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Posterior reversible encephalopathy syndrome (PRES) presenting as Status Epilepticus in a case of Autoimmune Hemolytic Anemia (AIHA): A Case report

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic state, caused by imbalance in autoregulation of posterior cerebral circulation. We report a case of young female, presented at emergency department with complains of nausea, vomiting and generalized tonic clonic seizures prior to admission. During the course of hospital stay patient landed in status epilepticus which was treated appropriately. Patient's magnetic resonance imaging (MRI) was done which had classical features of vasogenic edema in occipital and parietal region, suggestive of PRES. She was a known case of autoimmune hemolytic anemia that was treated with multiple blood transfusions and low dose oral steroids. She was discharged after complete resolution of symptoms with the advice to follow up in medicine outpatient department. Our case describes about autoimmune hemolytic anemia in which occurrence of PRES is uncommon. Early diagnosis and robust treatment can prevent permanent damage to the brain, and is often associated with complete recovery.

Key words: Posterior Reversible Encephalopathy Syndrome; Hemolytic anemia; Sporadic disease

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INTRODUCTION

Posterior Reversible Encephalopathy Syndrome is a disease of heterogenous etiologies commonly presenting as headache, vomiting, visual disturbances, seizures, and confusion. Acute changes in blood pressure are commonly associated with this.[1] Although PRES is being recognized and reported more often than before, the exact incidence is still unknown. Even though patients of all sexes and age groups are susceptible, it is more commonly seen in women. It is understood that many medical conditions and medicines raise the risk of posterior reversible encephalopathy syndrome.

Autoimmune hemolytic anemia (AIHA) is a disorder marked by presence of autoantibodies that attach to patient's erythrocytes causing hemolysis of red blood cells. AIHA is categorized as warm AIHA (reactive), cold AIHA and paroxysmal hemoglobinuria. AIHA can be either primary (idiopathic) AIHA or secondary AIHA in association with other systemic illnesses.

In a female patient with autoimmune hemolytic anemia, we report a rare case of posterior reversible encephalopathy syndrome.

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CASE PRESENTATION

Patient information

We present a case of 23-year-old female, a known case of Autoimmune Hemolytic Anemia diagnosed 1month back. She came to our tertiary care hospital in emergency department with history of headache, nausea, vomiting followed by generalized tonic-clonic seizures 3-4 episodes prior to admission.

Past history

Patient had past history of blood transfusions with 4 units of saline washed packed red cells,4 weeks ago at an outside hospital in view of low hemoglobin(4gm%). She was discharged on low dose oral corticosteroids.

On examination

She was afebrile with pulse rate of 100 beats/min regular, blood pressure was 190/110 mmHg in right arm, pallor was present and other general physical examination was normal. On admission, she was drowsy, pupils bilaterally equal and reacting to light, no neck stiffness and moving all four limbs. Fundus examination was normal. Cardiovascular, respiratory and abdominal examination was normal.

Management

During the course of hospital stay, patient landed up in status epilepticus, she received 4mg of iv diazepam followed by 1000mg of iv levetiracetam followed by phenytoin 1000mg. As seizures were not controlled, midazolam infusion was started at 15mg per hour with daily dosing of levetiracetam and phenytoin. Patient was intubated for airway protection and taken on volume control mode. After giving midazolam infusion, her seizures were controlled. In view high blood pressure tablet amlodipine 10mg was given, blood pressure monitoring was done and thereafter there was no requirement of any anti-hypertensive medication. MRI Brain was done suggestive of multiple posterior periventricular and subcortical T2/FLAIR hyperintensities noted in bilateral occipital, high parietal and right cerebellar region appearing isointense on T1 showing no DWI restriction and blooming on GRE (Figure A and B).

Laboratory studies

Showed hemoglobin 11.4 gm/dl, WBC 4500 cells/mm3 (neutrophils- 58%), platelets 3 lakhs/cumm. Blood gas analysis showed pH-7.32, PO2-78, PCO2-38, and HCO3-22. Blood sugar was 134 mg/dl. Direct Coomb's test was positive. Serum electrolytes, liver function test, renal function test and urine analysis were normal. CSF showed 2 cells with 100% lymphocytes with normal protein and sugar. Blood, urine and endotracheal cultures were negative for any growth. Chest x-ray, ECG and 2Dechocardiogram were also normal.

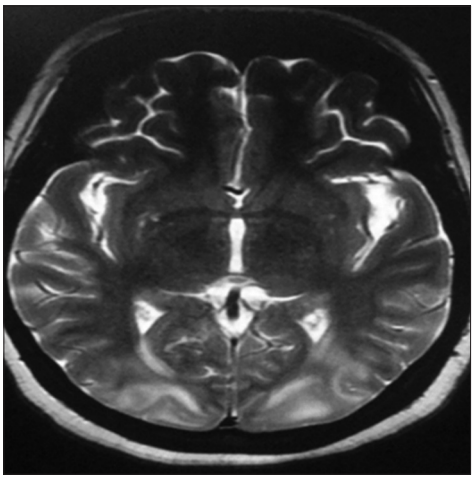

Figure A: T2 W images showing hyperintense lesion in occipital and temporal lobe

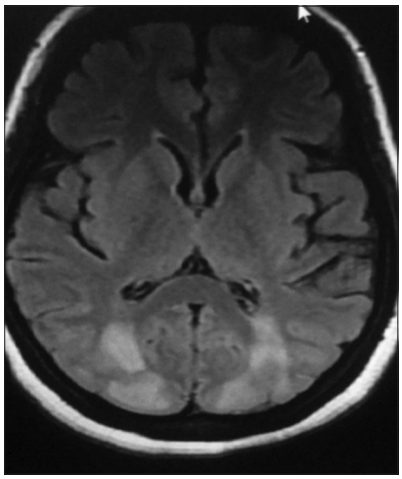

Figure B: MRI images Showing vasogenic oedema in occipital lobe

Therapeutic intervention

In view of classical clinical and radiological findings, PRES due to autoimmune hemolytic anemia was diagnosed. She was managed with supportive care- Antiepileptics, injection mannitol, antihypertensives along with once daily dose of prednisolone 40mg. She was discharged on oral supplementation of folic acid, zinc and vitamin B12.

DISCUSSION

Posterior reversible encephalopathy syndrome (PRES) was described first by Hinchey et al., in 1996.[2] Posterior reversible encephalopathy syndrome, also known as reversible posterior cerebral edema syndrome, reversible posterior leukoencephalopathy syndrome and reversible occipital parietal encephalopathy is a syndrome with heterogenous etiologies and characteristic clinical and

radiological features.[3] The characteristic clinical features and radiological criteria help in establishing the diagnosis of posterior reversible encephalopathy syndrome.[4,5] The incidence of PRES is still unknown due to its heterogenous presentation but the syndrome has female preponderance as it is more common in autoimmune conditions, preeclampsia, HELLP, etc.

The various etiologies leading to posterior reversible encephalopathy syndrome are heterogenous and can be broadly classified as follows, Table 1.

PRES is marked by symptoms such as headache, seizures, impaired consciousness and hallucinations (visual). It is usually associated with acute rise in blood pressure. Headache is the most prevalent clinical presentation, accompanied by improvements in the consciousness, which can range from lethargy to coma and somnolence.

The pathophysiology of PRES is still unclear, but it is often seen in conditions with immune challenge leading to T-lymphocyte and/or endothelial activation. Leukocyte activation and vasoconstriction, both systemic and cerebral may cause faulty cerebral autoregulation. Because there are many etiologies, different mechanisms are proposed for different clinical situations. The proposed mechanisms are; A) As the upper limit of autoregulation is crossed arterioles dilate allowing for hyper perfusion, causing breakdown of blood brain barrier. This leads to extravasation from vessels into the brain parenchyma.[9] B) Endothelial dysfunction especially in cases preeclampsia and cytotoxic drug use is associated with toxicity to vascular endothelium causing blood brain barrier disruption, capillary leakage and axonal swelling. Vasogenic edema seen with therapies may be seen in normotensive individuals and with therapeutic levels of these drugs.[2]

Table 1: Etiology of Posterior Reversible Encephalopathy Syndrome

General	Hypertension, sepsis and septic shock[6]
Pregnancy associated	pre-eclampsia, HELLP syndrome[6]
Autoimmune pathology	systemic sclerosis, polyarteritis nodosa Wegener's granulomatosis, Systemic lupus erythematosus Polyangitis[7]
Immunosuppressive/ cytotoxic drugs	cyclosporine, tacrolimus, paclitaxel, oxaliplatin, cisplatin, gemcitabine, bevacizumab, sunitinib, sorafenib, etc[8]

Usually, PRES is identified based on characteristic clinical symptoms, neuroimaging (computed tomography or images of MRI).[10] MRI is the gold standard and only 50% of the lesions were revealed by the CT scan.[11] In order to identify symptoms of cytotoxic oedema, which is a symptom of the progression of the disease, PRES clinicians should be aware of MRI findings in a suspected case.[12] In order to begin treatment and prevent death, a timely diagnosis is necessary.

The initial assessment of PRES patients should concentrate on rapid rectification of high blood pressure, the use of crystalloids for hydration and maintaining ample oxygenation. Aggressive management of underlying pathology and raised blood pressure is the usual treatment for neurological findings. Supportive treatment with fluids, analgesics, antiepileptics, etc and the prevention of possible causative factors is the line of management.[13]

Autoimmune hemolytic anemia is a moderately sporadic condition, estimated to be incidence of 1-3 cases per 100 000 per annum. In 48-70 percent of cases of AIHA, warm autoantibodies are responsible for destruction of RBC'S and consequent anemia.[14] Hemolysis may be acute, chronic, episodic.

In our patient with autoimmune hemolytic anemia, PRES could have been precipitated by either, Table 2.

Table 2: Review of cases of PRES after blood transfusion

Sr.no	Age	Hb pre and post transfusion	Onset of PRES after transfusion (days)	Cause of anaemia	Sequelae	Reference
1.	45	2.0gm-10.0gm%	2	Myoma uteri	None	16
2.	48	3.0gm%-8.0gm%	6	Myoma uteri	None	17
3.	47	1.5gm%-10.9gm%	7	Aplastic anaemia	Visual defect	18
4.	58	7.7gm%-10.9gm%	8	Cancer surgery	None	19
5.	77	9.2gm%-13.3gm%	17	Cancer surgery	None	19
6.	32	5.7gm%-12.5gm%	5	Myoma uteri	None	20
7.	42	5.7gm%-11.7gm%	6	CKD, CLD*	None	21
8.	56	2.0gm%-9.2gm%	6	Corpus uteri	None	22
9.	35	3.5gm%**	10	Unsafe abortion	None	15
10 (Present case)	23	4.0-11.4 gm%	28	AIHA	None	

*Chronic Kidney Disease, Chronic Liver Disease
**Patient received 5 units transfusion due to Hb of 3.4gm% at a local hospital and also had on going blood loss

a) Multiple blood transfusions causing activation of complement mediated (immune complex) activation of T cells/endothelial cells leading to PRES.
b) Patient was on long term oral steroids, consumption of oral steroids for prolonged periods may lead to systemic hypertension. High blood pressure can precipitate PRES by causing cerebral vasoconstriction.
c) The occurrence of PRES is thought to be caused by a rapid correction in the Haemoglobin levels and viscosity by blood transfusion.

Our patient's clinical findings suggest that severe cytotoxic oedema in the brain may have caused neurological manifestations. Furthermore, if anaemia is quickly reversed by blood transfusion, physicians should verify the existence of risk factors, including elevation of CRP levels, hypoalbuminemia, renal injury and female sex.

The rise in CRP levels could be associated with worsening of PRES by increasing the sensitivity of the blood-brain barrier to endothelial damage associated with inflammation. Hypoalbuminemia by decreasing colloid osmotic pressure affects the production of edema in PRES. Endothelial cell damage, which is a weak predictive marker, is reported to mediate renal injury. These factors can influence the incidence of PRES in patients with severe anaemia following transfusion of blood. However, in order to minimise the risk of this complication of the central nervous system, it would seem that in an environment of subacute to chronic anaemia, a gentler correction of haemoglobin over days is preferable as long as the patient is hemodynamically stable.

Review of literature

Till date only 9 cases of PRES associated with blood transfusion have been reported in literature, all of which were seen in female patients.[15] Our patient had prior history of blood transfusion 28 days ago. The pathophysiology of transfusion related PRES has been discussed above.

CONCLUSION

Our case shows that PRES is associated with multiple blood transfusions. High suspicion index with clinical symptoms, early brain imaging, prompt diagnosis and treatment can decrease morbidity, mortality and promote early recovery.

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Consent of the patient was asked and received

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