CASE REPORT

Posterior Reversible Encephalopathy Syndrome During Immunosuppressive Therapy in Aplastic Anemia

RAMITHA BHAT[1], MUKESH YADAV[2] AND SUNIL GOMBER[2]

From the [1]Department of Pediatric Oncology, Sri Shankara Cancer Hospital and Research Centre, Bengaluru, and [2]Department of Pediatrics, University College of Medical Sciences and GTB Hospital, Delhi
mukeshyadav32@yahoo.com, ***ORCID iD:*** 0000-0003-2541-6793

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ABSTRACT

An 11-year-old boy with acquired aplastic anemia on immunosuppressive therapy developed hypertensive encephalopathy, which was promptly treated. Neuroimaging was suggestive of Posterior Reversible Encephalopathy Syndrome (PRES). Various clinical conditions and drugs are attributed as causative factors of PRES. Early diagnosis and treatment is necessary to prevent permanent brain injury.

Keywords: Anti-thymocyte globulin, Hypertension, Seizure.

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological entity characterized by headache, confusion, seizures and visual disturbances associated with transient characteristic neuroimaging findings predominantly in the posterior part of the brain.[1] If promptly recognized and treated, the clinical syndrome usually resolves within a week. Delay in the diagnosis and treatment can result in permanent damage to the affected brain tissues.[2] It can occur in many settings, the most common being hypertensive crisis. We report a case of acquired aplastic anemia who developed PRES during immunosuppressive therapy which is an uncommon complication.

CASE DESCRIPTION

An 11-year-old boy with acquired severe aplastic anemia was started on immunosuppressive therapy with oral cyclosporine (8 mg/kg/day), oral prednisolone (2 mg/kg/day) and intravenous anti-thymocyte globulin (ATG) (40 mg/kg/day × four days). On day 4 of immunosuppressive therapy, he developed headache associated with vomiting. Examination revealed heart rate of 72 beats per minute and blood pressure of 150/90 mm Hg (>95th centile) and a positive Macewen's sign. He was started on labetalol infusion and ATG infusion was interrupted. Soon after, he developed generalized tonic clonic seizures for which he was started on intravenous valproate. Non contrast computerized tomography of the brain, performed to exclude any intracranial hemorrhage, was unremarkable. On day 5, there was clinical improvement and his sensorium had normalized and blood pressure had decreased to 124/80 mm Hg. Intravenous valproate was continued while treatment with cyclosporine and prednisolone were stopped. MRI brain showed hyperintensities in bilateral parietal, left posterior temporal, posterior limb of left internal capsule and left occipital subcortical white matter regions suggestive of PRES (**Fig.1**). Anti-hypertensives were continued and there were no further seizures episodes and his blood pressure normalized by day 6. Oral cyclosporine was restarted at a dose of 5 mg/kg/day after 10 days and the patient was discharged on oral antiepileptics and cyclosporine. No recurrence of hypertension was noted after restarting cyclosporine and the child remained trans-fusion free at 6 months of follow up.

DISCUSSION

Posterior reversible encephalopathy syndrome was first reported by Hinchey, *et al.* in 1996.[1] Various underlying conditions like hypertension, immunosuppressive/chemotherapeutic agents, eclampsia, porphyria, renal dysfunc-tion and stem cell transplantation are implicated as the causative risk factors of PRES.[2,3] Administration of ATG has also been reported to cause PRES.[4] Clinically, PRES is characterized by headache, seizures, confusion and visual disturbances.[1] Two theories are considered in the patho-physiology of PRES. The first being a sudden elevation in blood pressure causing vasospasm in cerebral blood vessels. This exceeds the auto-regulatory capacity of the brain vasculature resulting in focal transudation of fluid and petechial hemorrhages occur due to breakdown of the blood-brain

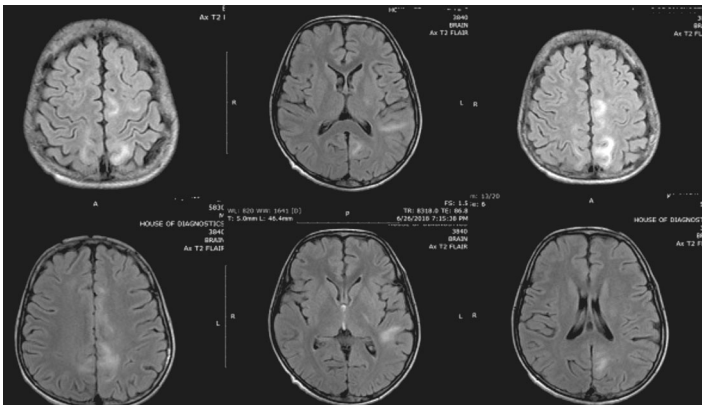

Fig.1 MRI brain showing hyperintensities in bilateral parietal, posterior limb of left internal capsule, left posterior temporal, and left occipital subcortical white matter regions on axial T2 FLAIR images.

barrier.[3] The relatively less sympathetic innervation in the posterior brain explains the preferential involvement of parietooccipital lobes. Children have a narrower range of cerebral autoregulation, hence are more susceptible. The other theory is direct cytotoxicity by antineoplastic and immunosuppressive therapies on cerebral endothelium. This explains the absence of hypertension in PRES which can occur in around 30% cases.[3]

Posterior reversible encephalopathy syndrome is a recently described variant of hypertensive encephalopathy (HE) which typically results in cerebral edema of subcortical white matter of the occipital and parietal lobes. It differs from HE in that it is not always associated with an increase in blood pressure.[5] The diagnosis of PRES is largely dependent on neuroradiological studies and MRI is the preferred modality for investigation.[3] Cerebral edema particularly involving the posterior parietal and occipital lobes seen as increased T2 and FLAIR signals[2] are commonly seen, although anterior hemisphere lesions have also been described.[1] Other areas which may be affected include the brainstem, thalamus, and cerebellum.[3] Treatment should be directed at stopping the precipitating factors whenever possible. Controlling hypertension and seizures and discontinuing or decreasing the dose of an offending immunosuppressive agent should be done immediately as it can progress to cause permanent brain injury.[3] Prompt diagnosis and treatment are the keys to achieving good reversal.[1] Our child improved without neurological sequelae due to early management of hypertension.

The possibility of PRES should be considered in the differential diagnosis of patients developing neurological symptoms, such as seizures, visual abnormalities, and altered mental state. Other conditions presenting with similar symptoms include benign intracranial hypertension, cerebral sinus venous thrombosis, infective meningitis or encephalitis and CNS vasculitis. Although few of these conditions have typical MRI findings, conventional MRI may not easily differentiate PRES from other acute vascular diseases. More specialized sequences may help identify ischemia, subtle hemorrhage, edema, or inflam-mation. Diagnosis requires a careful selection of appropriate imaging techniques. In our case, the child was on concomitant therapy with cyclosporine, prednisolone and ATG, all of which are implicated as causative factors of PRES.[2,3] Even though, the child was being monitored for hypertension, the symptoms developed over a matter of hours and early diagnosis led us to administer early and prompt treatment. PRES is usually reversible, though a mortality rate of 16% is noted.[3] One should keep the possibility of PRES in mind, while treating aplastic anemia with immunosuppressive therapy, as it can progress to cause permanent brain injury.

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