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NEPHROLOGY - CASE REPORT

Posterior reversible encephalopathy syndrome (PRES) induced by cyclosporine use in a patient with collapsing focal glomeruloesclerosis

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Abstract
Background Posterior reversible encephalopathy syndrome (PRES) is characterized by abnormalities in cerebral white matter and neurologic symptoms. It can be caused by immunosuppressive drugs or autoimmune diseases. We describe a case of PRES in a patient with collapsing focal glomeruloesclerosis (collapsing FGS) with complete recovery after withdrawal of cyclosporine (CSA).
Case report A 27-year-old male presented a corticosteroid-resistant nephrotic syndrome secondary to collapsing FGS corticosteroid. Treatment with CSA was started after a nonresponding course of prednisone. Three weeks later, he developed an abrupt elevation of blood pressure (210/120 mmHg), with headaches, mental confusion, and generalized seizures. Magnetic resonance imaging (MRI) showed lesions suggestive of PRES. CSA was withdrawn, and a new MRI was normal after 2 months.
Conclusions PRES is a rare syndrome that must be suspected in every patient presenting neurologic symptoms in the course of immunosuppression. It can be induced by CSA and is totally reversible when the drug is rapidly withdrawn.

Keywords Posterior reversible encephalopathy syndrome · Collapsing focal glomerulosclerosis · Cyclosporine · Headache · Neurologic symptoms

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Posterior reversible encephalopathy syndrome (PRES) is characterized by abnormalities in cerebral white matter and neurologic symptoms such as headache, mental confusion, vomiting, visual disturbances, multiple generalized tonic-clonic seizures, and occasionally focal neurological deficits or even coma [1, 2].

Most cases of PRES occur in patients with malignant hypertension, eclampsia or immunosuppression

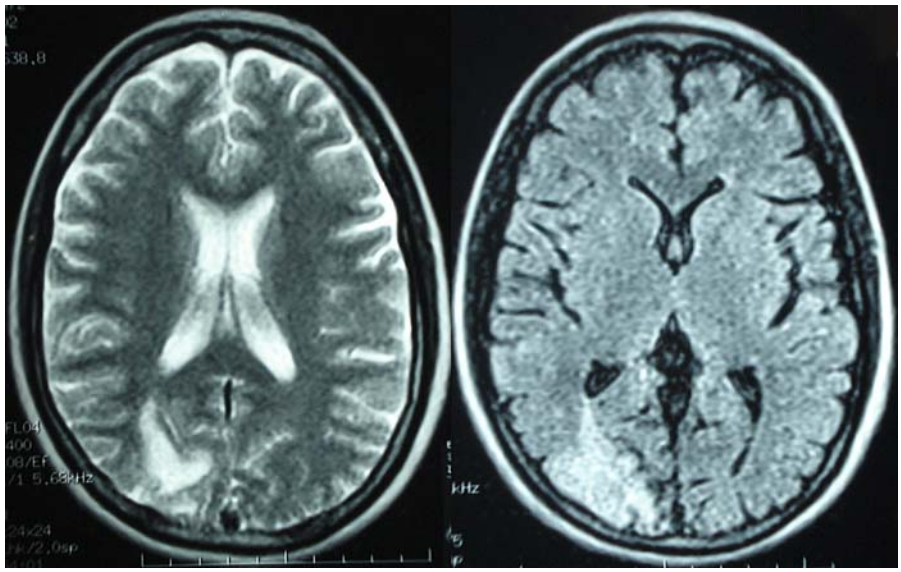

Fig. 1 Axial MRI on T2-weighted and fast fluid-attenuated inversion-recovery (FLAIR) showing area of high signal intensity in posterior parietal white matter during use of CSA

[3]. The association with cyclosporine use was first described in 1987 [4]. Other drugs can trigger PRES, such as interferon-α, erythropoietin, cisplatin, and cytarabine [1].

The clinical picture and the neurologic abnormalities in magnetic resonance imaging (MRI) are reversible after rapid cyclosporine withdrawal [1, 2]. The syndrome, despite its name, is not always reversible. Antunes et al. [5] described cases in which the symptoms did not completely disappear.

This syndrome can be present in many nephrology patients using different types of immunosuppressive drugs, and can be an underdiagnosed cause of neurologic symptoms in this setting [6].

We report the case of a 27-year-old male who presented a corticosteroid-resistant nephrotic syndrome secondary to collapsing FGS. The first laboratory tests showed serum urea 19.4 mmol/l, creatinine 0.25 mmol/l, haematocrit 33%, albumin 1 g/l, total cholesterol 13.79 mmol/l, triglycerides 6.08 mmol/l, fast blood glucose 6 mmol/l, urinary albumin excretion 21 g/24 h. Serology for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV) were all negative. Specific treatment was begun with cyclosporine (CSA) at a dosage of 5 mg/kg/day.

Three weeks later he developed intense headaches, nausea, vomiting, and abrupt blood pressure (BP) elevation (210/120 mmHg), and became confused. He was admitted at the emergency department and a few minutes after admission presented three episodes of generalized seizures. After neurological examination, computed tomography (CT) was performed, which revealed hypodense areas in the right parietal and left frontal areas, suggesting a stroke. PRES diagnosis was suspected and a brain MRI was carried out. The images showed a diffuse area of high signal intensity in the white matter of the right parietal posterior area (Fig. 1).

The CSA dose was reduced to 2.5 mg/kg/day. The patient presented complete recovery, with no permanent neurologic deficits. Headaches and high BP persisted and therefore, CSA was discontinued and replaced by mycophenolate mofetil (MMF) at a dose of 1,500 mg per day. His symptoms improved rapidly after CSA withdrawal. Two months later, another MRI was performed, showing complete resolution of the neurologic lesions (Fig. 2). The patient is currently undergoing conservative treatment for chronic kidney disease (CKD), without immunosuppression, as MMF was tried for two months without any success in NS remission.

The association of PRES with CSA use has been previously described, with successfully recovery after drug withdrawal [4, 7]. CSA was found to be efficient in decreasing proteinuria in both steroid-dependent and steroid-resistant nephrotic patients and is now largely used in nephrology [8]. PRES is typically characterized by headache, encephalopathy, visual symptoms, and seizures [2]. In a recent study by Lee

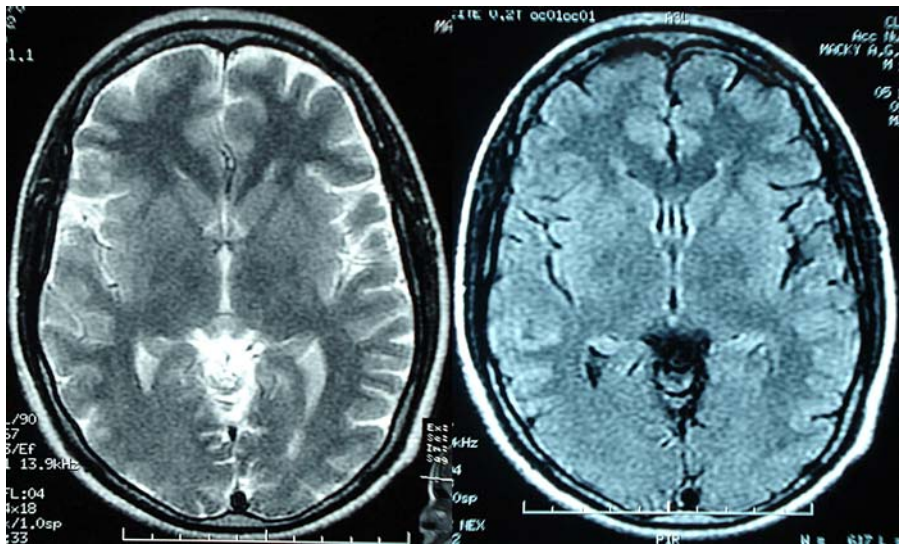

Fig. 2 Axial MRI on T2-weighted and FLAIR 3 months after CSA withdrawal showing complete resolution of the lesion

et al. [9], including 36 patients with PRES, the main clinical manifestations observed were seizures (87%), encephalopathy (92%), visual symptoms (39%), and headache (53%).

Several drugs have been implicated in the pathophysiology of PRES. CSA is the most common [4]. The time span between the drug initiation and development of symptoms is variable. In the case reported by Cosottini et al. [7] the clinical picture onset occurred 6 months after CSA initiation. This time span can be as long as 26 months [2] or as short as 1 week [1]. Our patient developed symptoms 3 weeks after the start of CSA use. PRES has also been reported in patients with chronic kidney disease, even without immunosuppression, and the suggested cause is hypertension [10].

The lesions disclosed by CT and MRI are asymmetrical, although symmetrical lesions are more common [2, 3]. The differential diagnosis should include cerebral venous thrombosis, demyelinating disorders, stroke, and hypertensive encephalopathy. The diagnosis should rapidly be done, considering that BP should be decreased as fast as possible in PRES and in stroke cases; BP should not be decreased fast and abruptly, as this can extend the ischemic area [3]. Delayed diagnosis can cause permanent cerebral injuries.

The use of immunosuppressive drugs is increasing, mainly in the setting of organ transplantation and autoimmune diseases. Physicians should be alert to the possible occurrence of PRES, because it is associated with high morbidity when not rapidly diagnosed and treated. PRES must then be suspected in every patient presenting neurologic symptoms in the course of immunosuppression. It can be induced by CSA and is totally reversible when the drug is rapidly withdrawn.

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