



Acute kidney injury and posterior reversible encephalopathy syndrome in a boy with β thalassemia major

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ABSTRACT

Renal involvement in thalassemia major is an important concern of both pediatric nephrologists and pediatric hematologists. Both glomerular and tubular injury may precede overt kidney dysfunction in these patients and may be due to deleterious effects of hemolysis, iron overload and iron chelator therapy. Here we present a case of thalassemia major with acute kidney injury with findings in favor of hemolytic uremic syndrome and consequent posterior reversible encephalopathy syndrome who needed multiple sessions of hemodialysis and finally recovered uneventfully.

Implication for health policy/practice/research/medical education:

Patients with β thalassemia major are at risk of renal damage due to multiple mechanisms. Frequent monitoring of kidney function and attention to level of iron overload, dose and duration of chelator therapy is highly recommended in this group of patients.

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Introduction

Renal involvement in thalassemia major is an important concern of both pediatric nephrologists and pediatric hematologists. Both glomerular and tubular injury may precede overt kidney dysfunction in these patients and may be due to deleterious effects of hemolysis, iron overload and iron chelator therapy (1,2).

Case Presentation

Patient is a 13-year-old boy, a case of thalassemia major who presented with chief complaint of gross hematuria since one week and epistaxis since two days before admission. He was diagnosed as thalassemia major at 6 months of age and then received pack cell transfusion every 3-4 weeks. He had history of headache, dizziness, hematemesis, pallor and tarry stool. He was

on deferoxamine 1500 mg subcutaneous 4 times weekly, deferiprone 500 mg 3 times daily and deferasirox 500 mg twice daily. He had family history of thalassemia minor in his parents. On physical examination he was pale, pulse rate (PR) = 102/min, respiratory rate (RR) = 25/min, blood pressure (BP) = 120/70 mm Hg, temperature = 36.5 axillary. Sclera was mildly icteric; heart and lung auscultation was normal. There was no organomegaly or abdominal distention but he had only mild tenderness over RUQ. In addition, he had +2 edema of lower extremities. Laboratory data was as follows: hemoglobin = 5.2 g/dL, white blood cell (WBC) = 4700 /mm³ (68% PMN, 30% lymph), platelet = 66 000/mm³, mean corpuscular volume (MCV) = 76.9 fl, prothrombin time (PT) = 13 seconds, partial thromboplastin time (PTT) = 30 seconds, blood urea nitrogen (BUN) = 220 mg/dL, creatinine = 10 mg/dL,

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total bilirubin = 6.9 mg/dL, direct bilirubin = 5.1 mg/dL, P = 7.8 mg/dL, Ca = 7.9 mg/dL, K = 5.9 mEq/L, pH = 7.24, HCO₃ = 8.7 mmol/L, HBsAg negative, D-dimer = 2553 ng/mL (high), fibrinogen degradation products (FDP) = 20 µg/mL (high), fibrinogen = 3.39 g/L (normal), C3, C4, ANA, P-ANCA, C-ANCA were all within normal range.

Peripheral blood smear showed; schistocytes and burr cells in favor of microangiopathic hemolytic anemia, G6PD assay was normal and direct coombs test was negative. Urinalysis showed; +1 blood, +1 ketone, 4-5 RBC/HPF. Renal sonography showed only bilateral enlarged kidneys with increased echogenicity.

Hemodialysis was started for him. His blood pressure was about 120-130/70 mm Hg and rose slowly but never went over 150-160/90 mm Hg. Anemia persisted and he received four transfusions of packed red blood cell (RBC). With high suspicion of hemolytic uremic syndrome and also antibody mediated hemolysis, fresh frozen plasma and prednisolone were started. Renal biopsy showed evidences of tubulitis, acute interstitial nephritis, changes in arterioles in favor of microangiopathy and significant iron deposition in renal tubules and interstitium. IF study was not significant. On 11th day of admission, after apparent satisfactory recovery he developed headache, repeated vomiting, and blurred vision. Cerebrospinal fluid analysis was normal with acceptable pressure. Polymerase chain reaction (PCR) for herpes simplex virus was negative. Brain magnetic resonance imaging (MRI) showed high intensity lesions in parieto-occipital region in favor of posterior reversible encephalopathy syndrome (PRES) (Figure 1). After a day, patient developed generalized tonic clonic seizure which recurred for several episodes and finally controlled with IV sodium valproate, phenytoin and phenobarbital. On 16th day of admission serum BUN and creatinine significantly decreased and the patient was discharged after 21 days with good general condition and withholding hemodialysis. On follow up visits blood pressure was normal, thus antihypertensive

drugs were discontinued, hemoglobin remained above 10 g/dL without pack cell transfusion, platelet count became normal and finally creatinine decreased to normal level according to age.

Discussion

Beta-thalassemia is a genetic disease caused by mutation of β globin gene resulting in defective hemoglobin synthesis and anemia which in most severe form (thalassemia major) needs multiple, often monthly blood transfusions (1-3). Frequent RBC transfusion with subsequent iron deposition in body organs such as heart, pancreas, thyroid and liver may cause several untoward complications. Without regular blood transfusions and also proper iron chelation patients with thalassemia major may not survive even to late childhood and adolescence (4). Traditionally excess iron removal has been achieved by subcutaneous injections of deferoxamine (desferal), but newer drugs such as deferiprone and deferasirox are used frequently in recent years.

Renal involvement in thalassemia major may be due to several pathophysiologic mechanisms; renal tubular injury, iron deposition and anemia may contribute to tubular injury in thalassemia major patients.

Iron deposition in renal tubules may lead to lipid peroxidation and oxygen free radicals production causing tubular damage (5). Anemia also can cause tubular damage per se or due to causing oxidative stress in thalassemia major patients (6). Glomerular hyperfiltration is a common finding in thalassemia major patients, which can cause renal damage and decline of GFR (7). Several studies highlighted that iron chelators caused renal injury presumably due to tubular necrosis or interstitial nephritis (8,9).

The main question in our case was: Is there any possible relation of thalassemia major and hemolytic-uremic syndrome (HUS)? Author found only an article which concluded that free heme from hemolysis (such as thalassemia major) can act as a trigger for atypical HUS (10). PRES is associated with hypertension in nearly 70% of cases but it may be due to in severe inflammation and endothelial injury such as sepsis, autoimmune disease, eclampsia and transplantation (11). More interestingly there are reports of PRES in patients with diagnosis of HUS (12,13).

Conclusion

Our experience with this case emphasizes close monitoring of thalassemia major patients especially ones receiving multiple iron chelators for early laboratory signs of renal dysfunction, keeping in mind that hemolysis may trigger atypical HUS in patients with genetic predisposition. Posterior reversible leukoencephalopathy syndrome should be considered as a possible cause of seizure and altered level of consciousness in these patients even in absence of significant hypertension.

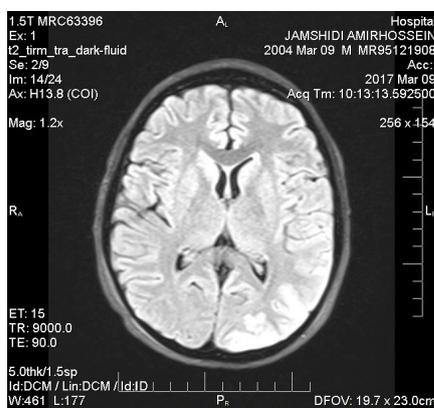


Figure 1. Brain MRI; hyperintense lesion in left parieto-occipital region in favor of posterior reversible encephalopathy syndrome (PRES).

Author's contribution

HEM is the single author of the paper.

Conflicts of interest

The author declared no potential conflicts of interest with respect to the case, authorship, and/or publication of this article.

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Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author. Informed consent was obtained from the patient for publication.

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