Pregnancy Induced Hemolytic Anemia in an Antenatal Mother: A Rare Case Report.

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Abstract:

Background: In an antenatal mother, pregnancy can exacerbate the underlying autoimmune hemolytic anemia. The features of anemia become apparent in third trimester, remits completely within 2 months of delivery, recurs in subsequent pregnancy and it may be severe and life threatening. The autoimmune hemolytic anemia may be due to warm antibodies, cold antibodies or due to biphassic antibody known as Donath-Landsteiner antibody. Case Report: 30 year old antenatal mother with 22 weeks of amenorrhea, G3P2L1AI, was referred to the hematology department with a known history of hemolytic anemia in previous pregnancies. She gave the history of jaundice and abortion at the 20th week of first gestation. During her second gravida also she developed evidence of hemolysis at 24th week of her pregnancy, for which she was investigated and diagnosed to have autoimmune hemolytic anemia. In the present pregnancy (3rd Gravida), at 22nd week her DAT, IAT and auto control were positive. The eluate was prepared and screened with panel cells, which showed the presence of anti-c antibody. Fathers and first child's blood were phenotyped and found to be c antigen negative. She was on corticosteroids and transfused c antigen negative least incompatible packed red cell units. She was transfused with around 12 units c antigen negative coombs compatible packed red blood cell during her entire gestation and her hemoglobin level was maintained at 7 gm. At term she delivered a healthy female child. Her subsequent follow up was uneventful. Conclusion: Pregnancy induced hemolytic anemia in an antenatal mother is very rare, unlike Hemolytic Disease of Fetuses. However, it can cause clinically significant hemolysis endangering both mother and fetus. The existence of such rare condition which appears during pregnancy and disappears following delivery has to be considered as one of the differential diagnosis in Hemolytic Anemia of Pregnancy.

Keyword: Pregnancy induced hemolytic anemia, AIHA, anti-c antibodies, elution

Introduction:

Immune hemolytic anemia is defined as shortened RBC survival mediated by immune response. It may be due to auto antibodies, where the patient produces antibodies against their own RBC antigens or alloantibodies where the patient produces antibodies against the foreign/ non-self RBC antigens introduced into the circulation or drug induced antibodies. In auto immune hemolytic anemia, the presence of underlying alloantibodies that is being masked by the auto antibodies should be ruled out especially in patients with history of transfusion. Pregnancy presents a special problem in immunohematological services as the mother potentially exhibits alloimmunization to fetal antigens. Auto immune hemolytic anemia associated with pregnancy is very rare. In an antenatal mother, pregnancy can exacerbate the underlying autoimmune hemolytic anemia. The features of anemia becomes apparent in third trimester, remits completely within 2 months of delivery, recurs in subsequent pregnancy and it may be severe and life threatening. Corticosteroids and intravenous immunoglobulin are sometimes helpful with RBC transfusion being the mainstay of treatment of severe anemia. Neonates born to women with pregnancy induced hemolytic anemia have transient hemolysis lasting 1 to 2 months but there has been no report of severe jaundice requiring exchange transfusion. The autoimmune hemolytic anemia may be due to warm antibodies, cold antibodies or due to biphassic antibody known as Donath-Landsteiner antibody. The work on samples with positive auto control, positive DAT and with recent history of transfusion is often complex, time consuming and needs a lot of experience on the part of the investigator. Adsorption and elution tests are carried out to find out whether there is any alloantibody along with the autoantibody. In fetus and new born Rh-D antigen is the major concern in causing hemolytic disease. Next to Rh-D, “c” antigen of the Rh system is most common in causing HDFN.

Case Report:

30 year old antenatal mother with 22 weeks of amenorrhea, G3P2L1AI, was referred to the hematology department with a known history of hemolytic anemia in previous pregnancies. She had symptoms of shortness of breath, palpitation and fatigue. On physical examination she had mild splenomegaly and hepatomegaly which was palpable 3 cms below the costal margin. Serological markers for HBV and HCV were Negative. RBC indices were as follows: HGB: 5.0 gms%, Hematocrit: 15%, RDW CV: 32.3%, MCV: 91.3 fl, MCH: 33.4 pg, MCHC: 36.6 %. Platelet count, total and differential WBC counts were normal. Red blood cells in her peripheral blood smear showed anisocytosis with few polychromatophilic cells, occasional late normoblasts and microcytosis. Her blood group was O positive. She gave the history of jaundice and abortion at the 20th week of first gestation. She was investigated and showed evidence for hemolysis with increased level of unconjugated bilirubin. She was transfused with packed red blood cells at the time of abortion and her
post-abortive period was uneventful. During her second gravida also she developed evidence of hemolysis at 24 weeks of pregnancy, for which she was investigated and diagnosed to have autoimmune hemolytic anemia. She was treated with corticosteroids and around 20 units of packed red blood cells till the term and delivered a full-term female child. In the present pregnancy, (3rd Gravida), at 22nd week she was referred to the hematologab therapy department from the candy clinic with complaints similar to the previous pregnancies. On investigation she showed above hematological parameters. Her DAT was positive. IAT and autocontrol were positive. This time to rule out the presence of any additional alloantibody her blood samples were subjected to adsorption and elution technique using acid glycine method. The eluate was screened with panel cells, which showed the presence of anti-c antibody. In order to find out whether anti-c antibody was against a paternal antigen or exposure to antigens present in the transfused red blood cells, father’s and first child’s blood were phenotyped and found to be “c” antigen negative. She was on corticosteroids and transfused “c” antigen negative least incompatible packed red cell units. Her hemoglobin level was raised from 5 gm% to 6.1 gm% after transfusion of 3 units of packed red blood cells. She was on corticosteroid treatment. She was advised to be on regular follow-up for once in six weeks duration. On her second visit, her blood sample was DAT positive and hemoglobin level was fallen to 5gm%. She was transfused again with 4 units of “c” negative least incompatible packed red cell units. Her hemoglobin was raised to 7 gm%. On her third visit after 2 weeks interval, her blood sample negative for DAT and autocontrol and positive for IAT. The serum sample was again screened with panel cells and found to contain the same “anti-c” antibody alone. Her hemoglobin was stable at 7gm%. On her fourth visit again her hemoglobin level had fallen to 5.5 gm%. However, her DAT was negative and IAT was positive. She was transfused with 3 units “c” antigen negative coombs compatible packed red blood cell. Her hemoglobin was raised to 7 gm%. Then on her subsequent visits once in four weeks till her term she showed similar results of her 4th visit and transfused repeatedly with around 3 units of “c” antigen negative coombs compatible PRBCs units and maintained at the hemoglobin level of 7 gm%. To rule out hemolysis in the fetus, throughout the pregnancy from 22nd week of gestation (i.e., first visit), periodical middle cerebral artery peak systolic velocity was measured and found to be within normal limits. At term she delivered a healthy female child. Her subsequent follow up once in a month for up to 6 months was uneventful.

Discussion: 
Auto immune hemolysis in pregnancy due to warm and cold antibodies occurs on an average of 1 in 50000 pregnancies.4 In a review of 19 reported instances of presumed autoimmune hemolysis during pregnancy revealed life-threatening anemia in nearly 50% of mothers.5 Autoimmune hemolysis associated with pregnancy is often mild and self limiting in the absence of other associated disorders like SLE.6 The incidence of alloimmunisation in multiply transfused patient has been reported to be 0-34%.6 Here in our patient the cause of alloimmunization was due to blood transfusion and not due to paternal antigen as the c antigen was absent on the RBC of the father on phenotyping. Smith et al showed a significant proportion of mothers who had previously received blood transfusion developed anti-c antibodies.7 Shipa single et al reported severe hydrops in an infant born to Rh D positive mother due to anti-c antibodies who have received multiple blood transfusions.8 Queenan et al reported that history of prior blood transfusion was 9 times more frequent among alloimmunized pregnant women.9 Benraad et al reported a patient with autoimmune hemolytic anemia in pregnancy who responded well to treatment with prednisone.10 Similarly, our patient also responded very well to steroid therapy with prednisolone. In warm autoimmune hemolytic anemia the destruction of red cells occurs by intravascular, extravascular and cell mediated mechanism. The reticuloendothelial systems i.e., the mononuclear phagocytic reticulums in the spleen and to a lesser extent the liver are the places where the extravascular destruction of red cells occurs. The presence of microspherocytes in the peripheral blood is a sensitive indicator for ongoing hemolysis. The diagnosis of hemolytic anemia rests on clinical findings and laboratory data such as hemoglobin or hematocrit values, reticulocyte count, red cell morphology, bilirubin, haptoglobin and LDH levels. Free hemoglobin may be present in the plasma and hemoglobinuria may be present. When the antenatal women develops auto antibody belonging to the IgG class the condition is potentially dangerous as the IgG antibody can cross the placenta and affect the fetus.11 Autoimmune hemolytic anemia has been associated with IgG, IgA and IgM warm auto antibodies. The target for these warm autoantibodies are mostly against the Rh antigens but antigens wrb, Ena, Ge, A, B, Vel, kbp, U and antigens within the Kell and Kidd blood group systems can also form autoantibodies. Some autoantibodies may mimic alloantibodies and are termed mimicking antibodies when the corresponding antigen on the red cell is weak or absent.12 Usually it is very difficult to rule out the presence of underlying alloantibody in the presence of autoantibody and even more difficult if the patient has been recently transfused. If the patient has not been transfused recently autologous adsorption can be done. If the patient is recently transfused in the previous 3 months then auto adsorption cannot be done. If the patient’s phenotype is not known then adsorption with selected cells of R1R1 R2R2 and rr are done.13 These cells should be selected so that they lack one or more antigens for the commonly encountered clinically significant alloantibodies of the Kell, Duffy, Kidd and SS. This requires initial preparation of patient’s red cell with gentle heat elution, Lui Freeze-thaw, acid elution kits, digitonin acid and ZZAP treatment can be done to elute the bound antibodies. Sudipa et al has found that PEG method is a rapid, cheap and effective way to remove autoantibodies to detect underlying alloantibodies.14

Conclusion:
Pregnancy induced hemolytic anemia in an antenatal mother is very rare, unlike Hemolytic Disease of Fetus and Newborn. However, it can cause clinically significant hemolysis endangering both mother and fetus. If the underlying mechanism is autoimmune, the disease responds well to the administration of corticosteroids, and transfusion of packed red blood cells. However, the transfusion of red cells is only to alleviate the symptoms of anemia, not merely to boost up the hemoglobin level, because, most often the transfused red cells will also be rapidly destroyed. This will avoid unnecessary exposure to alloantigens and worsening of hemolysis. In this regard, if the disease is idiopathic, the treatment response to steroid will be variable. Since autoimmune hemolysis in mother can sometimes cause severe hemolysis in fetus, it is imperative to monitor the fetus for development of hemolysis. If associated alloantibody is detected because of previous transfusion, for optimal survival of RBCs, transfused packed red cell must be negative for the corresponding antigen. Autoimmune hemolytic anemia in pregnancy may be either spontaneous or aggravation of the preexisting clinically undetectable condition. However, existence of such rare condition which appears during pregnancy and disappears following delivery has to be considered as one of the differential diagnosis in Hemolytic Anemia of Pregnancy.

Bibliography: 