TRIDHA
Journal of Clinical Cases & Reports
Volume 2022, Issue S1, 4 pages
https://doi.org/10.46619/joccr.2022.5-S1.1004

CASE REPORT

Alloimmune - Anti-c IgG and Mixed Warm & Cold Autoimmune Hemolytic Anemia in Young Female - Case report

Mitunkumar Mayani, Rateesh Sareeen*, Smitirupa Mishra and G N Gupta

Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India

Correspondence should be addressed to Rateesh Sareeen, Department of Pathology & Transfusion Medicine, Santokba Durlabhji Memorial Hospital & Research Centre, Jaipur, India

Received: 10 February 2022; Accepted: 22 February 2022; Published: 28 February 2022

ABSTRACT

We present a case of severe immune mediated hemolytic anemia in a 28-year-old woman who presented with severe unexplained anemia. The history of previous transfusion prompted immune hematology work up revealing presence of anti-c IgG (prior transfusion related); warm and cold auto antibodies making a diagnosis of allo and thermo labile antibodies induced hemolytic anemia. It emphasizes the importance of antibody screening in pregnant women to minimize risk of alloimmune life threatening hemolytic anemia.

KEYWORDS

Immune mediated hemolytic anemia; A antigen; Antibody screening

CASE REPORT

A 28-year-old female was admitted with complaints of headache, giddiness, generalized body ache, shortness of breath on exertion and an episode of fever. The patient was conscious, and the general examination showed pallor. The vitals were normal. The previous medical history revealed that she had fibromyalgia and hypothyroidism for which she stopped medications in 2019. The obstetrics history revealed a baby girl born in 2015 with normal vaginal delivery and the delivery was followed by post-partum hemorrhage. Two years later she had normal uneventful second vaginal delivery. There was an additional history of spontaneous abortion in 2019. Presently she has normal menstrual cycle with heavy and painful bleeding. Complete blood examination showed red cell count- 0.76 × 106/uL, hemoglobin 3.1 g/dL, MCV- 121.1 fL, HCT 9.3%, white blood cell count-7.80 × 103/uL, platelet count 150 × 103/uL. Peripheral blood smear showed marked agglutination of red blood cells obscuring the field (Figure 1). Hemoparasite was not seen. Reticulocyte count was 5.5%.

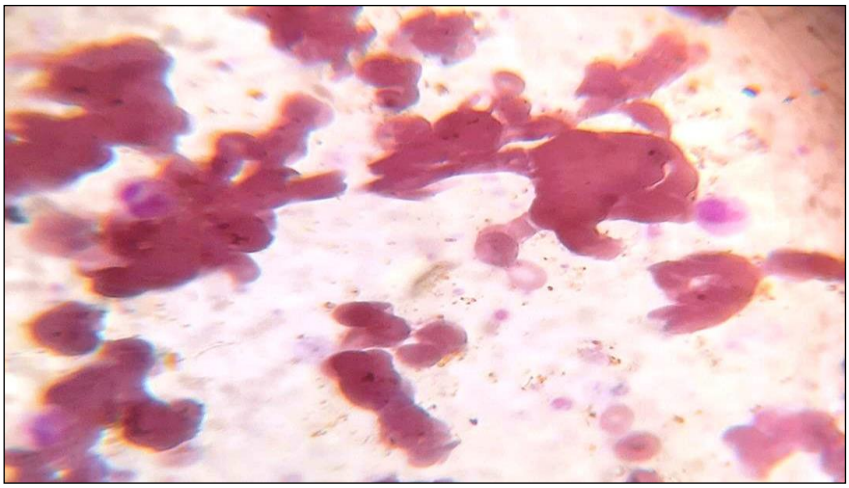

Figure 1: Peripheral blood smear showing agglutination of RBC (Leishman stain, 1000x oil).

The biochemical investigations revealed slightly raised total bilirubin i.e., 2.4 mg/dL (predominantly indirect bilirubin 2.2 mg/dL), Total protein 7.6 g/dL, Albumin 4.1 g/dL, A/G ratio 1.1, with normal serum electrolytes and renal function tests. Ultrasonography abdomen showed mild splenomegaly, there was absence of hepatomegaly or lymphadenopathy. The second line investigations were done. The direct and indirect Coomb's test was positive, whereas G6PD assay, osmotic fragility was unremarkable with normal serum Iron, B12 and Folate levels. A provisional diagnosis of hemolytic anemia was made.

The low hemoglobin required urgent blood transfusion and blood request was sent to blood bank. Blood grouping mandates both forward and reverse grouping by conventional tube method. The forward grouping showed agglutination in both A and B cells making it look like AB positive but reverse grouping did not validate it as there was 3+ agglutination with all reagent cells. The forward grouping was repeated after thrice washing of red blood cells with warm saline showing absence of agglutination with both A and B cells and hence blood group was O positive instead of erroneous AB positive due to allo/auto antibodies. The DAT was repeated using monospecific card (IgG, C3d and control; ortho clinical Diagnostics Mumbai, India) showed IgG and C3d positivity suggested of mixed (warm & cold) autoimmune hemolytic anemia (AIHA) (Figure 2).

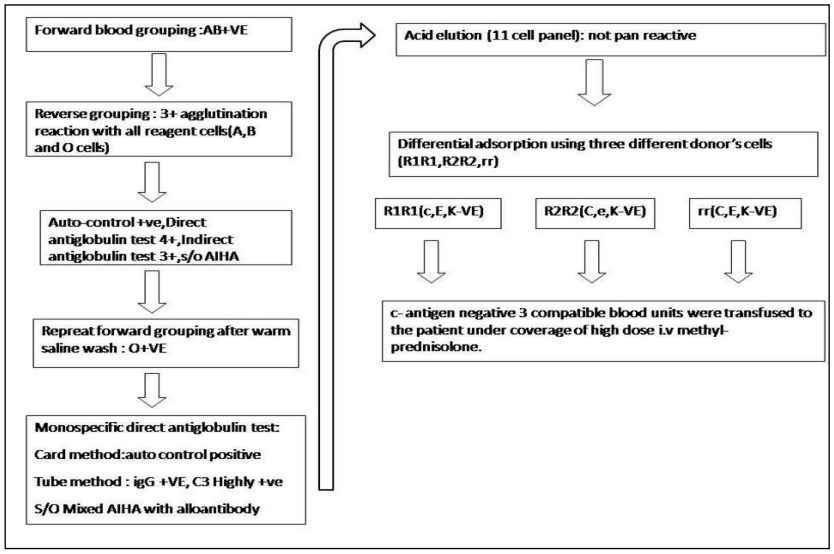

Figure 2: Immuno hematology work up.

Elution

Acid elution (Bag Systems; Germany) was performed to free the IgG antibody from sensitized red cells. The eluate did not show reactivity with all 11 reagent red cells suggesting c-alloantibody. To validate results positive and negative controls were used.

Differential Adsorption

We further did differential adsorption to adsorb auto antibodies so that underlying masked alloantibody(s) could be revealed. The cells used for adsorption were obtained from departmental rare donor registry and donor red cell inventory. Patient's serum sample was divided into three aliquots of 1 ml each. Each aliquot was adsorbed using three different donors' cells (R1R1, R2R2, and rr). Among the three cells, one was negative for c, E, and K; another negative for C, e and K, and the third negative for C, E and K. Adsorption were done at 37°C in incubator for 1 h with intermittent agitation. A total of four sets of cells were used to fully adsorb autoantibody. Following adsorption, 11 cell antibody identification panels were performed separately on each serum aliquot (R1R1, R2R2, and rr), and the reaction pattern was compared to reveal underlying allo antibodies, if any. In "R1R1" - the reaction pattern of 11 cell identification panels matched the pattern with c antigen suggesting "Anti-c" alloantibody as R1R1 cells were negative for c antigen. In "R2R2" - the reaction pattern of all 11 cell identification panels came negative. In "rr" - In 11 cell identification panels, all cells were negative (Figure 1). Three units were found compatible after typing around thirty O positive units considering c antigen negative. The units were transfused to the patient under observation and transfusion was uneventful. Post transfusion the patient was started on high-dose intravenous methylprednisolone to counteract rapidly evolving severe hemolysis.

DISCUSSION

The severity of anemia was driving force for urgent blood transfusion and gave us opportunity to work out the cause for hemolysis along with the past history of receiving blood transfusion. The Rh blood group system has 45 independent antigens, the most important of which are D, C, c, E, and e [1,2]. These antigens are encoded by the RHD and RHCE genes, located together on chromosome 1 [1]. The Rh system is one of the most immunogenic blood groups in humans and is well known for its role in hemolytic disease of the newborn (HDN) [3], in which mothers with Rh negativity are sensitized to the D antigen during their first Rh-positive pregnancy or exposure to Rh-positive blood and subsequently mount a severe immune response to the D antigen during subsequent Rh-positive pregnancies, producing a hemolytic reaction that is life threatening to the fetus [4]. The alloantibody produced is primarily IgG and react optimally at warm temperatures, with obvious clinical significance [5,6].

In this case the cause of hemolysis was alloantibody (anti c), warm and cold antibodies, thus both allo and thermo labile antibodies induced hemolytic anemia.

The c-antigen (little c) which is found in approximately 80% of the United States population, is considered the most clinically significant Rh antigen after D and is associated with severe HDN [7]. Anti-c antibodies arise through previous exposure, such as fetomaternal hemorrhage or transfusion and can produce acute and delayed hemolytic reactions. As with the D antigen, pregnant women and girls are usually sensitized to the c-antigen during an initial pregnancy, and complications occur with repeat exposure during subsequent pregnancies. Similar to the other Rh antibodies, anti-c is also primarily of the IgG type [8]. IgM anti-c however has been reported as well as other Rh IgM antibodies [9-11]. Most Rh-negative blood contains the c-antigen (due to the genetic mechanisms of the Rh system) [12]. Hence, when facing scarcity of Rh negative blood groups for transfusion to sensitized mothers one should opt for Rh-positive blood with c-antigen negative blood units [13].

CONCLUSION

The case demonstrates hemolytic anemia due to alloimmunization (formation of anti-c IgM and IgG) and mixed warm & cold antibodies. It emphasizes the importance of antibody screening in pregnant women to minimize risk of alloimmune life threatening hemolytic anemia.

CONFLICT OF INTEREST

Nil

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