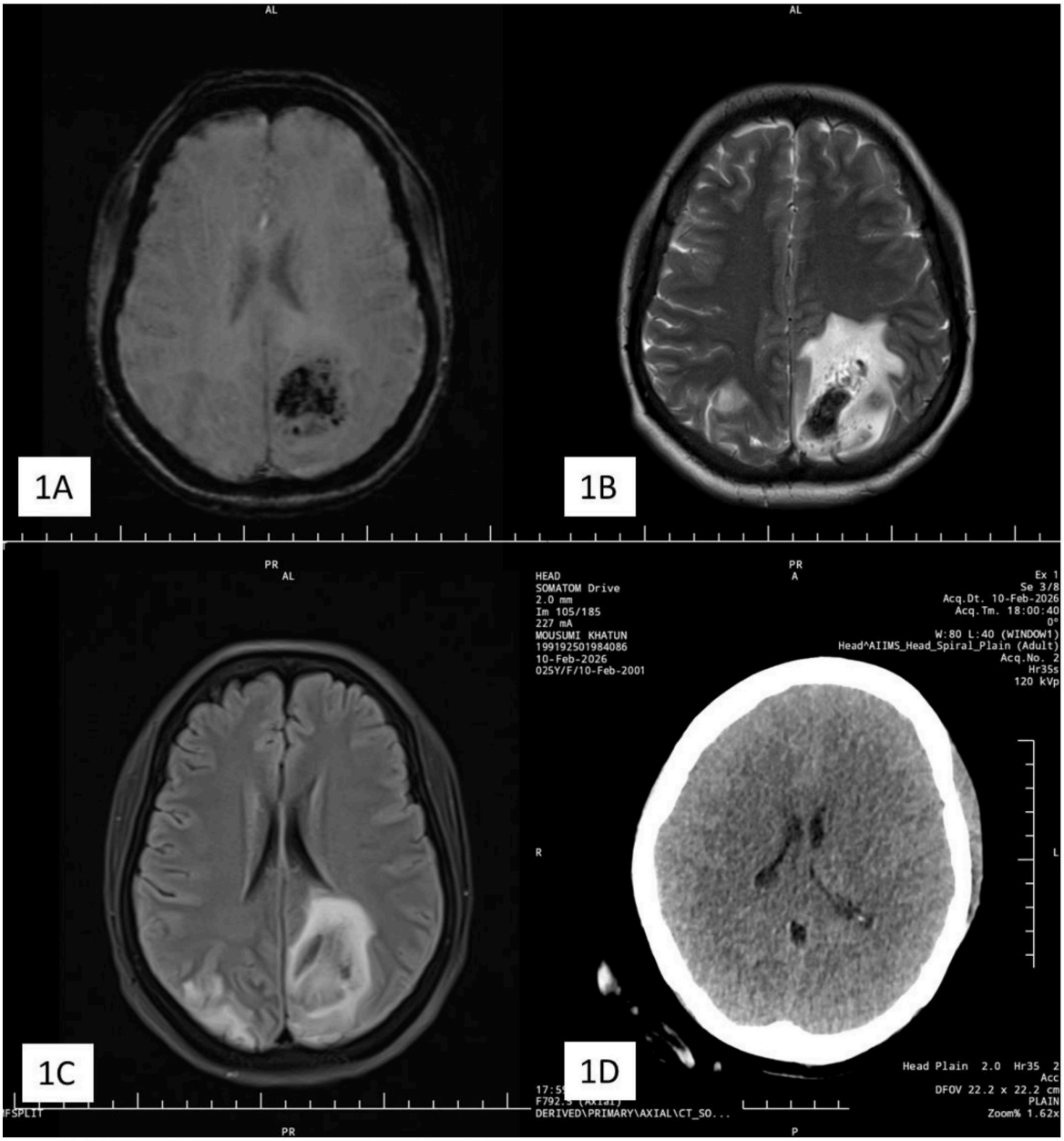


Figure 1 - The initial axial (MRI) scan of the brain shows changes consistent with haemorrhagic PRES. (1A) SWI displays a prominent blooming artifact in the left parieto-occipital region, indicating acute haemorrhage. (1B) T2-weighted and (1C) FLAIR sequences reveal extensive surrounding vasogenic oedema, characterised by hyperintense signals involving both sides, but mainly the left parieto-occipital lobes. (1D) A follow-up non-contrast computed tomography (NCCT) scan of the head shows significant interval resolution of both oedema and the haemorrhagic focus.

Figure 1

CASE 1 - The initial axial (MRI) of the brain shows changes consistent with haemorrhagic PRES. (1A) SWI displays a prominent blooming artefact in the left parieto-occipital region, indicating acute haemorrhage. (1B) T2-weighted and (1C) FLAIR sequences reveal extensive surrounding vasogenic oedema, characterised by hyperintense signals involving both sides, but mainly the left parieto-occipital lobes.

(1D) A follow-up non-contrast computed tomography (NCCT) scan of the head shows significant interval resolution of both oedema and the haemorrhagic focus.

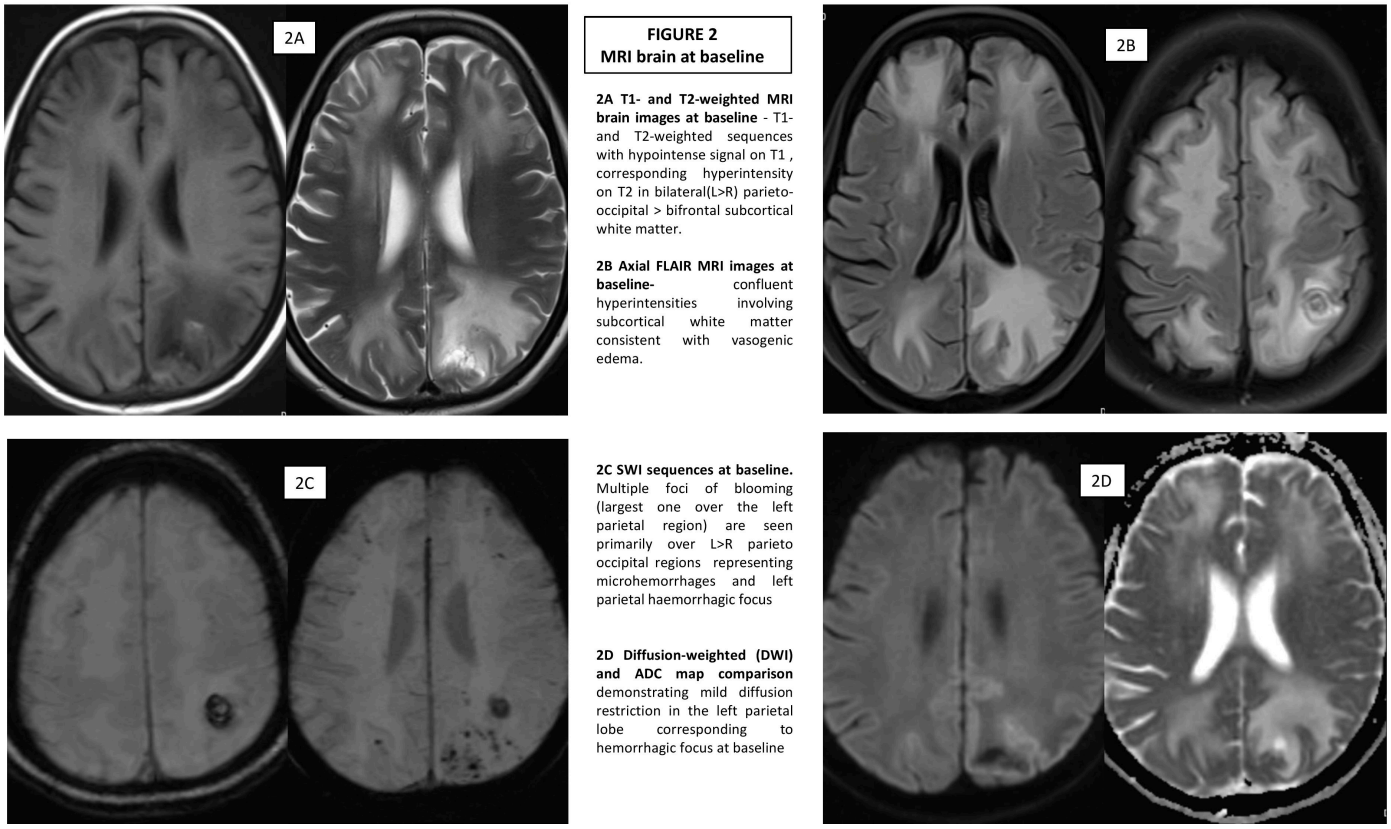


Figure 2

CASE 2 MRI Brain at Baseline - 2A: T1- and T2-weighted MRI brain images showing hypointense signals on T1 and corresponding hyperintensity on T2 in bilateral (L>R) parieto-occipital and bifrontal subcortical white matter. 2B: Axial FLAIR MRI images revealing confluent hyperintensities in the subcortical white matter, indicative of vasogenic oedema. 2C: SWI sequences displaying multiple foci of blooming, primarily over L>R parieto-occipital regions, including a large focus in the left parietal area, representing microhaemorrhages and a haemorrhagic focus in the left parietal region. 2D: Diffusion-weighted imaging (DWI) and ADC map comparison showing mild diffusion restriction in the left parietal lobe, corresponding to the haemorrhagic focus at baseline.

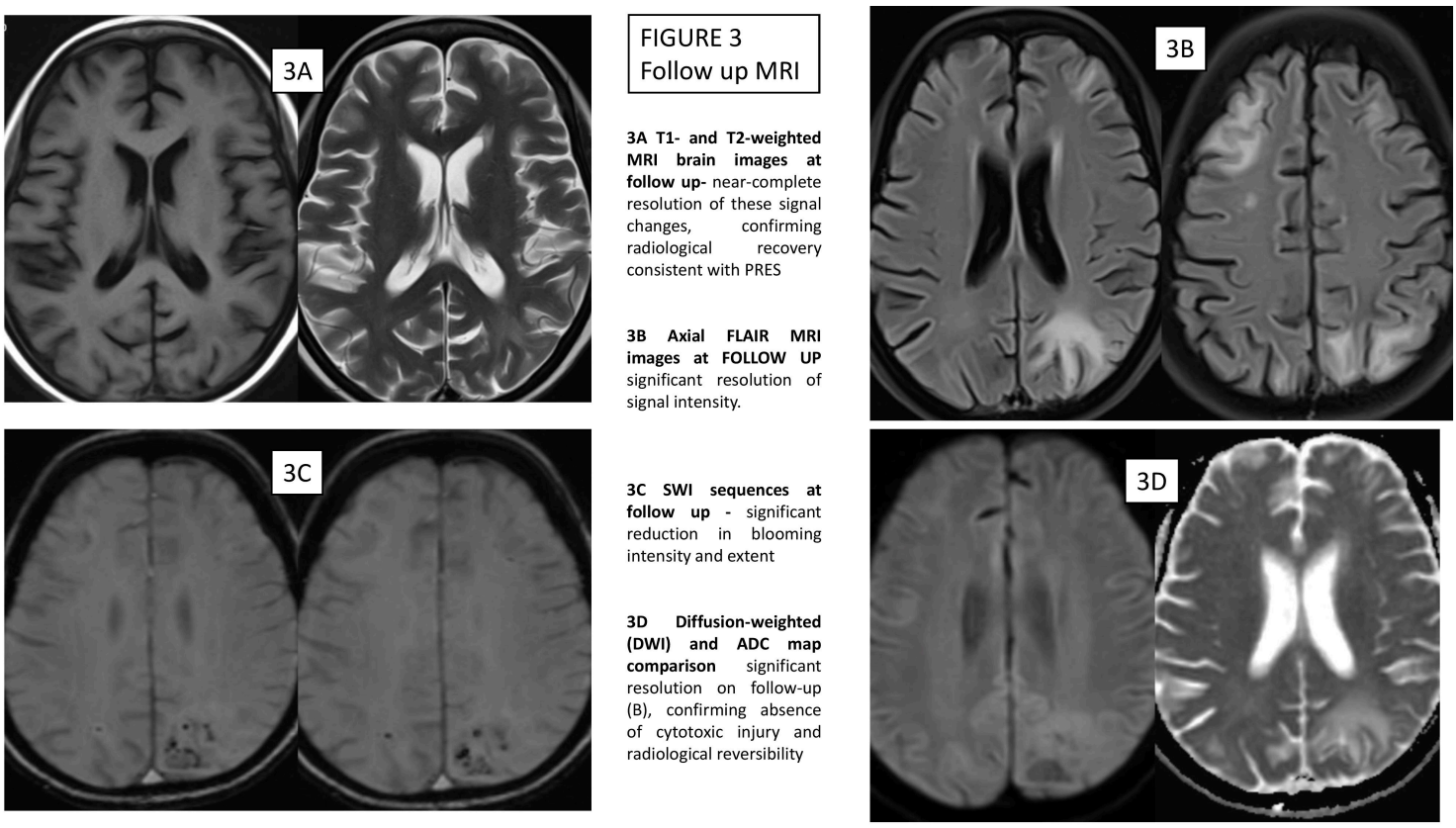


Figure 3

CASE 2 MRI brain at follow-up - 3A T1- and T2-weighted MRI brain images showing near-complete resolution of these signal changes, confirming radiological recovery consistent with PRES. 3B Axial FLAIR MRI images at follow-up demonstrate significant resolution of signal intensity. 3C SWI sequences at follow-up show a significant reduction in blooming intensity and extent. 3D diffusion-weighted (DWI) and ADC map comparison reveal significant resolution on follow-up (B), confirming the absence of cytotoxic injury and radiological reversibility.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- TABLES.docx
- SUPPLEMENTARYWORDARPHGEPRES.docx