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Case Report

Posterior Reversible Encephalopathy Syndrome in a Child with Acute Lymphoblastic Leukaemia: A Multifactorial Scenario

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Abstract

Posterior reversible encephalopathy syndrome is a clinicoradiologic disorder characterized by seizures, altered mental status, headaches and visual disturbance that is associated with white matter vasogenic edema predominantly affecting the occipital and parietal lobes of the brain. The most common neuroimaging presentation of PRES is the parieto-occipital subcortical T2 hyperintensity without enhancement. We report a case of seven years old boy that developed PRES during a clinical scenario with many possible triggers.

Keywords: Posterior Reversible Encephalopathy Syndrome, PRES, Chemotherapy, Acute Lymphoblastic Leukaemia, Tumour Lysis Syndrome, Blood Brain Barrier.

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiologic entity characterized by headaches, seizures, altered mental status, and visual disturbance that is associated with white matter vasogenic edema predominantly affecting the occipital and parietal lobes of the brain. This edema is potentially reversible in totality, but in some cases it can persist without recovery [1,2].

During the last years this syndrome was also called by reversible occipitoparietal encephalopathy, hyperperfusion encephalopathy, hypertensive encephalopathy, posterior leukoencephalopathy, reversible posterior cerebral oedema syndrome and potentially reversible encephalopathy. PRES has gained substantial recognition since its initial description by Hinchey et al in 1996 [1]. In 2000, Casey proposes the term Posterior Reversible Encephalopathy Syndrome (PRES) [3].

The most common neuroimaging presentation of PRES is the parieto-occipital subcortical T2 hyperintensity without enhancement; however, other structures (such as the brain stem, cerebellum, and frontal and temporal lobes) may also be involved, and although the abnormality primarily affects the subcortical white matter, the cortex and the basal ganglia may also be involved. In children, frontal lesions are reported to occur as frequently as parietal lesions [1,4-5].

Despite PRES has been widely studied in adults, clinical spectrum in the pediatric population are limited, mainly because it's heterogeneous presentation. Few data are available in literature about incidence or prevalence of PRES in children. Case series suggest that PRES is more common in women, even when pregnant patients are excluded; and this syndrome can occur in patients of all age [6].

Case Report

A 7 year old patient with the diagnosis of acute lymphoblastic leukaemia (ALL) was admitted to the hospital for persistent

pancytopenia and fever, following chemotherapy. Treatment with intravenous fluids along with cefepime for febrile neutropenia was begun. Also, innumerous accounts of plaquets transfusions were made. On 30th day of admission, oliguria developed, with a creatinine level rising to 1.46 (Normal Range: 0.70-1.20), an ionic calcium of 11 (NR: 4.4-5.1), phosphorus of 5.6 (NR: 2.5-4.5) and a uric acid level of 10.3 (NR: 3.5-8.5), receiving a diagnosis of tumour lysis syndrome.

He was admitted to ICU and started on pamidronate, hyperhydration, bicarbonate and pulsoterapy with metilprenidsolone (10mg/kg). On the third day of pulsotherapy, his creatinine raised to 1.86 and his blood pressure reached 163/109 mmHg (range systolic blood pressure – 163-126 and diastolic 112-74). He started to complain of increased difficult seeing and developed full cortical blindness in a matter of hours. Also, a partial seizure was noted in his left side, along with increasing mental confusion. A brain CT scan was ordered and showed low-densities predominating in the occipital areas. Brain MRI demonstrated hyper-intensities in the frontal, parietal and predominantly occipital areas, with increased signal on fluid attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) and decreased perfusion on apparent diffusion coefficient (ADC) in the occipital areas. (Figure-1 and Figure-2) A diagnosis of PRES was made and immediate discontinuation of pulsotherapy and establishment of blood pressure control were obtained.

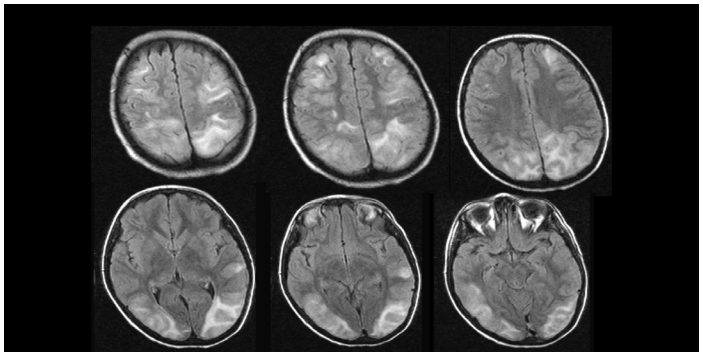

Figure 1: Brain MRI (FLAIR) showing an increase of signal in both hemispheres, predominantly in posterior zones.

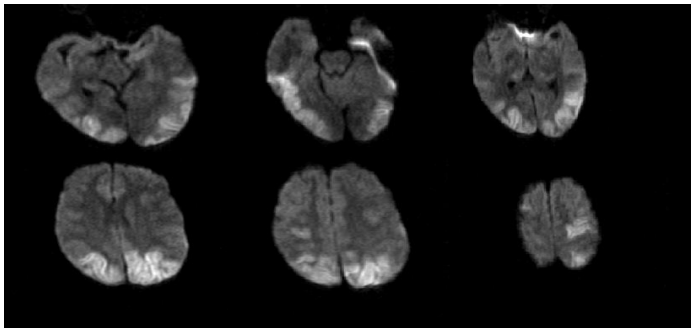

Figure 2: Brain MRI (DWI) showing an increase of signal in both hemispheres, predominantly in posterior zones.

Continuous focal seizures on his left face and arm began, which were controlled with diazepam. In the following days, his mental status, seizures and hemiparesis improved, but he remained with visual deficits. Nowadays, the patient persists with visual changes and follows in medical monitoring.

Discussion

The cause of PRES is unclear. Autoregulatory failure with resultant vasodilatation, as seen in hypertensive encephalopathy, is often cited as the underlying mechanism [1,7-8].

PRES is commonly seen in the setting of hypertension; probably due to a breakdown of autoregulation. PRES usually presents in the set of sudden or severe hypertension. Acute elevations on blood pressure interfere with brain vessels autoregulatory capacity, resulting in vasodilatation and hyperperfusion, along with capillary leakage and edematisation, a striking resemblance to hypertensive encephalopathy. However, PRES can occur without hypertension, suggesting endothelial dysfunction (such as caused by cytotoxic drugs) play an essential role in disrupting blood brain barrier [9].

Numerous factors can trigger the syndrome, most commonly: acute elevation of blood pressure, abnormal renal function and immunosuppressive therapy [1]. Other possible etiologies are eclampsia [10-12], transplantation [13], neoplasia and chemotherapy treatment [4,14,15] and renal disease acute or chronic [16].

Siebert and colleagues studied 18 patients younger than 18 years old with PRES. Acute kidney dysfunction, haematologic malignancies and immunossupression were the most common precipitant factors. In this serie, mean blood pressure was 140/73 mmHg, and for children this is quite elevated, since they are prone to develop failure of brain vessels autoregulation at a lower blood pressure threshold than adults. One interesting fact in this study is that frontal and parietal edema was more frequent than occipital location, which gives name to the syndrome [6].

Our patient had several reasons to develop PRES. First, acute kidney dysfunction due to tumour lysis syndrome (TLS) and hypercalcemia led to an important raise in blood pressure. Second, chemotherapy is known to be a cause of PRES [4,14]. Third, high dose corticosteroid therapy might also be implicated in the fisiopathogenia. By last, infection along with neutropenia certainly contributed to an increased inflammatory state. are known to damage endothelial cells, precipitating vasodilatation and disruption of blood brain barrier. Also, to our knowledge, only 3 cases of TLS [17-19] in association to PRES had been published, one of which in a 63 year old man with LLA who died during the course of PRES [17].

The treatment of PRES is not clear; however we think that the use of antihypertensive therapy like in hypertensive emergency cases and eliminate the possible cause/triggers (like drugs, immunosuppressive agents) could be the key of an adequate treatment and for a good outcome. Treatment of hypertension and seizures, and withdrawal of causative agents are the mainstays of therapy in PRES.

Although PRES is reversible in most patients, it is not uncommon to see residual lesions on follow-up imaging and persistent symptoms. In a serie of 53 patients with PRES, the complete resolution of radiological lesion occurred in 58% of the cases [20]. Our patient remained with visual deficits despite adequate therapy. Another point to be considered is that PRES, a usually benign pathology, is seen in complex and eventually life-threatening situations [1,20-22], requiring immediate suspicion along with control of precipitating factors. Rather than relief, the diagnosis of PRES must be seen as a marker of potentially serious illness. PRES remains an enigmatic syndrome.

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