Case Report

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A Rare Case of Successfully Treated Coombs Negative Immune Haemolytic Anaemia in Pregnancy

Obstetrics and Gynaecology Section

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ABSTRACT

Immune haemolytic anaemia in pregnancy, although rare, but it can be life threatening. Severe anaemia with jaundice, unresponsive to blood transfusion can clinch the diagnosis of immune haemolytic anaemia. Our patient was a 27-year-old second gravida, with all the above features, but there was diagnostic challenge as her Coombs test was negative. A high index of suspicion and rapid response to glucocorticoids, pointed towards the diagnosis. Thereafter, the course of pregnancy and postpartum period was uneventful. Thus, successful maternal and fetal outcome can be achieved with prompt diagnosis and treatment.

Keywords: Autoimmune, Direct coombs test, Haemolysis, Hyperbilirubinemia

CASE REPORT

A 27-year-old G2 P1 at 26 weeks period of gestation presented to a nearby local hospital with history of fever, generalized weakness and palpitations. Her first pregnancy was uneventful. There was no history of intake of haematinics or any other drugs. She was detected to have severe anaemia, with haemoglobin (Hb) of 5.3 g/dl. She was transfused two units of blood and started on oral haematinics. Then she was referred to higher centre in view of increasing bilirubin and no clinical or haematological improvement. She presented at our tertiary hospital-after five days, with fever (one episode), jaundice and severe anaemia. She had severe pallor, icterus and tachycardia (Heart Rate 120/min). Her blood pressure was normal and there was mild pedal oedema. There was no palpable hepatosplenomegaly or lymphadenopathy. Her haematological investigations revealed following: Hb=6.2 g/dl, peripheral smear showing mild anisopoikilocytosis, spherocytes, polychromatic cells, no schistocytes. Total leucocyte count and platelet count were normal. In her biochemistry total serum bilirubin (TSB)/ conjugated bilirubin was 5.3/1.99 mg%. However, her transaminases were mildly elevated (SGOT 58 U/L, SGPT 72U/L) and renal function tests were within normal limits.

Blood and urine cultures were sterile and investigation for malaria was negative. She tested negative for IgM HAV, IgM HEV, Anti HCV antibodies, HbsAg, HIV ELISA and Leptospira IgM. She was transfused two more unit of blood after extended cross match, but there was further drop in Hb to 4 g/dL and elevation in serum bilirubin. Reticulocyte count of 12% (Reticulocyte production index=2.6), serum Lactate Dehydrogenase (LDH) 1594µ/l, sonographic evidence of mild hepatosplenomegaly together-with a negative plasma and urine haemoglobin, suggested extravascular haemolysis. But direct (Anti-IgG, Anti C3d) and indirect Coombs tests and antinuclear antibodies were negative. Glucose -6-phosphate dehydrogenase deficiency and haemoglobinopathies were also ruled out. Considering her clinical picture, a final diagnosis of Coombs negative autoimmune haemolytic anaemia was made. Patient received four unit more blood transfusions, over one week, along with intravenous methylprednisolone pulse (1g once a day for three days) followed by oral prednisolone 40 mg daily. She was also given oral iron and parenteral cyanocoblamin supplementation. Within a week, she experienced symptomatic relief. She showed considerable improvement in haemoglobin (7.6g/dl), fall in serum bilirubin (0.36mg/dl) and serum LDH (336µ/l), thus consolidating the diagnosis. After one month, she was discharged with an Hb of 9.2 g/dL. Meanwhile she developed steroid induced diabetes, which was managed with low doses of insulin. On outpatient basis, her prednisolone was tapered to 15mg over 6 weeks. She was admitted at 36 weeks period of gestation in preterm labour. She delivered a healthy male baby with a birth weight of 2.4 kg. Neonate did not show any clinical or haematologic evidence of haemolytic disease. At the time of discharge, her Hb was 12.1 g/dl. She is currently asymptomatic, on prednisolone 5 mg once a day.

DISCUSSION

Autoimmune Haemolytic Anaemia (AIHA) is an uncommon disorder with an estimated incidence of 0.8-3 per 100,000/year and a prevalence of 17:100,000 in the adult population [1]. The autoantibodies are active at different thermal range; therefore they can be of the warm or the cold type. Most of the haemolysis, whether due to phagocytosis or complement mediated, is extravascular. Prevalence of AIHA in pregnancy, is around 1 in 50000 [2,3]. Presenting complaints include anaemia and its sequelae (shortness of breath, generalised weakness, easy fatigability) with jaundice as in this case. Patients commonly present in the third trimester and show improvement with delivery, with recurrence in future pregnancies. Diagnosis requires exclusion of other cause of haemolytic anaemia (haemoglobinopathies, enzyme deficiencies, drug induced haemolysis, hypersplenism) and evidence of hemolyis (spherocytosis reticulocytosis, hyperbilirubinemia and raised LDH levels). Normal Urine Haemoglobin and plasma haemoglobin cannot rule out haemolysis as it can be normal in extravascular haemolysis [2]. A positive direct agglutination test (Direct Coombs' test) clinches the diagnosis, although 5-10% cases may be Coombs' negative, as in our case. Causative explanation for Coombs' negative AIHA, include possible haemolysis by natural killer cells, small numbers of red blood cell bound IgG molecules below the threshold of the Coombs' test, low-affinity autoantibodies, IgA autoantibodies, and IgM autoantibodies [2,4]. Therefore, clinical suspicion is of paramount importance.

Corticosteroids are the first line drugs for treatment of autoimmune haemolytic anaemia. Usually prednisone is given at the initial dose of 1.0–1.5 mg/kg/day. Response is seen in two weeks in about 80% cases. After stabilization of haemoglobin, prednisone should be gradually and slowly tapered off. Intravenous methylprednisolone pulse therapy may be required for rapid haemolysis and severe

anaemia, which proved useful in our case. Side effects of corticosteroid therapy like derangement of blood sugars and osteoporosis are managed with insulin and calcium supplementation respectively. In cases of unresponsiveness/intolerance to steroids or requirement of maintenance dose more than 10 mg or multiple relapses, splenectomy is the most appropriate second-line treatment option. In pregnancy, splenectomy is feasible during second trimester. Rituximab (US FDA category C) used in a dose of 375 mg/m^2 weekly for a median of 4 weeks, is the alternative in steroid resistant cases [5].

Concomitant blood transfusion is an integral as well as challenging part of treatment. Packed red blood cells for transfusion are selected by extended crossmatch technique, in which all phases of compatibility tests including elution and adsorption are completed [6]. Small volumes of packed red blood cells, should be transfused slowly not exceeding 1mL/kg/min.

Intrauterine growth restriction and intrauterine fetal death may be seen in cases associated with other autoimmune disorders, probably due to the primary pathologic process. Preterm labor and low birth weight may be seen as a consequence of anaemia. Fetal haemolytic anaemia possibly due to transplacental passage of maternal antibodies has also been reported [7]. Successful maternal and fetal outcomes have been reported in the idiopathic cases similar to our case [8,9].

CONCLUSION

AIHA is rare in pregnancy but it can be life threatening. Severe anaemia with jaundice which is unresponsive to blood transfusion, can clinch the diagnosis. Plasma and urine haemoglobin can be normal. Coombs test can be negative in some cases of AIHA. Glucocorticoid is the mainstay of treatment. Successful maternal and fetal outcome can be achieved with prompt diagnosis and treatment.

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