E BETA THALASSEMIA COMPLICATED BY STEROID RESPONSIVE AUTO IMMUNE HEMOLYTIC ANEMIA DUE TO SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Thalassemia patients may have superadded acquired hemolytic diseases. This may cause a sudden increase in transfusion requirement. However, such acquired hemolysis is very difficult to diagnose in presence of Thalassemia. We here report a case of thalassemia complicated by hemolytic anemia secondary to SLE. This is probably the first report of this association from India. This combination of two hemolytic diseases is potentially fatal. The autoimmune hemolytic component responded well to immunosuppressive therapy and there was significant reduction in transfusion requirement.

Keywords: Thalassemia, SLE, hemolytic Anemia, immunosuppressive therapy

INTRODUCTION

Thalassemia is a very common congenital hematological disorder in India and of the different types, E Beta thalassemia is the commonest variant, especially in Eastern India¹. Beta thalassemia patients sometimes may show increased predisposition to some autoimmune diseases². We here report a case of E beta thalassemia with autoimmune hemolytic anemia secondary to Systemic Lupus Erythematosus (SLE). As far as we know, this is the first report of this association from India.

The Case Report

A thirty five years old female was admitted in November 2011 following rapidly developing pallor and weakness. She was a known case of E Beta Thalassemia, first detected at eighteen years of age (Figure 1).

From that age, she needed blood transfusion infrequently, usually one unit every six to seven months. However, from the beginning of 2011, suddenly her blood transfusion requirement increased steadily. At time of admission, she needed one unit packed red cells almost every week. On admission, she was markedly pale. There was no bleeding manifestation. On examination, there was enlargement of both liver (2.5 cm below right costal margin) and spleen (4 cm below left costal margin). There was no lymphadenopathy. After admission, the hemoglobin was found to be 3.6 gm% and after drawing blood for the tests, patient was transfused 3 units packed RBC for relief of symptoms. Initial results came as RBC count 1.66 million/cmm, Total Leukocyte Count 3500/cmm (neutrophil 68%, lymphocyte 30%, Eosinophil 1%), Platelet count 2 lakh/cmm. MCV- 91 fl, MCH – 28.3, MCHC- 31.1; RBC distribution width was 20.4. Peripheral Blood Smear showed Microcytic Hypochromic RBCs with Polychromasia, Target Cells and Anisocytosis. There were 2 nucleated RBCs/100 cells. Reticulocyte count was 7 % and ESR was 162 mm in first hour. After transfusion, the hemoglobin level increased to 6 gm% but within 5 days again came down to 4.7 gm%. Test results showed normal urine and stool analysis. Total bilirubin was 1.6 mg% with normal liver enzyme levels, albumin of 4 gm% and globulin of 4.1 gm%. Urea / creatinine levels were 30 and 0.7 mg% respectively. Tests for

viral markers like HIV and hepatitis B and C were negative. C Reactive protein and thyroid hormone levels were normal. Ultrasonographic scan of abdomen showed enlarged liver and spleen, but no other pathology. Now, from the initial blood sample of the patient (taken before current blood transfusion) further tests revealed a strongly positive direct Coomb's test. Also, serum anti- Nuclear factor, by Hep 2 method was positive at 1:640 with a homogeneous pattern. Anti dsDNA levels were positive at 1:80. Serum complement level (C3) was 69 mg/dl (N: 90—180). The qualitative tests for anti-SS A and anti Sm were also positive.

Multiple blood transfusions can cause all these autoimmune marker tests to be false positive. However in this case, considering the rapidly decreasing hemoglobin levels, autoimmune hemolysis was thought probable. We administered pulse methyl prednisolone (1 gm daily for 3 days) followed by oral prednisolone (1 mg/kg) and hydroxychloroquine sulphate (400 mg/day). Weekly blood tests showed hemoglobin levels to be 8 g% next week and 10.5 gm% after 2 weeks. The patient needed no more blood transfusions.

The patient is now in follow up and is on the above mentioned oral drugs. She has not needed any more transfusion for almost 2 months and her hemoglobin level remains stable. She has not developed any other feature of SLE like arthritis or muco cutaneous lesions. However, based on the blood markers, her hemolytic anemia is provisionally diagnosed to be secondary to SLE.

DISCUSSION

Thalassemia patients may have increase in transfusion requirement over time. This may be due to various reasons like formation of alloantibodies or secondary infections³. Rarely, the increased blood requirement may be due to acquired disorders like SLE². Additional hemolytic disorders associated with thalassemia are very difficult to diagnose clinically as the symptoms and signs are often identical. However, undiagnosed autoimmune diseases in thalassemia patients may lead to additional morbidities like atherosclerosis⁴. Thus, clinical suspicion needs to be high in a thalassemia patient with unexplained high transfusion requirement.

Figure 1: The hemoglobin electrophoresis report showing E beta thalassemia

Recent research has discovered that hemoglobin Beta gene is in close proximity to other genes for immune regulation like STIM1, CD151 and TC21/RRAS2². These genes are involved in anti inflammatory activity. This may account for the association of beta thalassemia with some autoimmune disorders like SLE as the anti inflammatory genes may also get deleted with the globin gene².

A recent landmark study from Italy analyzed the association between SLE and thalassemia⁴. In their series of 177 patients with SLE, they found thalassemia in 17 cases⁴. All the patients with dual disease were female, there was increased incidence of Sjogren's syndrome, Serositis and nephritis in this group and serum C3 was persistently low⁴. In our case too, we found positive anti-SS-A and low C3. However, our patient had no evidence of renal involvement or serous sac collection.

The diagnosis of SLE in a case of thalassemia is very difficult in absence of florid clinical features. The auto antibodies we use to diagnose SLE may be false positive in multi transfused thalassemia cases⁵. This is especially true for patients on iron chelator therapy⁵. However, anti-dsDNA is rarely positive⁵. Our patient had not received any iron chelation till admission and anti dsDNA was strongly positive.

The association of SLE with other hemoglobinopathies is rarely reported. Of the reported cases, there are more reports of sickle cell disease with SLE⁶. The association in potentially morbid and severity of both diseases can be aggravated². Also, in thalassemia with SLE sometimes the patients can develop lupus anticoagulant that can cause intracranial hemorrhage⁷. Prednisolone is said to be effective in lupus anti coagulant positive cases⁷. A recent report from India describes a case of SLE with sickle/ β thalassemia⁸. In that case, the patient had multi system involvement and needed aggressive immunosuppression⁸. In our case, our patient recovered with pulse methyl prednisolone therapy and is now being maintained on oral steroids and hydroxychloroquine.

CONCLUSION

Increase in transfusion requirement of thalassemia patients may be due to some other secondary cause like immune hemolysis. So, instead of blood product administration, proper diagnostic algorithm should be followed. Although various blood tests may show false positive results after repeated transfusions, the tests should be interpreted in light of the clinical situation. Then, harmful effects of repeated transfusions can sometimes be avoided.

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