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Case Report

Blood transfusion induced posterior reversible encephalopathy syndrome in a case of abnormal uterine bleeding-polyps with chronic very severe anaemia

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a rarely reported medical event across globe. Although PRES is primarily associated with pre-eclampsia, hypertension, auto-immune disorders and cytotoxic drug treatments, a rare fraction has been recently discovered due to transfusion of blood in rapid succession to the patients with chronic severe anemia. Postulated causation which is accepted overall; is due to hypoperfusion and vasogenic edema despite normal blood pressure. Pathology behind this disorder are endothelial dysfunction and breach of blood brain barrier. Cerebral lobes that are primarily affected are parietal and posterior occipital cortex which leads to headache, altered mental status, seizures, and visual disturbances. Its diagnosis is established only after proper clinicoradiological evaluation with aid of MRI. It is prudent to keep in mind about this rare clinical entity while assessing a patient in ward with visual disturbances, headache, and tonic-clonic seizures with normal blood pressure in the setting of chronic severe anemia and there is a history of multiple blood transfusions recently. Its prognosis is satisfactory with no report of fatality.

Keywords: PRES, MRI, Anemia, Seizure, Transfusion, Polyp, AUB

INTRODUCTION

The posterior reversible encephalopathy syndrome as clinico-radiological entity was first described by Hinchey et al based on 15 patients with MRI report showing sub-cortical edema without infarction.[1,2,4,5,10] It was previously called as posterior leukoencephalopathy syndrome, reversible occipito-parietal encephalopathy, and reversible posterior cerebral edema syndrome.[4] It is mainly characterized by symptoms like headache, altered sensorium, seizures, and visual disturbances which are manifestation of reversible vasogenic cerebral edema.[2,5,6,7,8,10] The parietal and posterior occipital lobes are predominantly affected.[4,9] The degree of blindness may vary from blurred vision to homonymous hemianopia to cortical blindness.[4] Other mild symptoms may be nausea, vomiting and brainstem deficits.[4] Its diagnosis is confirmed after MRI evaluation which shows hyperintensity on diffusion weighted imaging (DWI) and increase of apparent diffusion co-efficient (ADC) that denotes vasogenic edema.[2] The primary cause behind PRES is severe hypertension (70%) [SBP ranging from 170 to 190 mmHg] which is caused by eclampsia, acute kidney injury, chronic hypertension, auto-immune disorders (e.g., SLE, TTP), chronic kidney disease, autonomic disturbances (e.g., Guillain-Barre syndrome) and illicit drug use (e.g., LSD).[1,2,4,8,10] Known causes of normotensive PRES (10-30%) are exposure to immunosuppressive/cytotoxic drugs, bone marrow transplant, hemodialysis/peritoneal dialysis, massive blood transfusion, sickle cell disease, transplant rejection, sepsis, and shock.[5,7,10] Blood transfusion related PRES is reportedly very less in number (till date only 25 cases have been reported).[2,5] The possible mechanism is rapid

correction of severe anemia leading to increase in total blood volume and viscosity in the previously dilated anoxic cerebral vessels which in turn leads to cerebral blood volume overload with secondary vasoconstriction. This sudden change in cerebrovascular milieu alters the autoregulation and ultimately results in vasogenic and to some extent cytotoxic edema.[5] The underlying triggering factors are endothelial dysfunction and disruption of blood brain barrier.[4,5] Transfusion-related PRES has good prognosis with no reported fatality.[2,9] Here we will be discussing a case of transfusion-related PRES in a chronic very severe anemia patient with long standing menorrhagia due to cervical polyp.

CASE REPORT

A 36 years aged unmarried lady (height 142 cm, weight 44 kg) admitted in emergency department with complains of giddiness and generalized weakness over last 1 week. Outside report showed hemoglobin level-2.6 gm/dl. On clinical examination she was alert, blood pressure was 120/66 mmHg, pulse-88/min, temp-98.2^0 F, no edema/clubbing/icterus or prominent neck veins noted. She was admitted to medicine ward and urgent blood tests were sent. Blood reports were examined, and her test results were like this: Hb-1.7 gm/dl, total count- 8400, hematocrit-8.5, platelet count-6,47,000/cumm, sickling test-neg, red cell distribution width-52.4, erythrocyte sedimentation rate-45, International normalized ratio-1.35, serum albumin-2.1, liver enzymes-within normal limit, fasting sugar level-114 and post-meal glucose level-201 gm/dl. After seeing her hemoglobin level, she was advised 4 units of whole blood (each unit-350 ml) transfusion over 4 days and gynecological consultation was advised for her history of bleeding per vagina over the last 6 months. Gynecological history taking revealed that she is having menorrhagia for the last 1 year and her cycle is 7-10/15-20 days. Ultra-sound imaging of pelvis revealed that she is having a cervical polyp (6.83×6.89 cm). Then she was transferred to gynae ward and daily 1-unit whole blood transfused to her. After receiving 4 units of blood transfusion, she was planned for polypectomy under GA. She received 2 more units of blood transfusion after the procedure. On day 2 post-op she started complaining of severe headache and developed generalized tonic-clonic seizures over 2 mins for 2 times in 30 minutes interval. She was urgently rushed to ICU. Inj. Phenytoin 600 mg bolus in 100 ml NS over 30 mins given then inj. Phenytoin 100 mg TDS and inj. Pipzo 4.5 gm I. V. TDS started. Blood for serum Calcium sent and report came 9 mg/dl. Her T2 weighted MRI brain scan report revealed PRES i.e., diffuse T2 weighted hyperintense signal in deep white matter and subcortical white matter (Figure 1) in bilateral frontal and occipital regions with no evidence of diffusion restriction (Figure 2). She was transferred to gynae ward after her GCS returned to 15/15 and vision-6/6. Blood pressure was normal throughout her stay at hospital. She was discharged on day 10 post-op with tablet levetiracetam 500 mg twice daily and advised to return to OPD after 10 days for follow-up. Her follow-up MRI report showed disappearance of white matter hyperintensities and no episodes of seizures reported after discharge from hospital.

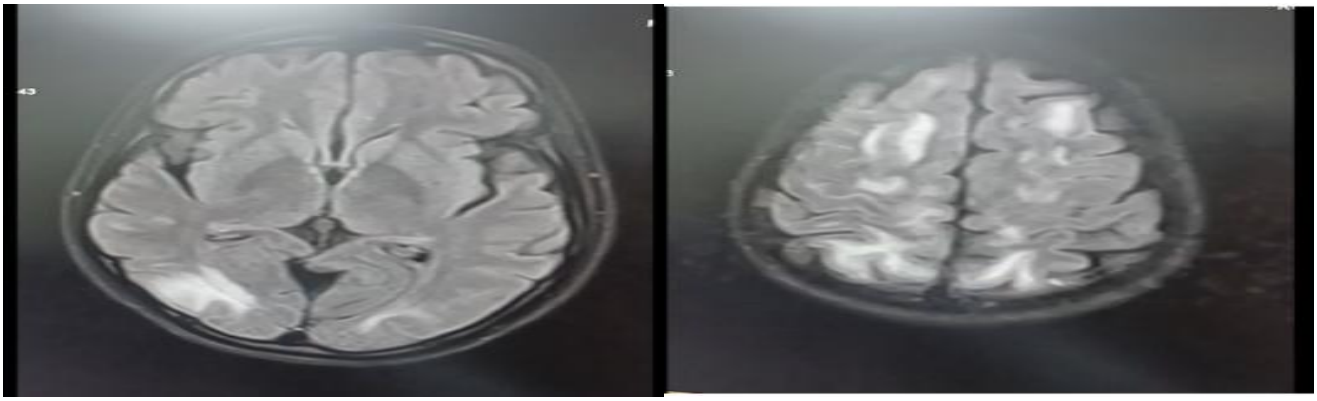

Figure 1 (A and B): T2 weighted MRI scan showing white matter hyperintensities in occipital and parietal lobe.

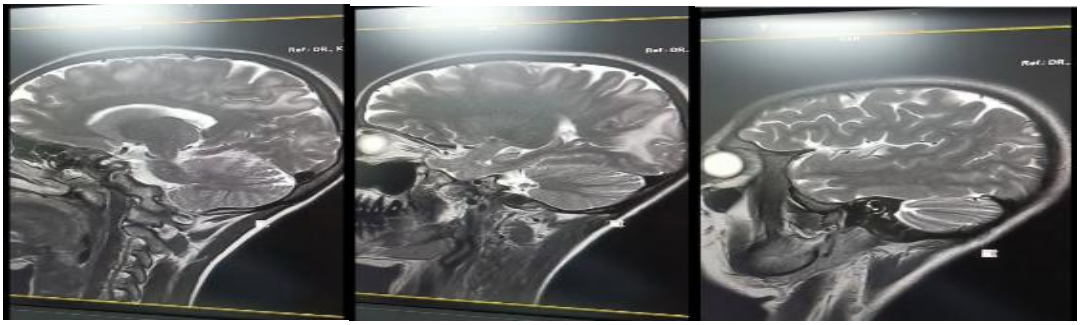

Figure 2: Axial MRI view of subcortical hyperintensities in frontal region and to some extent in parietal cortex.

DISCUSSION

Transfusion related PRES is very rare, and it is exclusively found in normotensive patients.[4] Apart from immunogenic and non-immunogenic complications of blood transfusion this rare disorder occurs due to rapid correction of chronic severe anemia (lasting over 1 month).[2,3] Several hypotheses have been made about its pathogenesis but the most accepted one is rapid increase in total blood flow with raised viscosity causes release of prostaglandin, calcium, serotonin, nitric oxide, and endothelin-1 damaging the endothelium which ultimately disrupts the integrity of blood-brain barrier and causes cerebral edema.[1,4,6,9,10] In the patients of chronic anemia, the cerebral vessels remain in hypoxic vasodilated state, triggering factors like comorbidities, massive and prolonged blood transfusion leads to disruption of cerebral blood flow autoregulation in vertebral artery and internal carotid artery leading to increase in perfusion pressure in cerebral capillaries resulting in vasogenic edema.[4,5,8,9] Low serum albumin aggravates the process of cerebral edema.[5] On T2 weighted MRI brain image high signals with raised ADC noted in the white matter of bilateral parieto-occipital lobes, brainstem, cerebellum, basal ganglia, and frontal lobes.[4,6,8,10] DWI is helpful to discriminate between arterial ischemic injury (reduced ADC) and vasogenic edema (increased ADC).[6] This disease affects more the cerebellar and occipital cortex than anterior cortex because of poor autoregulation and poorly developed sympathetic regulation in posterior circulation.[4]

Patients with transfusion related PRES usually complains of headache (64%), blurring of vision, altered sensorium and status epilepticus (45%) almost within 7 days (ranging from 1 to 18 days) after blood transfusion.[1,3,6,9]

Worldwide this rare entity has been found roughly in 25 cases and surprisingly 96% patients are females (within 40 to 50 years age group) who mostly belong to Asia continent indicating a genetic predisposition for transfusion related PRES in this region.[1,2,4-6,10] Chronic anemia in women is found in certain disorders namely-uterine leiomyoma, iron deficiency anemia, aplastic anemia, chronic renal failure, cancer surgery and dysfunctional uterine bleeding.[10] Patients with auto-immune disorders are prone to develop this disease that is why it is common among women.[9] Chronic severe anemia in the setting of BMI less than 25 has strong association with transfusion induced PRES.[8] Association of hypoglycemia also have been found in some cases with involvement of posterior limb of internal capsule, insula, hippocampus, and basal ganglia.[10] Low serum estradiol has been found to have caused cerebral vasoconstriction which indirectly contributes to transfusion-related PRES in perimenopausal women.[2,5,6,9]

Prognosis of blood transfusion related PRES is favorable with no recorded of fatality.[9] But in some literature, it has been found that older patients with multiple comorbidities are prone to develop irreversible PRES which presents with low level of consciousness at the onset, raised CRP values, thrombotic disorders, stroke, subarachnoid hemorrhage, and heart failure.[2,7,9] Blood component transfusion over prolonged duration is advised in chronically anemic patients to avoid this catastrophe.[4]

CONCLUSION

In this case it has been shown that repeated blood transfusions in a patient with chronic severe anemia with prolonged menorrhagia has caused vasogenic cerebral edema. If very severe anemia is corrected with blood transfusion certain blood parameters needs to be assessed like CRP level, serum albumin level, coagulation profile and renal function test. Blood transfusion should be performed slowly taking days. The best practice is to use blood component transfusion to treat chronic severe anemia with known autoimmune disorder in a female patient with low body weight. Prompt treatment of normotensive transfusion related PRES will relieve the patient of neurological sequel like in our case.

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