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CASE REPORT

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Posterior reversible encephalopathy syndrome in a known case of beta-thalassemia major after blood transfusion: a case presentation

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Abstract

Background Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic condition associated with a distinctive brain imaging pattern which typically occur in some complex clinical conditions. However, the leading offender to this condition remains not clear.

Case presentation We report a 6-year-old female with *β*-thalassemia major presenting with generalized tonic–clonic convulsions, repeated attacks of projectile vomiting, blurred vision, and altered conscious level after blood transfusion. The brain magnetic resonance imaging (MRI) FLAIR sequence revealed bilateral and symmetrical subcortical edema displaying high signal intensity. Follow-up MRI 1 month later showed complete resolution of the previously identified findings. The clinical presentation along with neuroimaging pattern as well as the reversible course indicated PRES as the most suitable diagnosis. Although PRES has been previously described in different clinical settings, this is a rare case of PRES recognized after blood transfusion in a child with *β*-thalassemia major.

Conclusion Acute neurological symptoms in children with thalassemia should raise high suspicion for PRES, especially after blood transfusion.

Keywords *β*-thalassemia, Posterior reversible encephalopathy syndrome (PRES), Blood transfusion, Case report

Background

Posterior reversible encephalopathy syndrome (PRES) remains a challenging clinical disorder due to continually changing knowledge regarding the terminology, pathogenesis, and clinico-radiologic characteristics of the disease [1]. PRES is defined as "a reversible hypertensive syndrome of headache, altered conscious level, seizures, and visual impairment along with extensive bilateral white matter changes suggestive of edema in the posterior areas of the cerebral hemispheres." However, this conception may be misleading, as other cerebral regions may be involved and the condition is not always connected to hypertension [1–3]. Hinchey et al. [2] first described PRES in 1996 after an observational study on 15 patients. Since then, few case series and case reports have been published [4–7]. The clinical picture of PRES might occur due to sudden disturbance of the autoregulatory mechanisms of the central nervous system (CNS) vasculature, causing endothelial dysfunction and breakdown of the blood–brain barrier (BBB). Sudden elevation of blood pressure could be a contributing factor to this disruption. Direct cytotoxic effect on the cerebrovasular endothelium is another reported cause for PRES [8]. There are a few case series and some case reports of PRES that occurred after

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blood transfusion [5, 9, 10]; nevertheless, none associated with β-thalassemia major. We present a case of PRES in a 6 years' age female with β-thalassemia major after blood transfusion.

Case presentation

A 6-year-old female child, known case of β-thalassemia major, diagnosed at age of 1 year, presented to the emergency department with sudden attack of generalized tonic–clonic convulsions, a total of four episodes in 3 h. In addition, repeated attacks of projectile vomiting, blurred vision, and altered conscious level (ACL) were experienced by the patient in association with the convulsions. There was no history of fever, head trauma, weakness, or facial asymmetry. Her vital signs at presentation were stable with blood pressure of 90/60 mmHg, pulse of 95 beat/minute, and respiratory rate of 27/min. Glasgow Coma Scale (GCS) score was 12/15 (E3V4M5); cranial nerves examination and superficial and deep tendon reflexes were normal, and no signs of meningeal irritation or abnormal movements were observed. Abdominal examination revealed hepatosplenomegaly (liver span 10.5 cm, spleen 5 cm below the costal margin). Systolic murmur was heard on auscultation of the heart with maximum intensity on the apex. Other systems examination revealed no abnormalities. Patient was admitted in pediatric intensive care unit (PICU) for seizures and ACL. On laboratory investigations, her complete blood count (CBC) revealed hemoglobin (Hb) 9.6 g/dL, total leucocytes count (TLC) 8.96×10^3/µL, and platelet count 179×10^3/µL. Renal function tests, serum electrolytes, and blood glucose level were all within normal range. Serum ferritin was 380 ng/ml. Laboratory tests to exclude autoimmune disorders (antinuclear antibody, anti-double-stranded DNA, C3, and C4) were within normal range. Cerebrospinal fluid (CSF) examination revealed normal results. Echocardiography was suggestive of mitral valve prolapse and mild mitral regurge, normal cardiac chambers diameter, and systolic function with impaired diastolic function (E/A ratio 0.75). Magnetic resonance imaging (MRI) of the brain during the acute stage was performed urgently at presentation with the first attack of convulsion, revealing bilateral nearly symmetrical posterior, mainly parietal and occipital and cortical and subcortical patchy areas of signal changes (low T1, high T2, and flair signals), denoting cerebral edema supporting the diagnosis of PRES (Fig. 1). Magnetic resonance arteriogram (MRA) showed preserved both internal carotid, vertebral and basilar flow-related enhancement, patent circle of Willis, and cerebral arteries with no evidence of occlusion, stenosis or aneurysmal dilatation. Magnetic resonance venogram (MRV) revealed normal flow-related enhancement of dural venous sinuses and superficial and deep cortical veins (Fig. 2). No radiological evidence of changes suggests angiopathy of autoimmune disorders.

The child received one unit of packed red blood cell (PRBC) transfusion 6 h prior to this event. She was on deferasirox film-coated tablets (20 mg/kg/day) as iron chelator and supportive therapy in form of L-carnitine, folic acid, and vitamin D. On admission, she received levetiracetam for seizure control, IV fluids, and mannitol. Patient showed complete recovery with no fever (gradually improved until complete resolution in the fifth day of admission) or convulsions (last episode was reported on the second day of admission), and the patient was discharged after 1 week. The levetiracetam was stopped

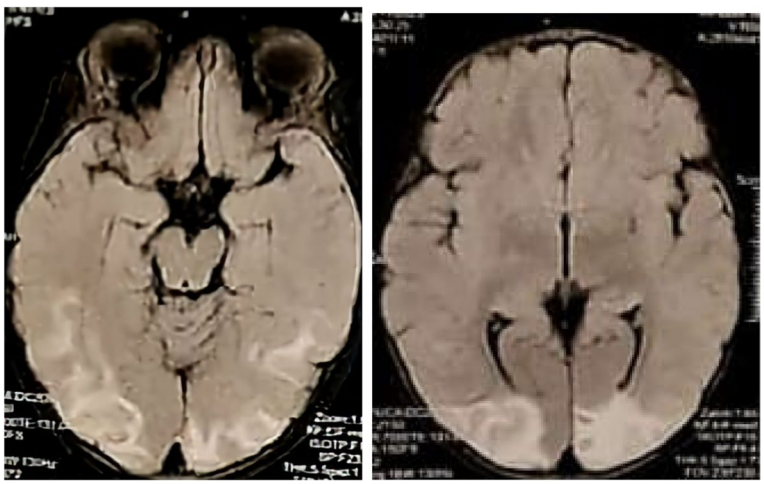

Fig. 1 MRI FLAIR sequence shows bilateral and symmetrical subcortical edema displaying high signal intensity

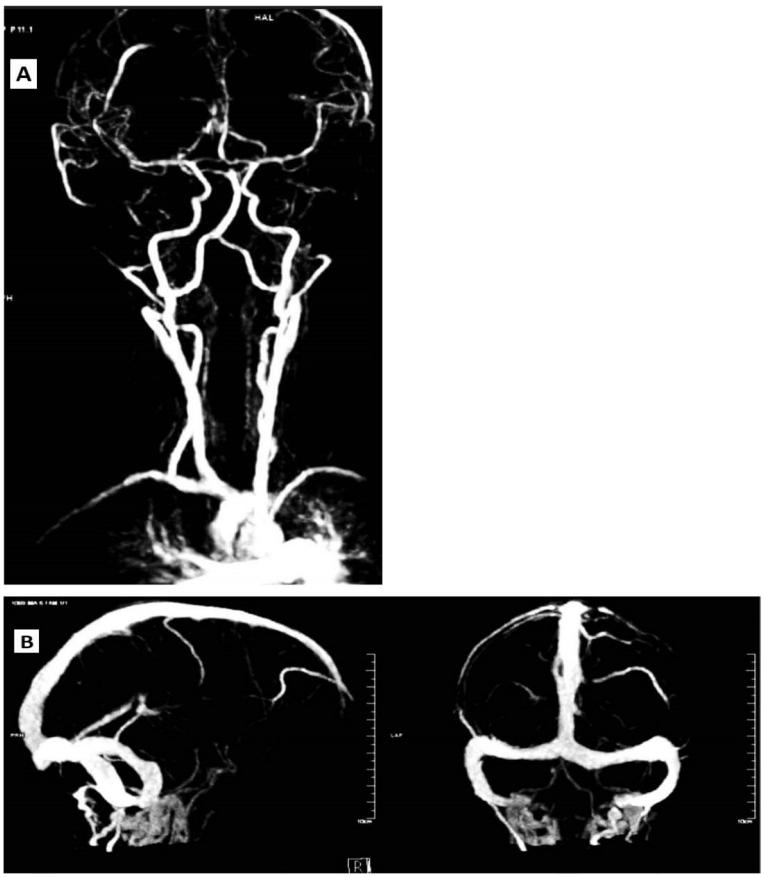

Fig. 2 **A** MRA reveals preserved both internal carotid and vertebral and basilar flow-related enhancement. Patent circle of Willis and cerebral arteries. No evidence of occlusion, stenosis, or aneurysmal dilatation. **B** MRV reveals normal flow-related enhancement of dural venous sinuses and superficial and deep cortical veins

gradually throughout the duration of 1 month after the MRI brain was repeated, and it was normal.

Conclusion

RPES has been identified in a wide range of hematologic conditions in adults and children, such as thrombotic thrombocytopenic purpura, hemolytic uremic syndrome (HUS), and also in acute or chronic renal failure, autoimmune diseases, and vasculitis [11]. Early clinical suspicion of RPES is crucial for early diagnosis, effective treatment, and good prognosis [12, 13].

The exact pathophysiology of PRES has yet to be clarified. About 70–80% are known to develop secondary to uncontrolled hypertension. Severe hypertension results in impaired cerebrovascular autoregulation, vasodilatation, and vasogenic edema. Literature reviews on hypertension and PRES widely discuss the "endothelial hypothesis" as the pathophysiological cause for a patient's hypertension [14].

Notably, our patient was normotensive at presentation and on repeated blood pressure measurements throughout the duration of admission. The patient did not have any evident cerebral anoxia but had received PRBCs transfusion preceding this event.

Although the exact mechanism of PRES after blood transfusion is not clear, in chronic anemic conditions, rapid transfusion of large blood volumes is thought to induce PRES due to vascular autoregulation disruption, hyper-perfusion, and hyper-oxygenation, leading to cerebral harm [15]. In addition, high blood viscosity as well as long-standing hypoxia-induced vasodilatation results in an increase in the vascular resistance and may evoke an acute vascular endothelium dysfunction [15]. Nandi et al. [8] reported PRES after blood transfusion in 5-year-old child with hemoglobin E (HbE) β-thalassemia. Similar cases of PRES after blood transfusion were reported [5, 9, 10, 12, 16], and a case series in Japan [17], but none associated with β-thalassemia major.

MRI of our patient showed T2-FLAIR hyper-intensities typically symmetrical and bilateral involving parieto-occipital regions. However, involvement of the anterior brain, brainstem, basal ganglia, thalamus, and cerebellum has been previously reported (atypical MRI findings) [1–3].

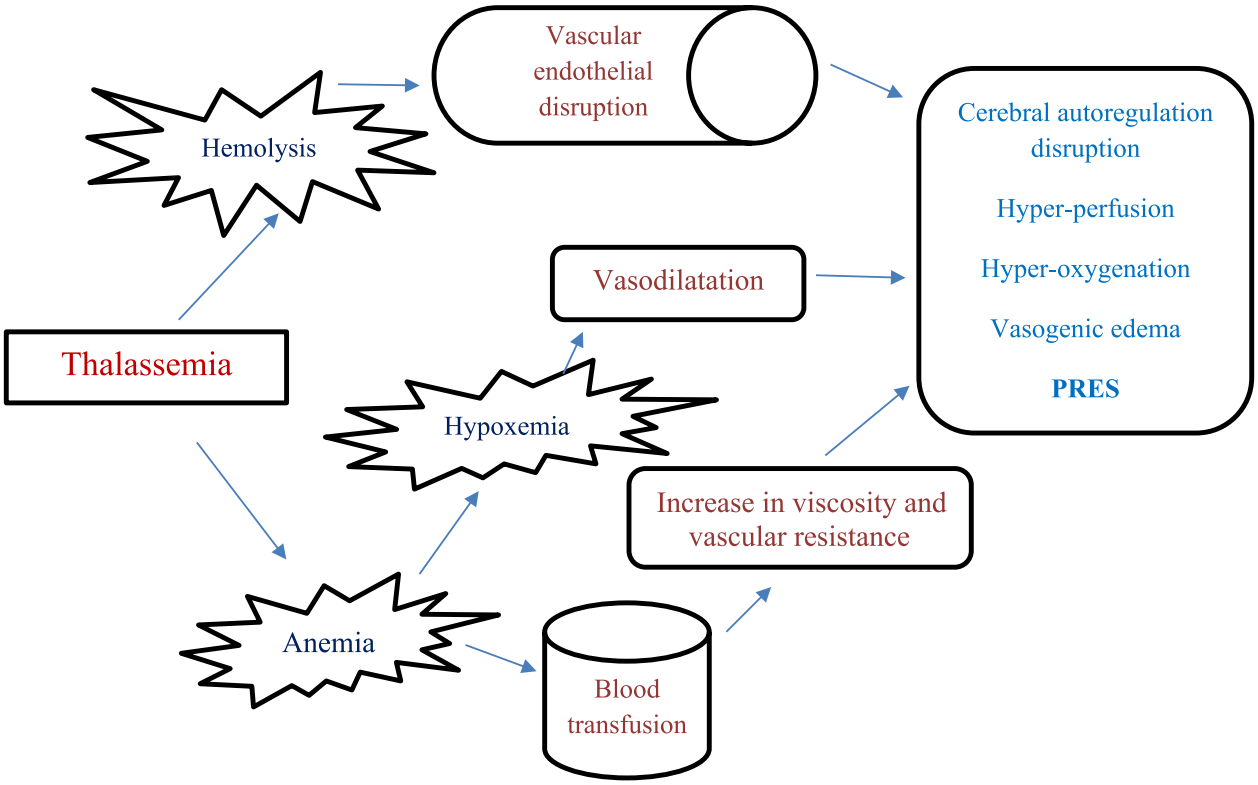

Fig. 3 Postulated pathophysiology of PRES in thalassemia

The development of RPES in thalassemia might be multifactorial, and it is difficult to determine the role of each factor in precipitating its development and challenging to identify the exact underlying pathophysiology. In our patient, in the absence of hypertension, we speculate that blood transfusion was the underlying culprit of RPES (Fig. 3).

The acute presentation and the complete recovery of our patient are noteworthy.

This highlight the fact that although PRES is considered a serious life-threatening disorder, it has an excellent prognosis with complete resolution if appropriate management is provided in the acute stage. More vigilance is crucial to early identify similar cases in practice. Further studies are still needed to investigate the exact pathogenesis and non-hypertensive mechanisms involved in this PRES, focusing on high-risk children with thalassemia.

Abbreviations

GCS	Glasgow Coma Scale
MRI	Magnetic resonance imaging
MRA	Magnetic resonance angiogram
MRV	Magnetic resonance venogram
PRES	Posterior reversible encephalopathy syndrome
PRBC	Packed red blood cell

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NA

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DH, MGN, and MMG, data collection and compiling; DH, writing of manuscript; and DH, MGN, and MMG, revising the manuscript and final approval. The manuscript has been read and approved by all the authors

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The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
NA

Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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