

Cold Autoimmune Haemolytic Anaemia with Blood Group Determination Challenge: A Case Report

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ABSTRACT

Autoimmune Haemolytic Anaemia (AIHA) is a rare, life-threatening condition characterised by the immune-mediated destruction of erythrocytes. AIHA can be classified as either warm or cold, based on the type of antibodies involved. Although idiopathic in many cases, AIHA necessitates a thorough work-up to exclude secondary causes such as infections, drug reactions, or autoimmune diseases. The present case report documents the presentation, clinical findings, diagnosis, treatment and outcome of a 15-year-old female patient with cold AIHA, who presented with fever and generalised bodyaches. Diagnostic evaluations included a positive Direct Coombs Test (DCT), elevated Lactate Dehydrogenase (LDH) and indirect hyperbilirubinemia, all suggestive of haemolysis. Management involved intravenous corticosteroids and supportive care, resulting in significant clinical improvement. The present report highlights the diagnostic complexity and treatment approach in managing cold AIHA, especially when compounded by challenges in blood typing.

Keywords: Cold agglutinin disease, Immunodeficiencies, Intensive care unit, Warm autoimmune haemolytic anaemia

CASE REPORT

A 15-year-old female presented to the Paediatric Outpatient Department at Dhiraj General Hospital with a 3-4 day history of fever and generalised body ache. On physical examination, her liver was palpable at 9 cm (smooth margin and non tender), while the spleen was non palpable. Laboratory findings included Haemoglobin (Hb) of 2.9 g/dL (normal range: 12-14 g/dL), Total Count (TC) of 12,800/mm³ (normal range: 4,500-13,500/mm³), Erythrocyte Sedimentation Rate (ESR) of 25 (normal range: 0-20 mm), Platelet Count (PC) of 3.50 (normal range: 1.5-3.5 lacs/mm³) and a reticulocyte count of 6% (normal range: 0.5-1%). Sickling tests returned positive, with indirect bilirubin of 1.6 mg/dL (normal range: 0.2-0.8 mg/dL), direct bilirubin of 0.7 mg/dL (normal range: 0.1-0.3 mg/dL) and a markedly elevated LDH level of 2,666 U/L (normal range: 157-272 U/L) [1]. No radiological investigations were performed. A positive DCT was observed with Grade 3 agglutination. Given the patient's negative High-performance Liquid Chromatography (HPLC) report, absence of drug history and positive Coombs test, a provisional diagnosis of AIHA is strongly supported. The patient's blood group was initially indeterminate due to autoagglutination. The autoimmune work-up was positive for Antinuclear Antibodies (ANA) with a strong reaction to the Ku antigen.

Treatment included injection of methylprednisolone at 2 mg/kg/dose every six hours for five days, followed by oral prednisolone at 2 mg/kg/day twice a day for 2-3 months. Transfusion support was also required due to the patient's significantly low haemoglobin level (2.9 g/dL), which posed an immediate risk for hypoxia and end-organ damage. The transfusion of O-negative packed red cells, despite challenges in blood typing, provided critical support in stabilising the patient's condition. The choice of O-negative blood was appropriate given the uncertainty around the patient's blood group, minimising the risk of alloimmunisation during transfusion. It is crucial to monitor such patients closely for transfusion reactions, especially when autoagglutination is a complicating factor.

The patient's gradual improvement with corticosteroids and transfusions allowed for a tapering of the steroid dosage over time,

demonstrating the effectiveness of the chosen therapeutic strategy. The decision to taper the steroids was based on the progressive stabilisation of haemoglobin levels and the resolution of active haemolysis, as evidenced by decreasing LDH levels and improving reticulocyte counts. A careful tapering process helps to avoid the risk of recurrence. The patient was discharged with a stable haemoglobin level of 9 g/dL, but regular follow-up is essential to monitor for relapse, especially during exposure to cold temperatures, which can exacerbate haemolysis.

Prognosis and Long-term Management: The prognosis of cold AIHA depends on factors such as the severity of haemolysis, underlying conditions and response to treatment. Patients with secondary causes, such as autoimmune disorders, may require long-term immunosuppressive therapy or specific treatments for the underlying condition. In this case, the positive ANA profile indicates the need for ongoing surveillance for connective tissue diseases or other autoimmune conditions that could influence long-term outcomes. Furthermore, the management of cold AIHA may include additional strategies such as plasmapheresis in cases of severe haemolysis or poor response to conventional therapy.

Follow-up: On follow-up, when the patient developed features of Systemic Lupus Erythematosus (SLE) symptoms like malar rash and arthritis along with a positive ANA profile, hydroxychloroquine and low-dose steroids were started and the dosage was gradually tapered upon symptomatic improvement.

DISCUSSION

The AIHA is a condition in which erythrocytes are destroyed by the body's immune system, leading to severe anaemia and related complications [2]. AIHA can be classified as either warm or cold, based on the type of antibodies involved. Although idiopathic in many cases, AIHA necessitates a thorough work-up to exclude secondary causes such as infections, drug reactions, or autoimmune diseases [3,4].

Cold AIHA is further subdivided into two primary types: Cold Agglutinin Syndrome (CAS) and Paroxysmal Cold Haemoglobinuria (PCH). CAS is the more common form and involves IgM antibodies

that react with Red Blood Cells (RBCs) at low temperatures (usually 4°C) but may continue to cause haemolysis at body temperature by activating the complement system [5]. This complement-mediated destruction occurs primarily intravascularly, leading to haemolysis. PCH, on the other hand, involves polyclonal IgG antibodies known as Donath-Landsteiner antibodies, which bind to RBCs at cold temperatures but trigger haemolysis when the blood is rewarmed. This biphasic nature of haemolysis distinguishes PCH from CAS. Although both conditions involve cold-reactive antibodies, they vary in their pathophysiology and management [6].

In the presented case, the patient demonstrated features consistent with cold AIHA, such as a positive DCT and significant auto-agglutination, which made blood grouping particularly challenging. This difficulty in blood typing is a known complication of cold AIHA, as cold agglutinins can cause the clumping of RBCs, interfering with standard blood typing procedures. This necessitates the use of special techniques, such as pre-warming of samples, to avoid false results. Despite these efforts, in this case, the blood type could not be reliably determined initially, complicating transfusion management [7].

The immunological profile of the patient showed a positive Antinuclear Antibody (ANA) profile with antibodies to Ku, indicating the potential involvement of an underlying autoimmune process. The association between cold AIHA and autoimmune disorders is well-documented in the literature, where AIHA can occur as a primary condition or secondary to autoimmune diseases, infections (especially respiratory viral infections), or lymphoproliferative disorders. A thorough immunological work-up is, therefore, crucial in such cases to identify any underlying causes that may influence treatment decisions and prognosis [8,9].

Management of cold AIHA involves a multifaceted approach aimed at reducing haemolysis, improving anaemia and addressing the underlying immunological triggers. In the present case, the use of high-dose intravenous corticosteroids played a pivotal role in controlling the autoimmune response and reducing haemolysis.

Corticosteroids help by suppressing the production of autoantibodies and reducing inflammation, leading to the stabilisation of haemoglobin levels. However, corticosteroids are often less effective in cold AIHA compared to warm AIHA, as the primary mechanism in cold AIHA involves complement-mediated destruction rather than direct antibody-mediated RBC destruction [10,11].

CONCLUSION(S)

The present case illustrates the complexities involved in diagnosing and managing cold AIHA, particularly when blood typing is challenging. The positive response to corticosteroid therapy highlights the effectiveness of immunosuppressive treatment for AIHA, while ongoing monitoring remains essential for preventing recurrence.

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AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Nov 30, 2024
- Manual Googling: Dec 26, 2024
- iThenticate Software: Jan 06, 2025 (3%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

Date of Submission: Nov 29, 2024
Date of Peer Review: Dec 19, 2024
Date of Acceptance: Jan 08, 2025
Date of Publishing: Mar 01, 2025