Posterior reversible encephalopathy syndrome due to pulse methylprednisolone therapy in a child

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SUMMARY: İncecik F, Hergüner MÖ, Yıldızdaş D, Yılmaz M, Mert G, Horoz ÖO, Altunbaşak Ş. Posterior reversible encephalopathy syndrome due to pulse methylprednisolone therapy in a child. Turk J Pediatr 2013; 55: 455-457.

Posterior reversible leukoencephalopathy syndrome (PRES) is a recently described disorder with typical radiological findings of bilateral grey and white matter abnormalities in the posterior regions of the cerebral hemispheres. It has been described in children in association with some medications, renal disease, autoimmune disease, transplantation, and sepsis. In this report, we discuss an eight-year-old boy with PRES during pulse methylprednisolone therapy. In conclusion, PRES is a neurological complication of pulse methylprednisolone therapy, which responds favorably to prompt therapy withdrawal and blood pressure control.

Key words: posterior reversible leukoencephalopathy syndrome, pulse methylprednisolone therapy, children.

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity, comprising symptoms such as headache, altered consciousness, visual disturbances, seizures, and radiological findings of bilateral grey and white matter abnormalities suggestive of edema in the posterior regions of the cerebral hemispheres[1].

The main causes of this condition include hypertensive crisis, renal failure, fluid retention, and some immunosuppressive drugs. However, it has recently been identified in a wide variety of conditions, including posttransplantation stage of liver diseases, hemolytic uremic syndrome, acute intermittent porphyria, malignancies, vasculitis, transfusion, autoimmune conditions, and erythropoietin, oxybutynin or intravenous immunoglobulin (IVIg) treatment[1-4].

In the literature, PRES associated with pulse methylprednisolone therapy has been reported in only one patient[5]. Here, we report an eight-year-old boy with PRES during pulse methylprednisolone therapy.

Case Report

An eight–year-old boy presented with fever and pallor for two days. In his medical history, he had been diagnosed with idiopathic autoimmune hemolytic anemia and followed up for two years. Because of hypersplenism, splenectomy was performed six months ago. His parents were not consanguineous, and there were no family history of diseases.

The physical examination revealed marked pallor, fever, tachycardia, tachypnea, and icterus. There was no lymphadenopathy, edema, rash, petechiae, or bruises. A non-tender soft hepatomegaly with a span of 5 cm below the left costal margin was noted. The neurological examination was normal.

His laboratory evaluation showed hemoglobin of 4.4 g/dl, a total white blood cell (WBC) count of $12.1\times103/mm^3$, and platelet count of $327\times103/mm^3$. Liver function tests showed a total serum bilirubin of 3.2 mg/dl with a direct fraction of 1.1 mg/dl and normal hepatic enzyme levels. Serum electrolytes and renal function tests were normal. Serology for human immunodeficiency virus, syphilis, Epstein-Barr virus, cytomegalovirus, hepatitis A, B, C viruses, and Mycoplasma pneumoniae were negative.

Rheumatoid factors and anti-nuclear antibody were negative.

On the day of admission, the patient was immediately transfused with packed red blood cells and started on prednisolone (2 mg/kg/day) and folic acid. Despite medical treatment, the hemolysis persisted. Plasmapheresis was initiated for a consecutive five days on day[3]. Then, IVIg (1 g/kg/day) was administered for two days on day[8]. Because the hemolysis persisted in spite of all therapy, pulse intravenous methylprednisolone (30 mg/kg/day for 5 days) was initiated on day[11]. On day 4 of the therapy, he suddenly started complaining of headache and confusion, and then developed seizures. These were controlled with intravenous levetiracetam. His blood pressure around that episode was 150/90–160/100 mmHg. His blood pressure was within normal limits on admission and until he was treated with pulse intravenous methylprednisolone. Magnetic resonance imaging (MRI) of the brain was performed, and PRES was diagnosed on the basis of clinical and radiological findings (Fig. 1). Pulse methylprednisolone therapy was stopped, and he was treated for hypertension. Clinical and radiologic findings of PRES resolved following withdrawal of methylprednisolone therapy and blood pressure control (Fig. 2).

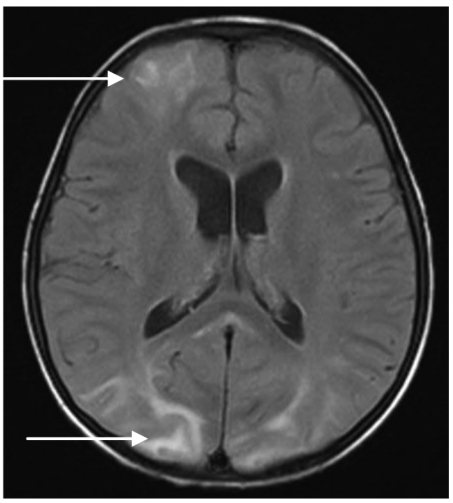

Fig. 1. MRI of cerebral signal intensity involving right frontal and bilateral parieto-occipital regions after pulse methylprednisolone therapy.

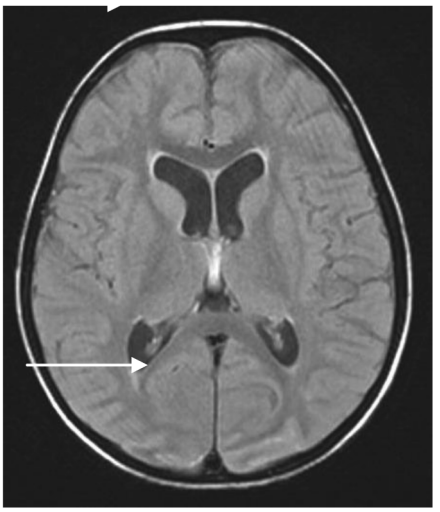

Fig. 2. Two weeks later, the brain MRI showed significantly resolved lesions.

Discussion

Posterior reversible encephalopathy syndrome (PRES) has become increasingly recognized in recent years. It has been associated with a variety of clinical conditions, including severe hypertension, pre-eclampsia or eclampsia, cerebrovascular events, renal disease, sepsis, autoimmune conditions, organ transplantation, and immunosuppressive agents and cytotoxic drugs[2-4].

Corticosteroids are used in the treatment of many different diseases. It is the first-line therapy of autoimmune diseases (such as hemolytic anemia)[6]. The most commonly seen side effects of corticosteroids are high blood glucose levels, fluid retention, hypertension, Cushing's syndrome, truncal weight gain, osteoporosis, glaucoma and cataracts, type II diabetes mellitus, and depression. PRES is a rare and potentially severe adverse event of corticosteroid therapy[5].

In the literature, there is a report of a patient who developed PRES associated with methylprednisolone pulse therapy[5]. In that report, Kumar et al.[5] described a six-year-old patient with juvenile idiopathic arthritis who developed PRES during treatment with pulse methylprednisolone. To our knowledge, our patient was the second patient to develop PRES during pulse methylprednisolone therapy. PRES is characterized by headache, seizures, confusion, and visual disturbance; other focal neurological deficits are uncommon[1]. Kwon et

al.[2] reported 12 patients who presented with seizures (42%), visual disturbances (33%), headache (17%), or altered mental status (8%). Our patient complained of headache, confusion and seizures after the administration of pulse methylprednisolone therapy. The brain MRI revealed increased signal in the bilateral parieto-occipital lobe and left frontal lobe on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences. These findings were considered consistent with PRES, attributable to a manifestation of vasogenic edema. We thus accepted that this may be a complication of pulse methylprednisolone treatment.

The pathophysiology of PRES is complex. Sudden elevations in blood pressure exceed the autoregulatory capacity of the brain vasculature. Focal transudation of fluid and petechial hemorrhages occur due to the breakdown of the blood brain barrier. It is probably a brain-capillary leak syndrome related to hypertension fluid retention and possibly the cytotoxic effects of immunosuppressive agents on the vascular endothelium[3,7].

In our patient, the underlying condition may have been hypertension or treatment with corticosteroid. Arterial hypertension is an observed side effect of corticosteroid treatment. The acute arterial hypertension can be an important provoking factor of PRES, but in addition, other autoimmune diseases-linked factors like cytokines and endotheliopathy may play a role in the pathogenesis of PRES. In his follow-up, we detected hypertension. Hypertension, induced or exacerbated by steroids, is the suspected cause because his blood pressure was previously normal. His blood pressure increased after pulse intravenous methylprednisolone therapy was started.

Treatment of PRES includes better blood pressure control, withdrawal/decreased doses of the offending medications, and seizure management[3,8]. Pulse methylprednisolone treatment was stopped in our patient. Following discontinuation of the infusion and control of the hypertension, his neurological complaints improved in the following days. Brain MRI repeated after 15 days showed significant reversal of the abnormal changes.

In conclusion, PRES is rare complication of different diseases and medications in childhood. We also want to emphasize that PRES can be seen during pulse methylprednisolone therapy. The diagnosis is made by recognition of the clinical syndrome in the appropriate clinical setting. Imaging, especially with MRI, is very helpful to rule out alternative causes and to confirm the diagnosis. A prompt diagnosis and correct treatment are essential to avoid irreversible brain damage.

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