Cold Agglutinin-Induced Haemolysis in SLE Patient: A Case Series

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can cause hemolytic anemia, usually linked to warm antibodies. Cold agglutinin disease (CAD) in SLE is rare. This report presents three cases of severe anemia in SLE patients, emphasizing diagnosis, treatment, and the role of corticosteroids and immunosuppressants in management. C**ase Series:** This case series presents three female patients with systemic lupus erythematosus (SLE) complicated by cold agglutinin disease. Severe anemia was confirmed with positive direct antiglobulin tests. Treatment included corticosteroids, immunosuppressants, and transfusions when necessary. All patients showed hematological improvement, emphasizing individualized therapy for effective management of SLE-associated hemolytic anemia. **Conclusion:** Thesecases effectively highlight the rarity of cold agglutinin disease in systemic lupus erythematosus (SLE) and emphasize the importance of tailored treatment strategies. The positive response to methylprednisolone and Rituximab underscores their therapeutic value, while safe RBC transfusion practices help mitigate complications.
Key words: Systemic lupus erythematosus (SLE), Cold agglutinin disease (CAD), Autoimmune hemolytic anemia (AIHA), Immunosuppressants, Antiglobulin test

Introduction

Systemic lupus erythematosus (SLE) is a well-known autoimmune, chronic inflammatory disease affecting virtually any organ system. Hemolytic anemia has been observed in fewer than 10% of patients with SLE, typically caused by warm antibodies. However, cold antibody-mediated hemolytic anemia in SLE is exceptionally rare, with only a handful of

documented cases in the literature.[1] Cold-antibody autoimmune hemolytic anemia, referred to as cold agglutinin disease in its primary form, is a type of hemolysis triggered by immunoglobulin M (IgM) antibodies targeting polysaccharide antigens on the red blood cell membrane. It represents 15%–30% of all autoimmune hemolytic anemias.[2] Autoimmune hemolytic anemia (AIHA) is an uncommon manifestation that may appear before the diagnosis of SLE or serve as an initial indicator of the disease. SLE-associated AIHA primarily affects females and can occur at any age, though it is more frequently observed in younger individuals. Patients with SLE who develop AIHA typically present with symptoms of anemia, such as fatigue, pallor, and dyspnea, along with signs of hemolysis, including jaundice, dark urine, and splenomegaly. The cornerstone of treatment for AIHA in SLE is high-dose glucocorticoids; for patients with severe, rapidly progressive hemolysis, intravenous methylprednisolone may be administered at doses ranging from 250 to 1,000 mg/day for one to three days.[3] Here we present a series of 3 cases of SLE who presented with severe anemia with cold agglutinin disease.

Case-1

A 17-year-old female patient came with severe anemia with the diagnosis of SLE. She also has malaria. The chief complaints are generalized weakness, fatigue, fever, night sweats, light-headedness, and dyspnea on exertion. On physical examination, the patient had mild pallor, icteric sclerae, and grade II edema in the lower limbs. The classification criteria for SLE were met. Her ANA was positive, and her Hb level was 5.3gm/dl. She has a history of multiple transfusions.

Autoimmune hemolytic anemia was also confirmed, with laboratory data revealing a cold agglutinin titer Positive dilution 1/128 at 4°C, Polyspecific Direct Antiglobulin Test (DAT): Grade 4 positive

Indirect Antiglobulin Test (IAT): Grade 2 positive

Auto Control: Grade 2 positive

Monospecific DAT: Grade 2 positive for C3d.

Other investigation: Increased level of Serum Bilirubin and LDH, Reticulocyte count: 27%

Treatment was initiated with Methyl Prednisolone at a dose of 200 mg daily orally and Hydrocloroquine. The patient showed clinical improvement and hematological recovery without requiring blood transfusions. Following outpatient treatment with oral prednisone (5 mg daily) and hydroxychloroquine (200 mg daily), they were discharged from the hospital.

Case: 2

A 16-year-old female patient was admitted to our hospital with severe anemia and with diagnosed case of SLE. Investigations showed positive ANA, anti-Smith & anti-RNP antibodies. She has a history of multiple blood transfusions. The patient's hemoglobin level was recorded at 4.0 gm/dL. Blood grouping and antibody screening were conducted to assess compatibility and identify potential immune reactions before proceeding with further medical interventions.

Polyspecific Direct Antiglobulin Test (DAT): Grade 3 positive

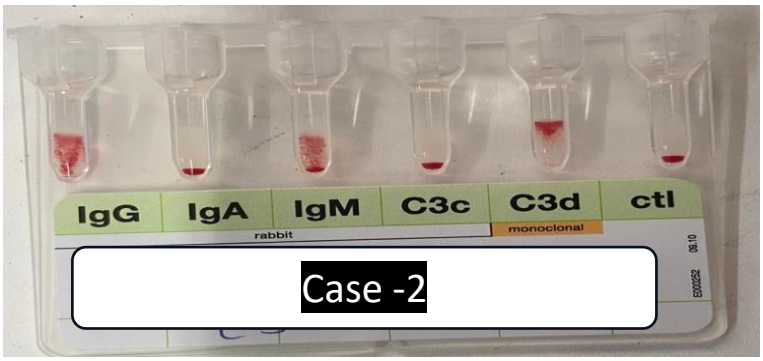
Indirect Antiglobulin Test (IAT): Grade 2 positive

Auto Control: Grade 3 positive

Monospecific DAT: Grade 2 positive for IgM & grade 3 positive for C3d and IgG.

Other investigation: Increased level of Serum Bilirubin (6.3) and LDH.

Treatment: Rituximab, Methyl Prednisolone, and Azathioprine.



Case-3

A 60-year-old female patient was admitted to the medicine department with severe anemia. She has been diagnosed with SLE with dermatomyositis. She has a history of 2-unit PRBC transfusions within 6 months. Her Hb was 6.0gm/dl. ANA and dsDNA positive. In our blood centre, Blood grouping and Antibody screening are done.
Polyspecific Direct Antiglobulin Test (DAT): Grade 3 positive
Indirect Antiglobulin Test (IAT): Grade 2 positive
Auto Control: Grade 3 positive
Monospecific DAT: Grade 4 positive for IgM & C3d.

Other investigation: Increased level of Serum Bilirubin and LDH.
The patient received treatment with Rituximab, Methylprednisolone, and Azathioprine. Additionally, one unit of PRBC was transfused at our blood center to manage anemia and support hematological recovery during the course of treatment.

Discussion

Autoimmune hemolytic anemia (AIHA) is a rare condition, affecting 1–3 individuals per 100,000 annually. It occurs in 10% of patients with systemic lupus erythematosus (SLE), typically linked to warm antibodies, though cold hemagglutinin disease is seldom observed. This paper discusses an AIHA case caused by cold agglutinins in an SLE patient.[4]

Remission occurs in fewer than 20% of cold agglutinin disease patients treated with corticosteroids, and those who respond often require high maintenance doses to sustain the effect. Due to the limited efficacy and potential risks of prolonged corticosteroid use, alternative treatments should be considered. Bendamustine or rituximab are preferred options, offering more targeted approaches with potentially better outcomes. These therapies can help minimize the adverse effects associated with high-dose corticosteroid regimens while providing effective disease control. Identifying the most suitable treatment strategy is crucial to improving patient outcomes and reducing the need for prolonged corticosteroid dependence.[5]

In cold agglutinin syndrome, treating the underlying disease remains the primary therapeutic approach. As observed in our patient, corticosteroid administration led to a positive clinical and paraclinical response. Similar cases reported in medical literature have demonstrated favorable outcomes with this treatment, reinforcing its effectiveness.[6] While no universally established therapy exists beyond managing the root cause, corticosteroids have been utilized successfully in cases like ours. The response observed aligns with previous findings, highlighting the beneficial impact of corticosteroid treatment. Further studies may provide deeper insights, but current evidence supports its role in achieving adequate patient improvement and symptom control.[7]

The cases reported here predominantly involve female patients in their second decades of life, with one exception—a female patient in her fifth decade. All individuals exhibited elevated bilirubin levels, primarily due to indirect bilirubin. Immunosuppressive treatment was administered across all cases, yielding favorable responses. However, in one instance (case 3), the patient required a PRBC transfusion in addition to immunosuppressive therapy. These findings suggest a consistent clinical presentation and response pattern, reinforcing the effectiveness of immunosuppressive treatment. While most patients benefited from this approach without additional interventions, the need for transfusion in one case highlights potential variations in disease severity and management requirements. Further studies could provide deeper insights into age-related factors influencing disease progression and response to treatment, helping refine therapeutic strategies for optimizing patient care and outcomes in similar cases.

Conclusion

Cold agglutinin disease is a rare form of autoimmune hemolytic anemia, infrequently linked to systemic lupus erythematosus (SLE). Treatment should prioritize addressing the underlying cause to achieve effective management. In this case, the patient exhibited a positive response to methylprednisolone and Rituximab, reinforcing their therapeutic role. Additionally, RBC transfusion can be safely administered in cold agglutinin disease when appropriate precautions are taken to minimize complications. This approach underscores the importance of individualized treatment strategies to optimize patient outcomes while mitigating risks associated with hemolysis and transfusion-related challenges in this rare condition.

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