




# Recurring Posterior reversible encephalopathy syndrome in a patient with polymyositis/systemic sclerosis overlap syndrome triggered by scleroderma renal crisis

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## Abstract

In posterior reversible encephalopathy syndrome (PRES) triggered by scleroderma renal crisis (SRC), modulation and adherence in immunosuppressive therapy are key for avoiding recurrence, complications, and death. A patient with polymyositis (PM)/systemic sclerosis (SSc) overlap syndrome developed PRES triggered by SRC. To our knowledge, this is the first report of a case with PRES associated with PM/SSc overlap syndrome. This manifested as altered mental status and headaches. Vasogenic edema was seen by magnetic resonance imaging in the brainstem and cerebral white matter. Antihypertension therapy resulted in improvement in both neurological symptoms and blood pressure (BP). Reversible clinical course and radiological change were consistent with PRES diagnosis. Here, the importance of BP maintenance and removal of precipitating factors of PRES is shown.

**Keywords:** Posterior reversible encephalopathy syndrome, Scleroderma renal crisis, Polymyositis/systemic sclerosis overlap syndrome, Adherence

## Introduction

Posterior reversible encephalopathy syndrome (PRES) is characterized by headaches, seizures, encephalopathy, and visual disturbances, as well as radiological findings of focal reversible vasogenic edema (1). Early detection and timely treatment are essential to avoid relapse and secondary complications. Though essentially reversible, PRES can cause substantial morbidity, and associated mortality is estimated to be approximately 3%–6%. Therapy usually consists of gradual blood pressure (BP) control and withdrawal of any potentially offending agents. Many factors have been reported to play causative roles in PRES, such as eclampsia, hypertensive encephalopathy, vasculitis, and immunosuppressive agents (2). PRES related to hypertension and immunosuppression is especially common; therefore, patients with systemic sclerosis (SSc) require precautionous evaluation. However, there are few reports of PRES in patients with SSc. Here we present a case with polymyositis (PM)/SSc overlap syndrome with scleroderma renal crisis (SRC) who developed PRES.

## Case Presentation

A 56-year-old female patient was transferred to our hospital in a coma. She had a history of SSc with interstitial pneumonia and PM overlap syndrome 8 months before admission. Her medication included 50 mg prednisolone (PSL)/day and 4 mg tacrolimus/day. After 4 months, she developed thrombotic microangiopathy that led to the revision of her prescription; tacrolimus was changed to azathioprine, and the dosage of PSL was decreased to 25 mg.

After 2 months, the patient was admitted to another hospital presenting with headache, abnormality in the visual field, and general convulsions. She was prescribed azilsartan and carbamazepine after diagnosis of PRES and reversible cerebral vasoconstriction syndrome. Magnetic resonance imaging (MRI) of the brain showed hyperintensities in fluid-attenuated inversion recovery imaging (FLAIR) at the white matter of the occipital lobe (Figure 1). However, owing to poor drug adherence, systolic BP remained >160 mm Hg. At 40 years old, the patient had developed hypertension, but family history was unremarkable.

On admission to our emergency department 2 months after the diagnosis, the patient presented with dull headaches and disturbance of consciousness with nausea and vomiting. Her headache involved the whole head. She had no seizures at this time. Consciousness was scored as E1V2M4, BP was 184/69 mm Hg, and

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heart rate was 126 bpm. She had bilateral leg edema and decreased tendon reflexes in the upper biceps, triceps brachii, brachiocephalic muscle, patellar tendon, and Achilles tendon. Other neurological findings were unremarkable.

Laboratory findings obtained on admission were as follows: white blood cell count 32,500 cells/mm<sup>3</sup> and serum creatinine level 4.37 mg/dL. The patient's baseline creatinine level for the previous 1 month was 2.81 mg/dL. Serum levels were 127 mmol/L for sodium and 5.1 mmol/L for potassium. Brain MRI revealed hyperintensities in FLAIR at the brainstem, cerebral white matter, basal ganglia, and thalamus with hyperintensity in the cerebellar sulci (Figure 1). MR angiography showed no vessel stenosis. The patient was transferred to the intensive care unit with a diagnosis of SRC.

The patient received continuous intravenous injection of nicardipine and was administered 6.25 mg captopril, 5 mg amlodipine, and 4 mg benidipine. On hospital day 2, her BP remarkably decreased from 184/69 to 121/78 mm Hg, and consciousness improved from E1V2M4 to E4V5M6. Owing to symptoms of headache and confusion in combination with radiological findings of focal vasogenic edema, the patient was re-diagnosed with PRES. Her symptoms

persisted; therefore, on hospital day 5, azathioprine was withdrawn, which is a known cause of PRES (3). Antihypertension therapy resulted in improvements to her lesions, BP, and general condition (Figure 1). On hospital day 18, no relapse of symptoms was observed, and the patient was finally discharged. The patient was regularly followed up. Initially, she was unwilling to take her medicine and hid and abandoned pills due to her poor recognition of the importance of medication. She was reluctant to take a large volume of tablets. We maintained regular communication with the patient and involved her in the decision-making regarding the intake of medication. She agreed to take single-pill combinations to avoid polypharmacy and consulted us when she had skipped taking medicine or when she was in poor condition. Adherence to antihypertensive medication improved, and she has remained free from any PRES events for 2 years with her serum creatinine levels fluctuating approximately 4 mg/dL.

Consent was obtained from the patient to publish these features of her case, and the identity of the patient has been protected.

## Discussion

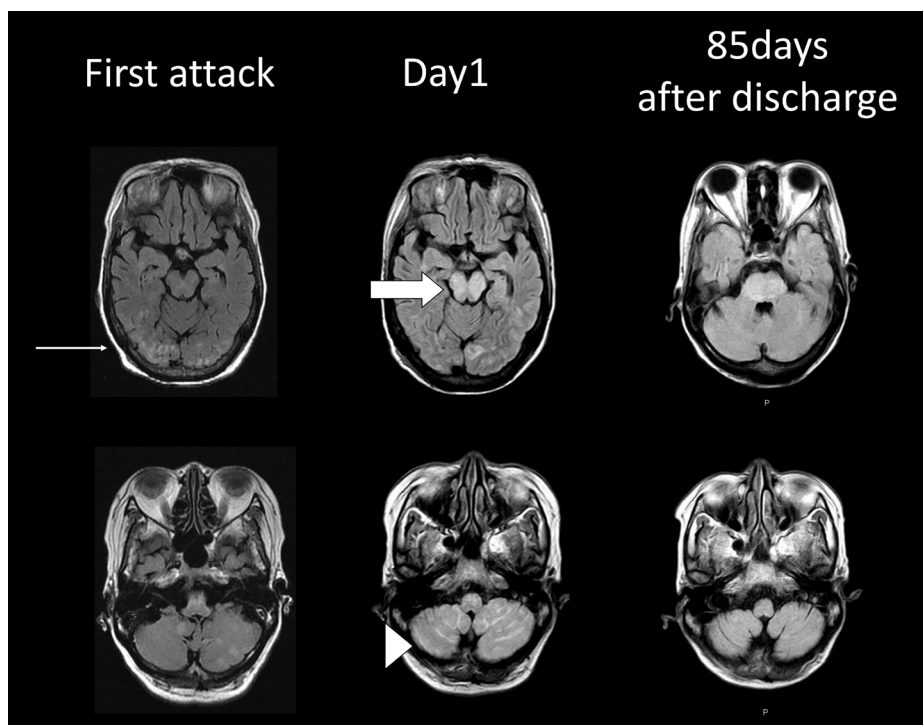
Hinchey et al. (4) described PRES in 1996 as a disease characterized by neurological symp-

toms, including headaches, blurred vision, altered consciousness, and seizures. Confusion is especially common among patients with PRES; it is reportedly present in 50%–80% of patients (1). Whereas headaches manifest in 50% of patients, visual disturbances and focal neurological deficit are less common (1). The present case manifested with altered mental status and headache, which are symptoms compatible with PRES diagnosis.

Posterior reversible encephalopathy syndrome is associated with multiple conditions, including hypertensive encephalopathy, pre-eclampsia/eclampsia, sepsis, bone marrow and solid organ transplantation, and thrombotic thrombocytopenic purpura, as well as during immunosuppressive drug treatment with, for example, cyclosporine and with autoimmune disease (2). We comprehensively searched PubMed and identified only six reported cases of SSc-related PRES (2, 5–9). To the best of our knowledge, this is the first report of a PRES case associated with PM/SSc overlap syndrome. Three patients had diffuse SSc, one had limited SSc, two had SSc/SLE overlap syndrome, and our case had PM/SSc overlap syndrome. As six of the seven identified patients had renal failure, we hypothesized that SRC might be a risk factor for PRES. Two patients experienced recurrence of PRES, including the present case. The mean duration of SSc before the onset of PRES was 4 years and 8 months. BP elevation is due to poor efficacy and discontinuation or switching of antihypertensive agents. Along with these factors, our case highlights the importance of adherence to antihypertensive agents. Poor adherence compromises optimal BP control, leading to the development of PRES within a short period after the onset of SSc. In the present patient, this led to recurrence.

There are several hypotheses regarding the pathophysiological mechanism of PRES (1). Rapid increase in BP provokes insufficient autoregulatory response. Hyperperfusion causes a blood–brain barrier breakdown that generates interstitial extravasation of plasma and macromolecules (1). In patients with SSc, endothelial dysfunction may occur secondary to autoimmune complication and SRC-related microangiopathic damage. The presence of overlapped PM requires the use of high-dose corticosteroids and cytotoxic drugs, which may precipitate SRC and PRES, respectively.

Hypertension control is the cornerstone of treatment against PRES, although no studies have been conducted to compare the therapeutic effects (1). However, there is still uncer-



**Figure 1.** Magnetic resonance imaging (MRI) of the brain on the first onset showed hyperintensities in fluid-attenuated inversion recovery imaging (FLAIR) at the white matter of the occipital lobe (arrow). On hospital admission, MRI of the brain revealed hyperintensities in FLAIR at the brainstem, cerebral white matter, basal ganglia, and thalamus (bold arrow) with hyperintensities in the cerebellar sulci (arrow head). Resolution of the lesion was confirmed 85 days after discharge

tainty as to which antihypertensive agents are most suitable for resolution of PRES (1). In an SRC-related case, angiotensin-converting enzyme inhibitor therapy is preferable (10). We administered continuous intravenous injection of nicardipine along with oral dosage of captopril, amlodipine, and benidipine. Retention of patient adherence to antihypertensive therapy is imperative for BP control. Along with BP control, removing or reducing the precipitating factors is also an essential part of management. We had a clinical dilemma, reducing the dosage of corticosteroid to reduce the risk of SRC or withdrawing azathioprine to avoid PRES, which has a part in reducing the dosage of corticosteroid for treatment of PM/SSc overlap syndrome. We gave priority to reducing offending agents by carefully taking into account patient adherence, as this plays a major role in PRES management.

In conclusion, our patient with PM/SSc overlap syndrome developed SRC-related PRES. Here, adherence to BP maintenance and removing precipitating factors for PRES were important to avoid non-reversible consequences.

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