Case Report

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Blood-transfusion-related posterior reversible encephalopathy syndrome - A description of a new case and review of the literature

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Abstract:

Posterior reversible encephalopathy syndrome (PRES) is a neurological syndrome associated with headache, altered mental status, seizures, and visual disturbances and characterized by white matter vasogenic edema affecting predominantly the posterior occipital and parietal lobes of the brain. Neurological complications of blood transfusion are uncommon, and blood-transfusion-related PRES is seldom reported. We report here one such case of PRES. A 61-year-old Asian woman with chronic anemia presented with a history of fall, causing fracture of the left femur neck. As her hemoglobin was 5 g per deciliter, she was transfused with four units of packed cells in three consecutive days. At the time of admission, she was alert, normotensive, and afebrile. Later, she developed mild headache and had a generalized tonic-clonic seizure. Her brain magnetic resonance (MR) imaging showed edema in bilateral frontal lobes and parieto-occipital lobes with normal MR venogram, consistent with PRES. We described her disorder as blood-transfusion-related PRES. Immunologic, as well as non-immunologic complications of blood transfusion, are known but, PRES is rare. Cumulative effects of blood transfusion on blood flow, blood viscosity, endothelial dysfunction leads to blood-brain barrier dysfunction, which culminates into vasogenic edema and vasoconstriction despite normal systemic blood pressure, leading to blood-transfusion-related PRES.

Keywords:

Blood-transfusion-related posterior reversible encephalopathy syndrome, posterior reversible encephalopathy syndrome

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome first described by Hinchey *et al*.,[1] characterized by headache, altered mental status, seizures, and visual disturbances and characterized by white matter vasogenic edema affecting the posterior occipital and parietal lobes of the brain predominantly.[2] PRES was previously called as (reversible posterior leukoencephalopathy syndrome, reversible occipital, parietal encephalopathy, and reversible posterior cerebral edema syndrome. The clinical symptoms are myriad, the visual disturbance can vary from blurred vision, homonymous hemianopsia to cortical blindness. Altered consciousness varies from mild confusion, agitation to coma. Seizures, status epilepticus, and non-convulsive status epilepticus are common presentations. Other symptoms include nausea, vomiting, and brainstem deficits.[2-4]

The conditions associated with acute hypertension may predispose to developing PRES. Peak systolic blood pressure (BP) ranging from 170 to 190 mmHg is common, but 10%–30% of patients have normal or

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only mildly elevated BP. Acute hypertension is caused secondary to acute kidney injury, eclampsia, autonomic disturbance, for example, Guillain-Barré syndrome, and after illicit drug use. Autoimmune diseases – including thrombotic thrombocytopenic purpura and systemic lupus erythematosus, exposure to immunosuppressive drugs such as cyclosporine, tacrolimus, or chemotherapy agents, transplantation including bone marrow or stem cell transplantation, chronic kidney disease, chronic hypertension also cause PRES. Rare causes include blood transfusion, peritoneal, and hemodialysis.[2,4-6] The underlying mechanisms common to all the triggering events are the breakdown of the blood-brain barrier and endothelial dysfunction. The exact pathogenesis is still debatable.

Case Report

A 61-year-old female was referred to us with a history of fall at home, the consequence of which she had difficulty in weight-bearing from the left lower limb. Her evaluation with an X-ray of the left femur showed fracture of the left femur neck. She was found to be anemic with Hb 5 g per deciliter. In view of her anemia she was transfused with 4 units of packed cells in three consecutive days. She was then referred to our orthopedics department for surgical management. At the time of admission in our hospital, she was alert, normotensive (BP 120/70 mm of Hg, and afebrile. She complained of mild headache. Later, in the ward, she had a generalized tonic-clonic seizure. After recovery, she developed a confusional state and complained of parieto-occipital distribution headache. Her brain magnetic resonance imaging (MRI) showed edema in bilateral frontal lobes and parieto-occipital lobes with normal magnetic resonance venogram, consistent with PRES [Figure 1]. Her repeat laboratory investigations showed Hb 15.1 g per deciliter, PCV 48.2%, RBC count 5.17 mill/mm^3 with normal blood biochemistry. Lumbar puncture was performed, which showed an opening pressure of 13 cms H_2O, colorless, Proteins 51.7 mg/dl (Normal 15–45 mg/dl), Glucose 76 mg/dl (Normal 50–80 mg/dl), Total cells 3/mm^3 (Normal 0–5/mm^3) with 100% lymphocytes. BP was normal throughout the hospital course. Her old records showed her Hb 8.8 g per deciliter. Her confusional state as well as headache gradually improved, and follow-up Brain MRI showed the disappearance of brain lesions [Figure 2]. There was no other episode of seizure.

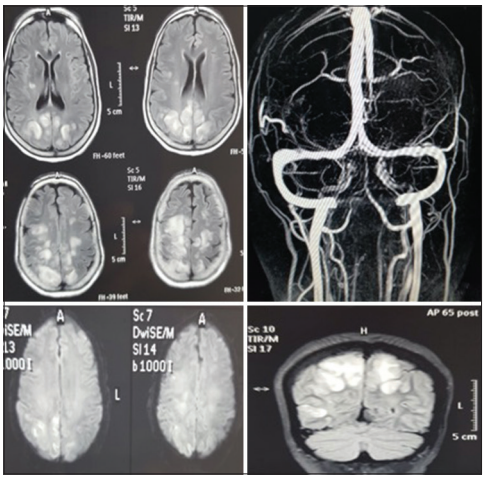

Figure 1: Vasogenic oedema involving parieto occipital lobes with normal magnetic resonance venogram

Discussion

Our patient had hallmarks of PRES by having typical clinical features, including seizures, benign clinical course, and rapidly changing MRI features of vasogenic edema.

Our patient was a middle-aged Asian female with chronic anemia with superadded acute insult. She was normotensive throughout her hospital course, and blood transfusion was the inciting cause after an extensive search for other causes. Previous reports on transfusion-related PRES show similar patient profiles who received blood transfusions and their hemoglobin level increased by at least 5 g per deciliter.[5,6]

There are few reports in the literature about blood transfusion-related PRES which have been tabulated [Table 1].

Immunologic as well as non-immunologic complications of blood transfusion are known, but PRES is rare.[3]

The etiopathogenesis leading to transfusion-related PRES in chronically anemic patients is that chronic anemia may result in compensatory cerebral vasodilatation. The blood transfusion leads to increased blood flow as well as blood viscosity, which results in impaired hypoxic vasodilation, thus an increase in vascular resistance, and ultimately, generalized cerebral vessel constriction.[5,17] Rapid increase in hematocrit levels with increased blood viscosity and release of prostaglandins, calcium, serotonin, nitric oxide,

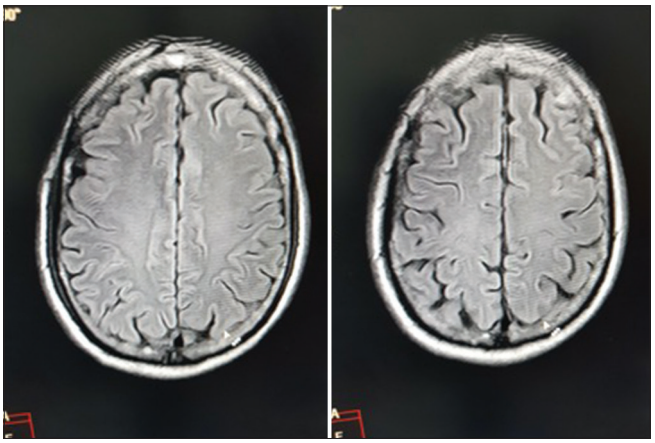

Figure 2: Complete resolution of oedema parieto occipital lobes

Table 1: Blood-transfusion- related PRES previous case reports including our case

Article	Anemia cause	Anemia course	Ictus symptom after blood transfusion (days)	Clinical findings	Brain MRI distribution of lesions	Sequelae	Reference
Ito *et al*. Post-transfusion reversible posterior leukoencephalopathy syndrome with cerebral vasoconstriction. Neurology 1997	Uterine myoma	Chronic	2	S, H	AC, PC	None	[3]
Boughammoura *et al*. Reversible angiopathy and encephalopathy after blood transfusion. J Neurol 2003	Uterine myoma	Chronic	6	E, S, F	AC, DS	None	[7]
Heo *et al*. Post-transfusion posterior leukoencephalopathy with cytotoxic and vasogenic edema precipitated by vasospasm. Cerebrovasc Dis 2003	Aplastic anemia	Chronic	7	E, S, H, V	PC	None	[8]
Kawano *et al*. Posterior encephalopathy syndrome in two patients after cancer surgery with transfusion. Rinsho Shinkeigaku 2004	Cancer surgery	NR, acute	9, 18	E, S	PC	E, None	[9]
Huang *et al*. Reversible posterior leukoencephalopathy syndrome caused by blood transfusion: A case report. Acta Neurol Taiwan 2008	Uterine myoma	Chronic	5	H	PC	None	[10]
Gümüş *et al*. Reversible posterior leukoencephalopathy syndrome in childhood: report of nine cases and review of the literature. Neurol Sci 2010	Iron deficiency anemia	NR	NR	S, V	AC, PC	None	[11]
Sato *et al*. Reversible posterior leukoencephalopathy syndrome after blood transfusion in a patient with endstage renal disease. Clin Exp Nephrol 2011	Renal failure	Chronic	6	S, H, V	PC	None	[12]
Wada *et al*. Posterior reversible encephalopathy syndrome induced after blood transfusion for severe anemia. Case Rep Clin Med 2013	Corpus uteri cancer	Chronic	6	E, S, V	PC	None	[13]
Dou *et al*. Reversible cerebral vasoconstriction syndrome after blood transfusion. Headache: The Journal of Head and Face Pain. 2014	Hypermenorrhea, Uterine myoma	Chronic	NR,15	S, H and H, V	AC, PC	None	[5]
Shiraishi *et al*. Case of post-transfusion posterior reversible encephalopathy syndrome with cerebral hemorrhage that may be associated with fat-soluble vitamin deficiency. Rinsho Shinkeigaku Clinical Neurology. 2014 Jan	Hypermenorrhea	Chronic	12	E, S	AC, PC, DS	V, F	[14]
Sarkar and Kumar. Posterior reversible encephalopathy syndrome after transfusion in Hb E-beta thalassemia. Indian Pediatr. 2014	Thalassemia	NR	2	E, H	PC	None	[15]
Zhao *et al*. Blood transfusion-related posterior reversible encephalopathy syndrome. J Neurol Sci 2014	Aplastic anemia, Iron deficiency anemia	Chronic	8,10	H, V and S, H	AC, PC	None	[6]
Singh *et al*. Posterior reversible encephalopathy syndrome secondary to blood transfusion. J Clin Neurosci 2015	Uterine myoma	Chronic	2	E, S, H, V	AC, PC	None	[16]
Liang *et al*. Reversible cerebral vasoconstriction syndrome following red blood cells transfusion: a case series of 7 patients. Orphanet J Rare Dis 2015	Renal failure	Chronic	4, NR	H, V and S, H, V	AC, PC and PC	None	[17]
Cevallos and Berman. Posterior reversible encephalopathy syndrome after blood transfusion. J Neurol Sci 2016	Hypermenorrhea	Chronic	4	S, H, V, F	AC, PC	None	[18]
Sudulagunta *et al*. Posterior reversible encephalopathy syndrome. Oxf Med Case Reports 2017	Abortion	NR	10	S	AC, PC	None	[2]

Contd...

Table 1: (Contd...)

Article	Anemia cause	Anemia course	Ictus symptom after blood transfusion (days)	Clinical findings	Brain MRI distribution of lesions	Sequelae	Reference
Nakamura *et al*. Posterior reversible encephalopathy syndrome with extensive cytotoxic edema after blood transfusion: a case report and literature review. BMC Neurology. 2018	Gastrointestinal bleeding	Subacute	1	E, V	AC, PC, DS	V	[19]
Mitaka *et al*. Posterior reversible encephalopathy syndrome induced by red blood cell transfusion. QJM: An International Journal of Medicine. 2019	Iron deficiency anemia	Chronic	14	H, F	AC, PC	None	[20]
Our case	Iron deficiency anemia	Chronic	5	H, S	AC, PC	None	

NR: Not reported, H: Headache, S: Seizure, E: Encephalopathy, V: Visual disturbance, F: Focal neurological deficit, PC: Posterior circulation, AC: Anterior circulation, DS: Deep structures, MRI: Magnetic resonance imaging

and endothelin-1 exacerbates endothelial dysfunction, which leads to blood-brain barrier dysfunction and culminating into vasogenic edema and vasoconstriction despite normal systemic BP.[5,6,17] Abrupt or acute cerebral hyperperfusion overwhelming the autoregulation of cerebral capillary perfusion pressure may result in vasogenic edema.[2] The release of catecholamines is also suggested as a possible mechanism of vasoconstriction.

The literature review suggests that cerebral vasoconstriction was seen in all reported cases.[2,3,5-20] Cerebral vasoconstriction *de novo* can be considered the inciting event of PRES rather than endothelial dysfunction leading to cerebral vasoconstriction and subsequently PRES. The triggering factors like patients' comorbidities, blood transfusion amount and duration, lead to the variable time frames in the cycle of autoregulation breakthrough to symptom onset and overt vasoconstriction of major cerebral arteries.[5] The temporal course of centripetal progression of the vasoconstrictions, as explained by the hypothesis that deranged cerebral vasomotor control might first involve small distal arteries that are beyond the resolution of imaging studies, might also explain for the delayed onset of vasoconstrictions.[5]

The predilection for the posterior brain is thought to be a result of the better-developed sympathetic regulation in the anterior circulation, with the posterior circulation more susceptible to impaired autoregulation and vasogenic edema in the setting of hypertension.[21]

In a retrospective study that compared the involvement of posterior circulation exclusively by PRES from anterior circulation involvement by PRES (either exclusive or in addition to the posterior circulation), the mean BP was higher in the latter group ($P < 0.01$), which supports the vasogenic theory.[22]

PRES has been associated with several radiological patterns, asymmetrical versus symmetrical, unilateral versus bilateral, atypical region involvement such as brainstem and cerebellum both or only brainstem or cerebellum.[23] In the literature review of cases of blood transfusion-related PRES, only three case reports[7,14,19] show involvement of deep brain structures (basal ganglia, deep white matter, and corpus callosum), while all the remaining reports show predominant posterior circulation involvement.[2,3,5,6,8-13,15-18,20]

PRES generally presents in the fifth or sixth decades, but literature review of cases of blood-transfusion-related PRES showed nearly 50% of the patients in the fourth or fifth decades.[3,5-9,12,17,18] It was seen in children also.[11,15] Thus, it can be summarized that blood-transfusion-related PRES has its uniqueness when compared with other causes of PRES. This study suggests that chronically anemic patients should be transfused blood components with caution as transfusion-mediated autoimmunity may predispose to PRES.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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