CASE REPORT

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Autoimmune hemolytic anemia in a patient with systemic lupus erythematosus: a case report

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ABSTRACT

Introduction: Autoimmune hemolytic anemia (AIHA) is a rare disorder characterized by the destruction of red blood cells due to the presence of autoantibodies that target the patient's own erythrocytes. Given the increasing incidence of AIHA in cases of systemic lupus erythematosus (SLE) and the urgent need for prompt treatment, accurate diagnostic and therapeutic approaches are essential to achieving favourable clinical outcomes. The aim of this study is to report autoimmune hemolytic anemia in a patient with systemic lupus erythematosus.

Case description: A 38-year-old female patient was referred with a diagnosis of anemia, suspected autoimmune hemolytic anemia (AIHA), and suspected systemic lupus erythematosus (SLE). The patient reported experiencing paleness, which she had noticed for the past month, and a history of blood transfusion at a previous hospital. She also complained of fatigue that had been present for the past nine months.

Conclusion: Knowledge of appropriate diagnostic and therapeutic approaches is essential to prevent misdiagnosis and mistreatment. In this case, it can be concluded that the diagnosis and management of AIHA were carried out in accordance with the hospital's standard operating procedures.

Keywords: Autoimmune hemolytic anemia, hematology, paleness, systemic lupus erythematosus.
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INTRODUCTION

The rare condition known as autoimmune haemolytic anaemia (AIHA) is typified by the death of red blood cells as a result of autoantibody reactions that specifically target the patient's erythrocytes. With an average death rate of about 11%, its incidence is estimated to be between one and three cases per 100,000 population annually. Children have a lower mortality rate (about 4%), however diseases like mixed-type AIHA and Evans syndrome (autoimmune thrombocytopenia) can have higher mortality rates (up to 10%). Around 75% of cases of AIHA are classified as warm-type (mediated by IgG and involving high-temperature extravascular haemolysis), 15% as cold-type (mediated by complement activation at low temperatures and involving intravascular haemolysis), and less than 5% as mixed-type. This classification is based on the range of temperatures at which the pathogenesis-related autoantibodies are active. The causes of AIHA vary greatly. Idiopathic causes account for almost half of instances, with the remaining 20% being linked to lymphoproliferative disorders, 20% to autoimmune diseases such systemic lupus erythematosus (SLE), and the remaining 1% to infections and cancers.[1–3]

Clinical signs and symptoms of AIHA usually appear gradually over months to years, depending on how severe the anaemia is. Compensated anaemia, reticulocytosis, and moderate hyperbilirubinemia are examples of asymptomatic cases; fulminant haemolysis might manifest as jaundice, hepatosplenomegaly, tachycardia, and angina. The degree of haemolysis and the underlying disease can affect these clinical characteristics, which are influenced by the type of autoantibody that is implicated. In comparison to patients with cold-type AIHA, individuals with warm IgM-mediated AIHA typically have more severe haemolysis and a greater fatality rate. The body's compensatory response, specifically its capacity to boost reticulocyte production, often determines how severe anaemia is. Individuals with reticulocytopenia typically have more severe symptoms and frequently need transfusions of red blood cells.[4]

The general diagnostic strategy for AIHA entails confirming hemolysis-induced anaemia with serological evidence of anti-erythrocyte antibodies, which are usually found by the direct antiglobulin test (DAT).[5] Additionally, AIHA is intimately linked to systemic lupus erythematosus (SLE), a multi-organ system autoimmune disease with different clinical manifestations depending on the organs affected. One of the common haematologic symptoms of SLE is AIHA. Other organ involvement that is typical of SLE is frequently seen in patients with AIHA secondary to SLE.[6]

Given the increasing incidence of AIHA in SLE patients and the urgency of initiating timely treatment, accurate diagnosis and management are critical for achieving optimal outcomes. The aim of this study is to report autoimmune hemolytic anemia in a patient with systemic lupus erythematosus.

Table 1. Complete blood count results at Prof. I.G.N.G. Ngoerah General Hospital

Parameter	22/04/24	23/04/24	26/04/24	29/04/24	30/04/24	Reference Range
WBC (10^3/µL)	12.14	11.06	8.68	9.87	6.54	4.1 – 11.0
% Neutrophils	82.70	95.00	84.10	80.30	74.70	47.0 – 80.0
% Lymphocytes	11.70	3.20	12.30	15.70	19.60	13 – 40
% Monocytes	5.30	1.80	3.50	3.90	4.70	2.0 – 11.0
% Eosinophils	0.20	0.00	0.10	0.00	0.80	0.0 – 5.0
% Basophils	0.10	0.00	0.00	0.10	0.20	0.0 – 2.0
# Neutrophils	10.05	10.51	7.30	7.93	4.89	2.50 – 7.50
# Lymphocytes	1.42	0.35	1.07	2.57	1.28	1.00 – 4.00
# Monocytes	0.64	0.20	0.30	0.01	0.31	0.10 – 1.20
# Eosinophils	0.02	0.00	0.01	1.55	0.05	0.00 – 0.50
# Basophils	0.01	0.00	0.00	0.38	0.01	0.0 – 0.1
RBC (10^6/µL)	1.67	1.74	2.25	2.57	2.86	4.5 – 5.9
Hemoglobin (g/dL)	5.10	5.30	6.80	7.70	8.40	13.5 – 17.5
Hematocrit (%)	17.30	18.60	22.80	25.30	27.40	41.0 – 53.0
MCV (fL)	103.60	106.90	101.30	98.40	95.80	80.0 – 150.0
MCH (pg)	30.50	30.50	30.20	30.00	29.40	26.0 – 34.0
MCHC (g/dL)	29.50	28.50	29.80	30.40	30.70	31 – 36
RDW (%)	23.10	23.00	19.70	18.10	17.30	11.6 – 14.8
Platelets (10^4/µL)	333	300	350	284	246	150 – 440

Table 2. Complete blood count results at KLB Regional Hospital

Parameter	14/04/2024	17/04/2024	20/04/2024	Reference Range
WBC (10^3/µL)	26.8	19.3	7.98	3.80 – 10.60
# Neutrophils	23.5	16.1	6.56	1.5 – 7.0
# Lymphocytes	2.50	2.01	1.03	1.00 – 3.70
Hemoglobin (g/dL)	4.2	4.0	4.4	13.2 – 17.3
Hematocrit (%)	13.1	12.5	14.6	40.0 – 52.0
MCV (fL)	95.3	96.2	99.3	99.38 – 100.0
MCH (pg)	30.6	30.8	29.9	26.0 – 34.0
Platelets (10^4/µL)	381	298	283	150 – 440

CASE DESCRIPTION

A 38-year-old female patient was referred with a diagnosis of anemia, suspected autoimmune hemolytic anemia (AIHA), and suspected systemic lupus erythematosus (SLE). The patient reported experiencing pallor for the past month and had a history of blood transfusion at a previous hospital. She also complained of fatigue that had persisted for the past nine months, accompanied by intermittent fever, hair loss, and frequent joint pain. Upon arrival at the referral hospital, the patient remained fatigued and reported epigastric pain and bilateral lower limb edema. She was afebrile and denied experiencing cough or shortness of breath.

In September 2023, the patient began experiencing fatigue, intermittent fever, significant hair loss, and joint pain. Upon evaluation at the hospital, she was suspected of having an autoimmune disease and hypertension. Since then, she had been prescribed methylprednisolone 4 mg every 8 hours and amlodipine 5 mg once daily; however, medication adherence was inconsistent.

In March 2024, she was hospitalized for five days with a hemoglobin level of 6 g/dL and received two units of packed red cells (PRC), after which she was discharged.

In April 2024, the patient again presented with intermittent fever and reported heavier-than-usual menstrual bleeding. She was brought to the hospital, where her hemoglobin level was found to be 4.2 g/dL. A PRC transfusion was planned; however, four major crossmatch attempts resulted in incompatibility, and the patient subsequently left the hospital against medical advice.

Family history revealed no similar complaints among other family members, and there was no known history of systemic diseases within the family. From the social history, the patient is the first of two siblings; her younger sibling is in good health. The patient's current medications include: Candesartan 8 mg once daily, Vitamin D3 1000 IU once daily, Folic acid 1 mg three times daily, Methylprednisolone 16 mg three times daily, Bisoprolol 2.5 mg once daily, Omeprazole (OMZ) 40 mg once daily, and Methylprednisolone 62.5 mg twice daily.

Physical examination revealed a moderately ill general condition, with a Glasgow Coma Scale (GCS) score of E4V5M6. Vital signs were as follows: blood pressure 140/80 mmHg, pulse rate 81 beats per minute and weak, respiratory rate 20 breaths per minute, and body temperature 36.7°C. The patient's height was 158 cm and weight 45 kg. On physical examination, both conjunctivae appeared pale, alopecia was observed, there was

tenderness in the epigastric region, and bilateral pretibial edema was present. Other physical findings were within normal limits.

According to the ACR/EULAR classification criteria, the patient scored +2 for alopecia, +6 for joint involvement, and +4 for proteinuria. Based on the MEX-SLEDAI scoring system, the patient scored +2 for arthritis, +2 for mucocutaneous involvement (alopecia), and +1 for fatigue. To support the diagnosis, several investigations were performed, including complete blood count, clinical chemistry, Coombs test, antinuclear antibody (ANA) testing, peripheral blood smear, urinalysis, and chest X-ray. Complete blood count revealed severe anemia, and reticulocyte analysis indicated evidence of hemolysis, as shown in Tables 1, 2, and 3.

Clinical chemistry evaluation revealed hypoalbuminemia and elevated LDH levels, as shown in Tables 4 and 5 below.

Coomb's test results revealed positive findings in both the direct and indirect tests, as demonstrated in Tables 6 and 7.

Interpretation of Tables 6 and 7 were described as: the patient has blood type B, Rhesus positive.; sensitization of red blood cells by IgG components and complement was observed in vivo (indicated by a positive direct Coomb's test); the presence of incomplete antibodies or complement in the plasma was demonstrated after incubation with red blood cells in vitro (positive indirect Coomb's test). The ANA immunofluorescence (IF) test revealed a homogeneous staining pattern with a titter of 1:10,000. This pattern may be observed in conditions such as systemic lupus erythematosus (SLE), drug-induced SLE, and juvenile idiopathic arthritis. Further testing with an ANA profile is recommended if there are clinical indications suggestive of autoimmune disease, as illustrated in Table 8 and Figure 1.

The peripheral blood smear examination revealed signs of hemolysis, as presented in Table 9.

The complete urinalysis revealed hematuria and proteinuria, as presented in Table 10.

The patient was found to have pneumonia and pulmonary edema, as demonstrated in Figure 2.

Based on Figure 2, the impression was: pneumonia; cardiomegaly accompanied by early-stage pulmonary edema. Based on the history taking, physical examination, and supporting investigations, the working diagnosis was Autoimmune Hemolytic Anemia (AIHA) and suspected Systemic Lupus Erythematosus (SLE) with high disease activity. Therefore, the therapeutic management administered included: intravenous fluid drip at a rate of 20 drops/minute; low-sodium diet (1,900 kcal/day); packed cell transfusion (1 unit/day), continued until hemoglobin reaches 10 g/dL; Methylprednisolone pulse therapy at a dose of 500 mg intravenously; Ranitidine 50 mg intravenously every 12 hours; Candesartan 8 mg orally every 24 hours; Amlodipine 5 mg orally every 24 hours.

Table 3. Reticulocyte count results at Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

Parameter	Unit	Result	Reference Range
% Reticulocytes	%	16.52	0.76 – 2.21
# Reticulocytes	10^6/µL	0.29	0.03 – 0.10

Table 4. Clinical chemistry laboratory results at Prof. I.G.N.G. Ngoerah General Hospital

Parameter	Unit	22/04/2024	26/04/2024	Reference Range
Albumin	mg/dL	2.5	2.5	3.40 – 4.80

Table 5. LDH examination result at Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

Parameter	Unit	Result	Reference Range
LDH	U/L	358	125 – 220

Table 6. Direct Coomb's Test Results Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

IgG	C3d	Control	Method
4+	3+	Negative	Gel Test

DISCUSSION

The autoimmune reaction that causes autoantibodies to target erythrocyte surface antigens causes red blood cell lysis in autoimmune haemolytic anaemia (AIHA), a diverse set of disorders. Red blood cells are directly attacked by the patient's immune system's anti-erythrocyte antibodies, which results in haemolytic anaemia.[7] AIHA is regarded as an uncommon cause of anaemia, with a prevalence of 9.5 per 100,000 people and an incidence rate of 1.8 per 100,000 people annually. AIHA is most frequently identified in older persons, with most patients being over 40 at the time of diagnosis, even though it can happen at any age.[8]

Based on the temperature at which autoantibodies bind to red blood cells

Table 7. Indirect Coomb's Test Results Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

Identical Cells	Same Blood Type Cells	Autocontrol	Temperature	Method
2+	2+	3+	37°C	Gel Test

Table 8. ANA IF Test Results at Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

Parameter	Unit	Result	Reference Value
ANA IF	Qualitative	Pattern: Homogeneous, Titer 1:10,000	<1:100

most effectively, AIHA is categorised. Atypical forms of AIHA, mixed-type AIHA, paroxysmal cold haemoglobinuria (PCH), warm autoimmune haemolytic anaemia (wAIHA), and cold autoimmune haemolytic anaemia (CAD) are among these categories.[9] About 60 to 70 percent of cases of AIHA are warm autoimmune haemolytic anaemia (wAIHA). IgG antibodies, which attach to red blood cells at a temperature of about 37°C, are usually the mediators. In these circumstances, anti-IgG antisera or a low titer combination of anti-IgG and complement typically result in a positive Direct Antiglobulin Test (DAT). 20–25% of cases are cold agglutinin disease (CAD), which is brought on by IgM autoantibodies that respond best at 4°C, trigger the complement system, and result in a DAT positive for anti-C. The serum frequently has high cold agglutinin titers. A DAT positive for both IgG and complement, as well as high cold agglutinin titers, are indicative of mixed-type AIHA, which makes up 5–10% of cases and presents with overlapping characteristics of both wAIHA and CAD. IgG antibodies that attach to red blood cells at low temperatures but cause severe intravascular haemolysis at 37°C catalyse paroxysmal cold haemoglobinuria (PCH), a less common variant that affects 1–5% of people. The Donath–Landsteiner test supports the PCH diagnosis.[10] Whether or not an underlying ailment is present allows each AIHA subtype to be further categorised. It is known as primary or idiopathic AIHA if no underlying condition is found. Secondary AIHA, on the other hand, occurs when AIHA develops as a symptom or consequence of another illness.[11]

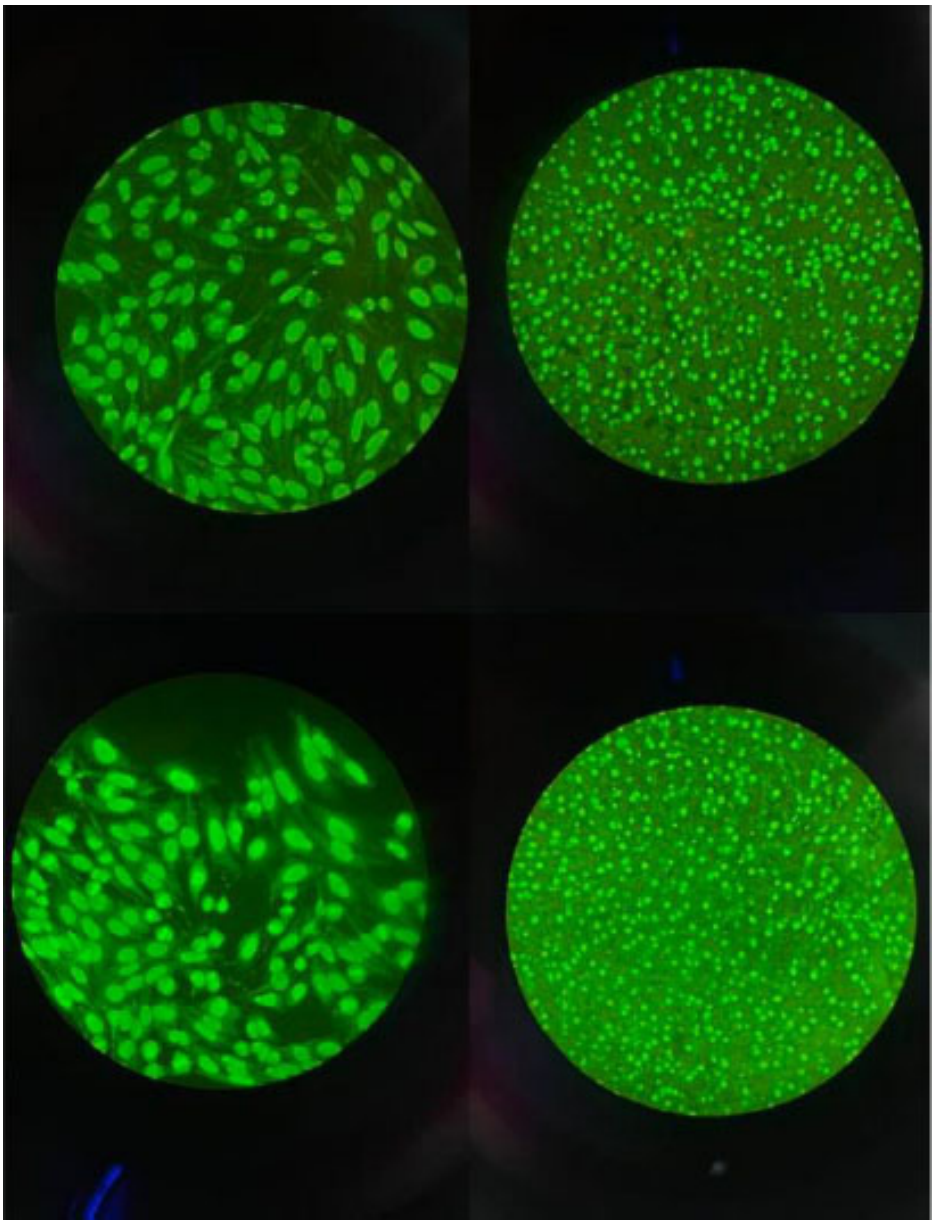

Figure 1. Homogeneous pattern observed in the ANA IF examination. (1) Titer 1:100 HEP; (2) Titer 1:100 PL; (3) Titer 1:1000 HEP; (4) Titer 1:1000 PL.

A combination of the clinical history, physical examination, and laboratory tests are used to make the diagnosis of AIHA. Pallor that had persisted for the past month and a history of blood transfusions were the patient's main complaints when they first arrived. In addition, the patient complained of joint discomfort, hair loss, and sporadic fever for the previous nine months. Upon physical examination, pallor in both conjunctiva was noted. An examination of the abdomen showed that the epigastric area was painful to the touch. A haematocrit of 17.3%, a peripheral blood smear that was compatible with normocytic normochromic anaemia, and a haemoglobin level of 5.1 g/dL were all reported in the laboratory. Indirect immunofluorescence of antinuclear

Table 9. Peripheral blood smear examination results at Prof. I.G.N.G. Ngoerah General Hospital (23/04/2024)

Peripheral Blood Smear	Result
Erythrocytes	Normochromic normocytic, with anisopoikilocytosis (presence of tear drop cells, fragmented cells, spherocytes), and positive polychromasia
Leukocytes	Impression of increased count; differential count shows neutrophilia, absence of toxic granules, absence of vacuolization
Platelets	Normal count impression, no giant platelets, normal distribution
Impression	Normochromic normocytic anemia and leukocytosis

Table 10. Urinalysis results

Parameter	Unit	SLB Hospital (13/04/24)	RSUP PN (22/04/24)	Reference Value
Leukocytes	Leuco/uL	Negative	Negative	Negative
Blood	Ery/uL	(+4)	(2+)	Negative
Protein	mg/dL	(+4)	(3+)	Negative
Glucose	mg/dL	Negative	Negative	Negative
Ketones	mg/dL	Negative	Negative	Negative
Urobilinogen	mg/dL	Negative	Normal	Normal
Bilirubin	mg/dL	Negative	Negative	Negative
Nitrite	mg/dL	Negative	Negative	Negative
Urinary Leukocyte Sediment	/LPB	29	2	< 2
Urinary Erythrocyte Sediment	/LPB	6	6	< 2
Casts	/LPK	–	3.98	< 2.25
Epithelial Cells	/LPK	–	1	< 1
Bacteria	/LPB	–	261.8	< 2.64

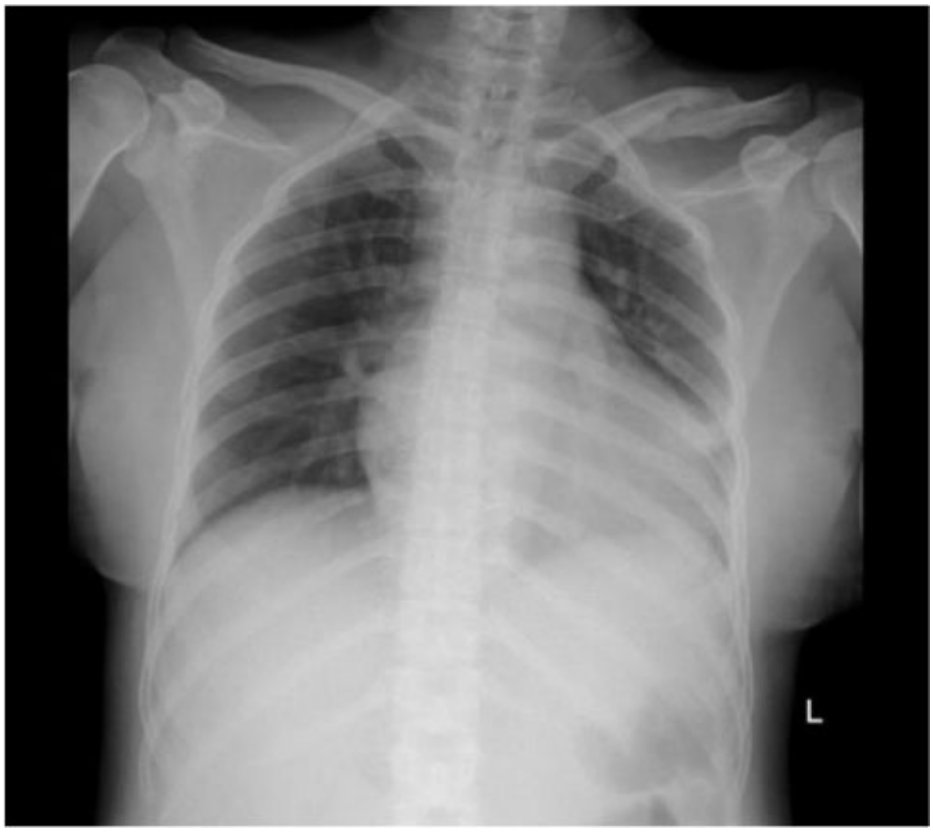

Figure 2. Chest X-ray from Prof. Dr. I.G.N.G. Ngoerah General Hospital (22/04/2024).

antibodies (ANA IF) showed a high titer of 1:10,000, and the Coombs test came back positive.

Women make up about 66% of autoimmune haemolytic anaemia (AIHA) patients, according to Das et al. AIHA's clinical signs and symptoms are typically comparable to those of other forms of haemolytic anaemia. Classic symptoms of anaemia, such as pale skin and conjunctival pallor, are often present in patients. Haemolytic anaemia can also present with jaundice and reticuloendothelial system (RES) organs like the liver and spleen enlarging. Although all patients with AIHA have these common clinical characteristics, those with AIHA brought on by autoimmune conditions, like systemic lupus erythematosus (SLE), typically show primarily the symptoms of the autoimmune disease, as was the case in this instance.[12]

A thorough medical history, including past diagnoses, prescription drugs, and any personal or family history of haemolytic anaemia, should be acquired if haemolysis is suspected. Additional vague symptoms could be tachycardia, hypotension, tiredness, and dyspnoea. The symptoms of chronic haemolysis can include cholestasis, choledocholithiasis, lymphadenopathy, and splenomegaly. The indications of haemolytic anaemia are usually seen in laboratory tests. These include decreased haptoglobin levels because of the binding of free haemoglobin, increased levels of lactate dehydrogenase (LDH), a marker of red blood cell lysis, and reticulocytosis, which is a bone marrow reaction to anaemia. Polychromasia or more specialised characteristics like spherocytes, schistocytes (fragmented red blood cells), and teardrop cells is frequently observed in peripheral blood smears, as in this instance. Usually, spherocytes are caused by membrane loss or abnormalities brought on by macrophage activity.[9,13,14]

An autoimmune disease that affects several organ systems, systemic lupus erythematosus (SLE) is characterised by persistent inflammation that can cause serious tissue damage and organ failure. Tissue damage from the disease is linked to the accumulation of immune complexes and autoantibodies. Overproduction of interferon-alpha (IFN-α), increased apoptosis, and complement deficits are the underlying pathophysiology of SLE. Between people of different ages, races, and clinical characteristics, disease processes, development, and outcomes can differ significantly.[15–17]

An estimated 5.1 instances of systemic lupus erythematosus (SLE) occur for every

SLE Classification Criteria

ANA ≥ 11:80 on HEp-2 or an equivalent positive test required. Immunofiuoreseen recommended. Recommender recommendations under high performance at an additive criterion to declarte tininot occur ≥710.

If absent, SLE is not classified
If absent, SLE is not classified *uddditive criteria*

Additive Criteria (entry-*criterion*)
A point criterion not counted if an explanation exists that is more likely SLE.
A minimum of 1 criterion within a given domain must be present for arin additive criterion, Classification of SLE requires a minimum of 1 clinical domain criterion and a total score of ≥10 points. Criteria need not occur simultaneously. Only criteria altributed to SLE are counted

Clinical Domain and Criteria	Point	Immunologic Domain and Criteria	Point
Constitutional		**Antiphospholipid attbody**	
Fever	2	Anti-cardiotipin atau	
		Anti-B2GP1 antibody or	2
Hematologic	3	Lupus anticoagulant	
Leukopenia		**Complement protein**	
Thrombocytypenia	4	Low C3 or	4
Autoimmune hemolysis	4	Low C4 or	4
Neuropsychiatric		Low C3 and Low C4	
Delirium	2	**Specific antibody**	
Psychosis	3	Anti-dxDNA antiody	6
Seizure	5	Anti-Sin (Sm) antibody	6
Mucocutaneous			
Non-scarring alopecia	2	**Renal**	
Oral olcers	2	Proteinuria > 0,5 g/24 hour	4
Subocute cutaneous lapus or Discold cutancous	4	Renal biopsy class II or lupus nephritis grade V	8
Acute cutaneous lupus	6	Renal biopsy class III or lupus nephritis grade IV	10
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		

Total Score

SLE is classified with a score total ≥10 if if entry criterion is fulfilled

Figure 3. SLE criteria based on ACR/EULAR 2019.[21]

100,000 people in the United States, with women accounting for the majority of cases (9–14:1). Hormonal variables are a major element in the etiopathogenesis of the disease, especially throughout a woman's reproductive years, as this is probably caused by hormonal impacts. The precise prevalence of SLE is unknown in Indonesia.[18] Malar rash, discoid rash, photosensitivity, alopecia, oral or nasal ulcers, myalgia, polyarthralgia/polyarthritis, pericarditis, leukopenia, thrombocytopenia, haemolytic anaemia, proteinuria, haematuria, psychosis/seizures, and cranial or peripheral neuropathies are among the common clinical signs of SLE. Depending on the age range, SLE presents differently clinically.[19]

The diagnosis of SLE is based on criteria established by the American Rheumatology Association (ARA) in 1982, which were later revised in 1997 to include immunological disorders as part of the diagnostic criteria. Additionally, the Systemic Lupus International Collaborating Clinics (SLICC) criteria of 2012 emphasized that SLE is fundamentally an autoantibody-driven disease, requiring at least one immunologic criterion for diagnosis. In 2015, the SLICC criteria were revised further, removing the previous requirement for the presence of at least one clinical and one immunologic criterion.[20]

According to the 2019 ACR/EULAR criteria, the entry criterion is a positive antinuclear antibody (ANA) test with a titer of ≥1:80 on HEp-2 cells or an equivalent test, performed at least once. This criterion offers superior diagnostic performance due to the high sensitivity of ANA (98%) as a screening tool. Consequently, patients with persistently negative ANA results are not eligible for SLE classification. If the ANA is positive, the diagnosis is established by evaluating the presence of additive criteria. Classification of SLE requires at least one entry criterion and a total additive score of ≥10 points. These additive criteria include fever, hematological abnormalities (leukopenia, thrombocytopenia, autoimmune hemolysis), neuropsychiatric symptoms (delirium, psychosis, seizures), mucocutaneous manifestations, serositis, musculoskeletal involvement (joint involvement), renal disorders, positive antiphospholipid antibodies, complement protein alterations, and SLE-specific antibodies. In this case, ANA testing yielded a titter of 1:10,000 with a homogeneous pattern, and clinical manifestations included alopecia, joint pain, pulmonary edema, and renal involvement characterized by hematuria and proteinuria. The total score was 24, thereby fulfilling the classification criteria for SLE.[21]

Serum albumin is a negative acute-phase reactant that decreases in response to systemic inflammation. Previous studies have shown that an increase in the SLE Disease Activity Index (SLEDAI) score correlates with a decrease in serum albumin levels. In this case, the patient

Table 11. Sensitivity, specificity, and disease association of specific antinuclear antibodies (Adapted from Nashi and Shmerling, 2021)[26]

Specific Antinuclear Antibody	Associated Disease	Sensitivity (%)	Specificity (%)
Anti-Sm, Anti-dsDNA	Systemic Lupus Erythematosus (SLE)	40	98.66
Anti-SSA (anti-Ro)	Systemic Lupus Erythematosus (SLE)	90	96
Anti-SSB (anti-La)	Primary Sjögren's Syndrome	29	95
Anti-RNP	Primary Sjögren's Syndrome	49	87.5
Anti-Scl-70	Systemic Sclerosis	28	100
Anticentromere	Mixed Connective Tissue Disease	100	84–100
Anti-SSA (anti-Ro)	Limited Scleroderma	33	99.9
Anti-SSB (anti-La)	Limited Scleroderma	33	99.9

also presented with hypoalbuminemia. Hypoalbuminemia may result from systemic inflammation and is associated with pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α), which shift metabolism toward a catabolic state. These pro-inflammatory cytokines are believed to play a role in the pathophysiology of SLE and have been shown to be elevated in patients with active disease.[22]

The severity of Systemic Lupus Erythematosus (SLE) can be classified into three categories: mild-to-moderate, severe, and life-threatening. Mild-to-moderate SLE is characterized by clinical stability, absence of organ dysfunction, and no life-threatening events. Severe SLE is identified by the presence of nephritis, cerebral lupus, serositis, or hemolytic anemia. Life-threatening SLE should be considered in the presence of critical complications such as cardiac tamponade, pulmonary hypertension, mesenteric vasculitis, pancreatitis, psychosis, or transverse myelitis. In this case, the patient's SLE severity falls within the severe category due to the occurrence of hemolytic anemia, nephritis, and serositis.[23]

Anemia occurs in approximately 50% of SLE patients. Although it was initially thought that anemia in SLE was primarily due to antibody-mediated erythrocyte destruction, current research shows that the causes are varied, and the pathogenesis may involve both immune and non-immune mechanisms. Common etiologies include anemia of chronic disease, iron deficiency anemia (IDA), autoimmune hemolytic anemia (AIHA), anemia secondary to chronic kidney disease, and cyclophosphamide-induced myelotoxicity. Among these, anemia of chronic disease is the most frequently encountered type. One underlying mechanism involves the presence of autoantibodies against erythropoietin. Additionally, hemolytic mechanisms play a role, where erythrocytes become targets of the immune system. Furthermore, anemia is also a clinical manifestation of chronic kidney disease, marked by decreased erythropoietin production (primarily synthesized in the kidneys), reduced erythrocyte lifespan, uremic toxicity, and secondary hyperparathyroidism. In this case, complete blood count results showed severe normochromic normocytic anemia. A peripheral blood smear revealed normochromic normocytic anemia with anisopoikilocytosis (presence of tear drop cells, spherocytes, and schistocytes), which supports the diagnosis of SLE.[24]

The patient had a homogenous pattern of positive antinuclear antibody (ANA) test results. A positive ANA test could mean that there are antibodies against a number of nuclear antigens. This pattern is most frequently linked to anti-double-stranded DNA (anti-dsDNA) and anti-histone antibodies, which can both be correlated with the activity of SLE disease, especially in lupus nephritis patients. SLE and mixed connective tissue disease are more commonly linked to anti-RNP antibodies, albeit their existence by themselves does not prove either diagnosis. Antibodies against Ro (anti-SSA) and La (anti-SSB) have been associated with both SLE and primary Sjögren's syndrome. Anti-Ro antibodies are also closely linked to the onset of newborn lupus. About half of patients with SLE have anti-histone antibodies, and drug-induced lupus nearly always had them. Systemic sclerosis or CREST syndrome (which includes calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) are the conditions most strongly linked to anti-centromere antibodies, while SLE patients may also have them on occasion. These antibodies' high specificity makes them useful in clinical settings, despite their variable sensitivity. Anti-DFS70 antibodies are generally considered markers of non-systemic autoimmune conditions. Only about 1% of patients with systemic autoimmune diseases test positive for DFS70, while 2–22% of healthy individuals may yield positive results. Other studies have reported anti-DFS70 positivity in 11% of patients with Sjögren's syndrome and 6% in those with SLE. In this case, the patient's ANA result was positive at a titer of 1:10,000 with a homogeneous pattern, further supporting the diagnosis of SLE.[25,26]

On laboratory testing, the Direct Coombs Test yielded a positive result. Abnormalities in the production and clearance of immune complexes are fundamental to the pathogenesis of systemic lupus erythematosus (SLE). Complement receptor type 1 (CR1) plays a critical role in the binding, transport, and endocytosis of complement-bound immune complexes. CR1 is differentially expressed on erythrocytes, eosinophils, monocytes, dendritic cells, and renal podocytes. Erythrocytes are particularly important in clearing circulating immune complexes by binding them via CR1. The Direct Coombs Test detects both the binding of anti-erythrocyte antibodies to erythrocyte surfaces and the attachment of immune complexes to CR1 on erythrocytes. While the binding of anti-erythrocyte antibodies is a hallmark of autoimmune hemolytic anemia (AIHA), the attachment of immune complexes to CR1 is not associated with hemolysis.[27]

Management of AIHA includes both pharmacologic and non-pharmacologic approaches. In this patient, pharmacologic therapy included transfusion of packed red blood cells (PRC) until the hemoglobin level reached 10 g/dL. According to the literature, transfusion should be conducted under careful monitoring and is recommended in cases of life-threatening anemia. In general, for warm-type AIHA, transfusion is considered when hemoglobin levels fall below 5 g/dL. Studies have shown that 75–96% of AIHA cases secondary to SLE respond to corticosteroids, such as prednisone at a dose of 1 mg/kg/day (or an equivalent dose of another corticosteroid) administered in divided doses. Typically, a clinical response is observed within 2–3 weeks of initiating therapy. Dose tapering of corticosteroids should only be considered once hematocrit levels rise and reticulocyte counts begin to decline.[28]

The primary goals of treatment in systemic lupus erythematosus (SLE) are to control inflammation, achieve clinical remission (absence of disease manifestations), improve quality of life, prevent severe exacerbations, avoid irreversible organ damage, and ultimately reduce mortality. Initial treatment during the first 4–6 weeks is indicated in severe cases and typically involves high-dose intravenous methylprednisolone at 30 mg/kg/dose infused over 60 minutes for three consecutive days, or oral prednisone at 15–60 mg/day (0.5–2 mg/kg/day) in divided doses. This is followed by a tapering regimen of prednisone or methylprednisolone, combined with the administration of Disease-Modifying Anti-Rheumatic Drugs (DMARDs). In the present case, the patient was initiated on a high-dose intravenous methylprednisolone regimen at 10 mg/kg/dose as induction therapy to achieve remission.[24]

In addition to pharmacologic management, the patient was also provided with education regarding the Systemic Lupus Erythematosus Disease Activity Index (Mex-SLEDAI) prior to discharge. This index serves as a validated measure of disease activity and helps monitor the clinical progression and overall impact of SLE on the patient's quality of life.[29,30]

CONCLUSION

Autoimmune hemolytic anemia (AIHA) secondary to SLE is a relatively rare clinical entity encountered in routine medical practice. Therefore, a thorough understanding of its diagnostic and therapeutic approach is essential to prevent misdiagnosis and ensure appropriate treatment. In this case, the diagnosis and management of AIHA were carried out in accordance with the hospital's standard operating procedures. Further studies with different designs and larger samples are needed to develop this topic.

DISCLOSURES

Ethical Considerations

The patient and family have agreed regarding using cases in this case report.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

All authors collaborated equally in the writing and editing of the manuscript.

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