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Case Report

Status Epilepticus and Reversible Hemiplegia During Induction Chemotherapy in Acute Lymphoblastic Leukemia

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Abstract: Posterior reversible encephalopathy syndrome (PRES) is one of the major causes of neurologic impairment commonly presenting with seizures or headaches, mental alterations or visual disturbances usually associated with hypertension in those children. It is known to be a potentially reversible entity with typical neurologic findings corresponding MRI abnormalities including hyperintense lesions within occipital-parietal subcortical or deep white matter regions bilaterally. In here, we share significant clinical and MRI findings of PRES, which emerged in a 10 year-old girl, recently received chemotherapy protocol for acute lymphoblastic leukemia (ALL). We aimed to increase familiarity of clinicians to PRES especially during treatment of leukemia which can be confused with some other severe neurologic complications including stroke or hemorrhage for early and appropriate management in order to avoid neurological sequel.
Keywords: Status epilepticus, Acute lymphoblastic leukemia, Posterior reversible encephalopathy syndrome, Magnetic resonance imaging, Diffusion weighted imaging.

INTRODUCTION

PRES is a reversible entity has been more commonly described in adults, especially with hypertensive encephalopathy, eclampsia and renal failure or transplantation [1-4]. Other etiologic factors associated with PRES reported in literature cover a wide spectrum of conditions including immunosuppressive or cytotoxic drugs, analgesics, sepsis, connective tissue diseases, and hemolytic uremic syndrome [4-9]. MRI is essential diagnostic method for the PRES, demonstrates vasogenic edema as increased signal intensity in parietal-occipital regions, visible on T2 weighted and FLAIR (fluid attenuated inversion recovery)sequences in combination with diffusion weighted imaging [10].

In here, we share significant clinical and MRI findings of PRES, which emerged in a 10 year-old girl, recently received chemotherapy protocol for acute lymphoblastic leukemia (ALL). We aimed to increase familiarity of clinicians to PRES especially during treatment of leukemia which can be confused with some severe other neurologic complications including stroke or hemorrhage for early and appropriate management in order to avoid neurological sequel.

CASE REPORT

A 10 year- old girl with diagnosis of ALL was admitted to hospital with status epilepticus on the 25th day after completion of chemotherapy treatment consisting Dexamethasone, Vincristine, Methotrexate, Cyclosporine and L-asparaginase. Her blood pressure waselevated (130/95 mmHg). Thereafter, she was in a confusionalstate, had developed aphasia and right-sided hemiplegia with eyes deviation to the right side. Elevation of blood WBC (25040x10^9/L), liver enzymes (aspartate aminotransferase/alanine aminotransferase 131/233 IU, lactate dehydrogenase 773 IU), and D-Dimer (2.4 mg/dL) levels were determined. A non-enhanced cranial CT scan was within normal limits excluding intracranial hemorrhage or acute dural sinus thrombosis. Also contrast-enhanced cranial MR, diffusion MR and time of flight MR angiography (TOF) were achieved. T2 and FLAIR sequences revealed areas of patchy high signal intensity in subcortical white matter and gray matter along with sulcus with bilateral asymmetrical distribution in left temporal and bilateral parietal-occipital regions. Enlargement of affected gyrus and neighboring sulcus effacement was also noted due to edema (Fig. 1). Any hemorrhage or contrast enhancement or dural sinus filling defect was not noted.

A history of cytotoxic medication in an ALL patient, with the presentation of seizure and paraplegia with vasogenic edema in parietal-occipital regions on MRI, prompted the diagnosis of PRES. ACE inhibitorand valproicacid were used for treatment. Her confusion state and hemiplegia resolved within 2 days. Control MRI was achieved 19 days after the initiation of PRES, which showed no signal of abnormality within brain parenchyma (Fig. 2).After this, despite having subsequent high risk chemotherapy blocks, any neurologic problem was noted again.

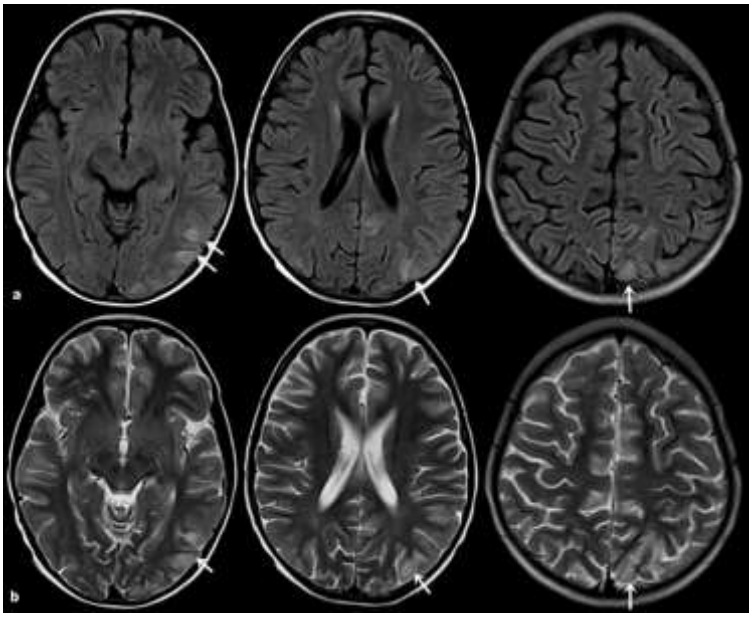

Fig. 1: MRI achieved 4 hours after beginning of symptomis revealing areas of patchy high signal intensity lesions on FLAIR (a) and T2 weighted (b)axial slices, involving subcortical white matter and gray matter along with sulcus in left parietal-occipital regions (arrows). Enlargement of affected gyrus and neighboring sulcus effacement is also seen due to edema

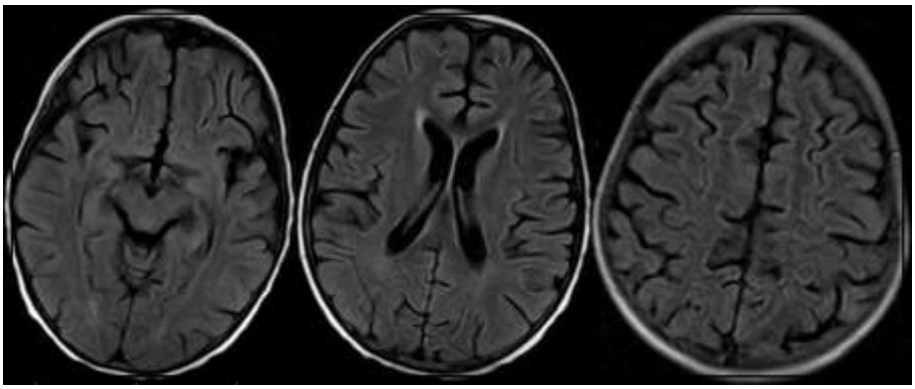

Fig. 2: Control MRI achieved after 19 days from the event, FLAIR slices are showing normal findings on which vasogeniced emasites have all dissappeared

DISCUSSION

Pathogenesis of PRES has been suggested to be failure of cerebral auto-regulation either due to hyper-perfusion, induced by accelerated hypertension or endothelial damage by some toxic effects currently. Another theory claims development of hypo-perfusion triggering hypoxia and consequently vasogenic edema[11].Capillary leak occurs firstly and basically through white matter having looser junctions inside so this is why white matter is the primer site for vasogenic edema. Reversibility of brain lesion is all explained by vasogenic edema. Nevertheless, it was also declared that cytotoxic edema should develop in untreated patients which is explained by excessive vasogenic edema causing ischemic changes within neurons [11].

Common and typical neurologic manifestations of PRES in children include seizures, mental alterations, suddenly onset headache and visual disturbances [12]. Although motor deficit such as hemiparesis or quadriparesis was stated as clinical manifestation, hemiplegia was not declared before. The time of PRES emerging during childhood leukemia treatment was reported to be within different times in the literature ranging from 21 to 27 days [13].

Hypertension is commonly (86%) declared to be associated with PRES as a contributor factor [12]. Most of PRES patients with leukemia in literature had high BP values usually promoted by corticosteroid therapy or renal dysfunction [13, 14]. It still remains unclear whether hypertension is a result of PRES causing cerebral edema or not.

There were PRES cases reported in the literature attributed to neurotoxicity of intratechal methotrexate, cyclosporin, L-asparaginase, vincristineto the vascular endothelium as well as hypertensive effect of steroids individually or combination of these[13, 15-17]. Vincristine is known to have a side effect on autonomic system which may also interferes cerebral auto-regulation mechanisms of posterior circulation causing PRES[13]. Thus PRES in leukemia is suggested to have multifactorial mechanisms overlapping during induction treatment of ALL.

Neuroradiological findings in PRES can demonstrate patchy as well as linear or confluent pattern [18]. They are clearly visible on both T2 weighted and especially FLAIR sequences. FLAIR is most sensitive sequence indicating cerebral edema[19]. These lesions in current patient were hypo to isointense on DWI and hyper intense on ADC as characteristic of vasogenic edema. No contrast enhancement was noted in places of involvement. In areas of cytotoxic edema, restricted diffusion is displayed as high signal on DWI and low signal on ADC. Lesions of vasogenic edema are reversible besides this hemorrhage or restricted diffusion sites will develop encephalomalasia [20].

Neuroimaging plays a key role in diagnosing PRES. Clinical signs of PRES mimic ischemic or hemorrhagic stroke, encephalitis or dural sinus thrombosis or initially. Radiologists should also be aware of typical and atypical findings of PRES particularly on MR and DWI. They should also help clinicians for excluding the differential diagnosis list of PRES including stroke, venous thrombosis, hemorrhage, and encephalitis or leptomeningeal infiltration of primary disease.

Management of PRES warrants antihypertensive and anti-epileptic treatment as well as withdrawal of the possible responsible agent following prompt diagnosis. PRES in leukemia usually cause a delay in treatment. It is favored to restart the therapy as soon as possible.

PRES has almost good prognosis overall ALL patients in literature (86%). Recovery after PRES varies within 1 to 5 months [12, 14]. Neurologic findings are almost reversible except in 12% of cases those represent epilepsy as a neurological sequel. Death is also reported due to seizures, primary disease, septic shock or coma [12].

In conclusion, acute onset of status epilepticus and hemiplegia in a child with ALL, within weeks after chemotherapy is an unpredictable and scary problem which should be solved immediately. PRES should be kept in mind, presenting neurologic symptoms in leukemic patients commonly after induction therapy. Prompt diagnosis and management will provide recovery of patient without sequel since manner of the disease is expected to be reversible in most of cases. Although neurological symptoms including hemiplegia seem to be devastating, they resolve within the first days in the great majority of the patients after controlling the blood pressure and eliminating the etiologic factor. The essential diagnosis in PRES with the suspicion is the neuroimaging with FLAIR-MRI. The clinicians should keep in mind this under diagnosed entity to avoid persistent deficits.

Abbreviations: PRES: Posterior reversible encephalopathy syndrome; ALL: Acute lymphoblastic leukemia; MRI: Magnetic resonance imaging; DWI: Diffusion weighted imaging; ADC: Apparent diffusion coefficient; FLAIR: Fluid attenuation inversion recovery; WBC: White blood cell count; TOF: Time of flight angiography; BP: Blood pressure

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