

A rare incidence of Auto Immune Haemolytic Anaemia due to insect bite revealed with blood group discrepancy

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Abstract

Auto Immune Haemolytic Anaemia is a type of immune haemolytic disorder that becomes acquired variety, characterized by shortened red cell survival as a result of altered immune response. In this type of antibody directed against one's own red cell antigen. Moreover, haemolytic anaemia due to autoantibodies which usually occurs due to infection, autoimmune diseases like SLE, Rheumatoid arthritis and some drugs are also responsible for such kind of problems. But insect bite is a very rare occasion for causing such type of incident. The venom of certain spiders, bees, ants, wasps, and some snakes may become responsible for such kind of rare incidence as well as intravascular haemolysis. Here in this description, a very interesting case of Coombs positive haemolytic anaemia has diagnosed due to insect bite. This case is extremely rare for performing any diagnosis for recovering from systemic manifestation. Therefore, this was referred from the department of Haematology for a complete evaluation and for resolving blood group discrepancy as well as for arranging compatible unit of blood for transfusion as it owes to a critical lifesaving condition. Hence early diagnosis of this kind of disease could be able to manage the problem as well as to identify the reason and the consequences for saving the patient life from developing a critical stage as well as for early recovery.

Keywords: Insect bite • Auto immune haemolytic anaemia • Blood group discrepancy

Introduction

Autoimmune hemolytic anemia This is a type of immune haemolytic disorder, this type of anaemia is of acquired variety characterized by shortened red cell survival as a result of altered immune response, "antibody directed against one's own red cell antigen. "The fundamental law of immunity that's the immune antibodies is only produced in an individual to antigens which the individual himself lacks. The cause of such abnormal behavior is not clearly understood in some special cases as lots of reasons are behind this. Sometimes such auto antibodies are easily identifiable against a well known and easily identifiable. However almost all auto antibodies are pan reacting, So that the patient's serum is incompatible not only with his or her own cell but also with those of donors who could be usually chosen for him. These pan reacting antibodies are normally only detectable by the Indirect anti human globulin technique, trypsin or haemolysin techniques. Some also detected by cord blood speciality if possess anti-I or anti-i.

Insect bites are not so common cause to causing any anaemia especially immune antibody usually not produced due to such kind of incidence. Therefore, these manifestations may be mild, self-limiting or sometimes fulminant and in rare case life threatening if not treated properly.

Case Report

A 14 years old girl reside in Dinajpur, northern area of Bangladesh, presented with a history of insect bite on her left arm about 12 days back. Initially she was well tolerated with her indwelling pain but after 3-4 hours,

she developed an agonizing pain which could not be able to be treated at her home. Then she was taken to a nearby local health care center for treating the itching and tender area. After visiting local center she came back to home but developed continuous fever within 24 hours. Therefore, she was presented with weakness and more itching over the bite area. She went to the local health care center where after primary management in OPD she was advised to go home, but within 24 hours of the incidence she developed fever which was high grade (39 c), continuous, subsided with taking paracetamol, associated with fatigue After 4-5 days, the fever subsided but the tiredness and itching in biting site persisted and also she developed jaundice. At this point she again sought help in local health care center where she undergone some investigation which revealed that her Hb level 10.5 gm/dl, MCV 115 f l and reticulocyte count 25%. Total leucocyte count was $13 \times 10^9/L$ (Neutrophil 56%, Lymphocyte 31%, Eosinophil 8%, monocyte 3% and others 2%). Platelet count was $2 \text{ lac} \times 10^9/L$, LDH 1200IU/L. Serum albumin 4.2 g/dl. Total bilirubin 7.47 ng/dl. Indirect Bilirubin 6.5 ng/dl. Alkaline Phosphatase 111IU/L, SGPT 24 IU/L and SGOT were 80 IU/L. Her routine urine examination showed yellowish coloration with plenty of RBC casts, serum creatinine level was normal, coagulation profile: prothrombin time. APTT and FDP were also within normal range. Later (within how many days?) when her hemoglobin level falls to 6.0 gm/dl, periferal blood film was evaluated which showed marked anisocytosis, macrocytosis, schistocytes, spherocyte, nucleated RBC, mild neutrophilic leukocytosis with few reactive lymphocytes and toxic granules and agglutinin also noted. Blood grouping was advised by her physician for planned blood transfusion and it was determined that her blood group was A (RhD) positive but no compatible A (RhD) positive donor was found due to crossmatch incompatibility. Her blood grouping and cross matching were done in another two centers of that region but no compatible unit

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Received date: 09 April, 2021; **Accepted date:** 23 April, 2021; **Published date:** 30 April, 2021

was found, moreover two centers reported that her blood group was AB (RhD) positive. For further evaluation and management she was referred to a tertiary level hospital of Dhaka. After 8 days of insect bite she was admitted at the Department of Hematology and was examined thoroughly. She was found to have severe anemia with dyspnea, jaundice and mild hepatosplenomegaly. She had no history of taking any herbal medication or blood transfusion. As her hemoglobin was 3.2 gm/dl during admission, her blood sample was sent to Transfusion Medicine laboratory for urgent blood grouping and finding a compatible unit.

Later she was advised for confirming her blood group for prompt transfusion. She has three blood grouping report from different centers, which shows that she was A or AB, Rh D positive but cross matching could not be found compatible in periphery with respective three donors. She gave a history of never transfused before. She also added nothing about drug or any herbal remedies to cure from such ongoing condition.

In laboratory, her blood group reactions were as follows (at room temperature): (At the first day) (Table 1)

| Forward grouping | | | Reverse grouping | | | Rh (D) typing | |
|------------------|----|------|------------------|--------|--------|---------------|-----|
| -B | -A | -AB | A cell | B cell | O cell | -D | A/C |
| (+) | ++ | (++) | +- | ++ | +- | ++ | ++ |

Table 1. At the first day

(Therefore, reveals) forward as AB and in reverse O group At 4°C (Table 2)

| Forward grouping | | | Reverse grouping | | | Rh (D) typing | |
|------------------|----|-------|------------------|--------|--------|---------------|-----|
| -B | -A | -AB | A cell | B cell | O cell | -D | A/C |
| (+) | ++ | (+++) | ++ | +- | +- | ++ | ++ |

Table 2. At 40C

Tube method: at 37°C (Table 3)

| Forward grouping | | | Reverse Grouping | | | Rh (D) typing | |
|------------------|-----|------|------------------|--------|--------|---------------|-----|
| -B | -A | -AB | A cell | B cell | O cell | -D | A/C |
| (-) | (+) | (++) | - | ++ | +- | ++ | - |

Table 3. Tube method: at 370C

After 3 days, again her fresh blood sample was rechecked for grouping (Table 4)

| Forward grouping | | | Reverse Grouping | | | Rh (D) typing | |
|------------------|----|-----|------------------|--------|--------|---------------|-----|
| -B | -A | -AB | A cell | B cell | O cell | -D | A/C |
| (-) | ++ | ++ | - | ++ | - | ++ | +- |

Table 4. After 3 days, again her fresh blood sample was rechecked for grouping

So, she was reported as a case of blood group A Rh D positive. In this present case, DAT showed positive reaction with antihuman globulin C3d but negative with IgG specific antihuman globulin (using both poly specific and monospecific antihuman globulin reagent). Indirect Coombs test was also positive. Her extended red cell phenotype was done which showed presence of Rh C, D and e antigen and genotype was R1R1, others shows K-k+, Fya-b+, Jka – b+ and others could not be done due to resource limitation.

After group confirmation patient was transfused with 2 unit of phenotypically matched A RhD positive packed red cell following IAT cross matching with no obvious transfusion reaction. Hence, treatment of the itching area though it was recovering. Therefore, she found incompatible with more three A Rh D positive donor. Moreover, she was further on steroid coverage and responding well. Next, she was transfused with phenotypically matched two units of A Rh D positive compatible packed red cell and there was no obvious hemorrhagic transfusion reaction was noticed with total blood unit

transfusion.

Besides blood transfusion, the patient was also on systemic steroid, Iron supplementation, antibiotics, diuretics and care of biting site. The patient's clinical condition began to improve. She was discharged 4 days later on a quick tapered oral steroid regimen, and was instructed to continue her wound care. During follow up visit, her bite site was completely healed, and she had no further evidence of anemia.

Discussion

Autoimmune hemolytic anemia is a fairly uncommon disorder with an estimation of the incidence at 1–3 cases per 100,000 per year [1-3]. In contrast, alloimmune hemolytic anemia requires exposure to allogeneic red cells through pregnancy, transfusion or transplantation. The incidence of acute hemolytic transfusion reactions has been estimated to be 0.003%–0.008%, while 0.05%–0.07% of transfused patients develops a clinically recognized delayed hemolytic transfusion reaction [4-6]. Delayed serologic transfusion reactions are more common and are a frequent finding in patients who receive multiple transfusions [7].

This is the first case reporting in our country of insect bite induced Auto Immune Haemolytic anaemia associated with blood group discrepancy and cross matching incompatibility. Envenomation by bees, wasps, certain spiders and snakes can rarely cause intra vascular hemolysis. The manifestations may be mild, self-limited or fulminant and life threatening. Usually, there is history of allergic reaction due to insect bite, but cases with severe systemic disturbances in absence of any cutaneous lesion have also been described [1].

In case study of Céline Phan shows a case of 67 year old man got a bed bugs bite and developed erythematous papules on the abdomen, limbs, and bottom for over 1 week, with a general feeling of malaise. He was given topical steroids and came back 3 days later because of asthenia, fever, inflammatory bilateral edema, and arthralgia of both wrists and hands without palpable synovitis. He also reported conjunctivitis, as well as a sore throat at the beginning of the eruption that had spontaneously regressed within 48 hours [3]. It has been reported in many countries, presumably due to insecticide resistance and growing international trade and travelling. Bed bug bites usually cause localized reactions such as itchy maculopapular wheals. Systemic reactions have rarely been described, even if severe bullous reactions and anaphylaxis have been reported [1].

In a case from David R Lane et al. a 19 years old African American woman presented with similar type of case after a painless bite from a "brown spider" in her bed that she went to her physician after 2 days. At this initial evaluation, she had a diffuse maculopapular rash with mild systemic symptoms including malaise and arthralgia. No laboratory workups were done, and she was started on a 5 day steroid dose pack. Her laboratory workup at this time showed a mildly elevated total bilirubin level, mild leukocytosis, anemia with a hemoglobin level of 11.7 mg/dL and later dropped to 6.9 gm/dl and later she had 5.7 gm/dl. Her DCT was positive but ICT remains negative. Later she also developed nausea, peripheral edema, lymphadenopathy, fever, and dysuria, along with worsening pain and erythema at the bite site. She was admitted for hematologic monitoring and supportive measurements [2].

Warm autoantibodies are responsible for 48%–70% of autoimmune hemolytic anemia cases [8,9]. Positive direct antiglobulin test may be the first serological evidence. Anemia is of variable severity and some patients present with fulminant hemolysis, jaundice, pallor, hemoglobinuria and hepatosplenomegaly [10].

In this current case, the patient was grouped wrongly and later after confirmation of blood group transfused with A positive blood after referral to our center. She presented with severe life threatening anemia, jaundice, mild hepatic as well as splenic enlargement and evidence of hemolysis. The direct and indirect antiglobulin tests were positive. Therefore, cross

matching incompatibility was found with several donors. But antibody screening was done with prompt effort but could not be able to find out the causative antibody as we don't have panel cell for antibody identification. Moreover, due to time limitation we couldn't go through elution and adsorption technique.

Approximately 57% of patients with warm autoimmune hemolytic anemia have free serum autoantibody and a positive indirect antiglobulin test [11]. Due to pan agglutinin in the serum of patients with autoimmune hemolytic anemia, cross matching blood is a difficult and time consuming process since the pan agglutinin reacts with all donors' red blood cells. Moreover, the most pressing problem is detection and identification of RBC alloantibodies that may be masked by the autoantibodies [12]. In our patient, the anemia was life threatening with time constraints to perform adsorption studies with subsequent identification of underlying alloantibodies.

In this patient after thorough serological evaluation, the optimal blood for transfusion was still likely to be mismatched. And after administration of steroid, we could be able to give her a compatible unit of blood for transfusion. When a decision to transfuse least incompatible blood has to be made, transfusion of small aliquots to provide relief of symptoms and to avoid fluid overload has been recommended. It has also been recommended to transfuse using leucocyte reduced blood products if patient can afford or with pre-medication with antihistamines and antipyretics to prevent febrile and allergic reactions, respectively, in patients with multiple antibodies [12-14].

The final decision to transfuse should depend on the proper evaluation of the patient's blood group discrepancy, clinical condition of the patient and availability of experienced and competent health care provider.

Conclusion

Insect bite is a rare incidence to cause such type of AIHA. And this is the first case report in our country that went for such evaluation. This case suggests that insect bites may trigger multi systemic inflammatory reaction. So, each patient with AIHA should be treated with a detail history. According to American Society for Apheresis, AIHA is Category II for indication of plasma exchange. We can perform adsorption and elution test for identifying the autoantibody. Moreover, we can arrange panel cell of R2R2, rr and R1R1 and other minor cell reagents for proper evaluation and management. In special cases (Rh) 'e' negative blood transfusion is also recommended if Evans syndrome is suspected. We can also treat the

patient with immunosuppressive drugs like Rituximab, Azathioprine etc. Follow up these patients with proper counseling. Even patient's attendance counseling is also a part to evaluate the cases properly. Sometimes family screening could be able to guide us to solve the discrepancy.

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How to cite this article: Miah SS, Doha MA, Sharmin M, Islam A, Khatun A and Sharmin Net al., (2021) A rare incidence of Auto Immune Haemolytic Anaemia due to insect bite revealed with blood group discrepancy. *J Blood & Lymph Res* 11: 253