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Management of Severe Warm Autoimmune Hemolytic Anemia in Chronic Systemic Lupus Erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multi-organ involvement, often complicated by hematologic disorders such as warm autoimmune hemolytic anemia (AIHA). AIHA in SLE patients can lead to severe anemia, jaundice, organ dysfunction, and increased mortality, yet data on its management, particularly in severe cases, remain limited. This study aimed to describe the diagnosis, management, and clinical outcomes of severe warm AIHA in a patient with chronic SLE. A qualitative case report methodology was employed, collecting data through anamnesis, physical examination, laboratory testing, imaging studies, and treatment documentation. The patient, a 28-year-old female with chronic SLE, presented with severe normochromic-normocytic anemia, jaundice, splenomegaly, and discoid lesions. Management included methylprednisolone pulse therapy, hydroxychloroquine, packed red cell transfusions, supportive care, and vitamin D supplementation. Clinical monitoring demonstrated progressive improvement in hemoglobin levels, reduction in autoimmune activity, and resolution of systemic symptoms over five days of hospitalization. The study concludes that integrated medical and supportive therapies are effective for stabilizing severe warm AIHA in chronic SLE, emphasizing the need for individualized care and close monitoring. Future research should focus on larger cohorts to validate treatment protocols, explore adjunctive therapies, and identify predictive markers for severe hemolysis to enhance early diagnosis and improve long-term patient outcomes.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by a variety of clinical and immunological manifestations (Fava & Petri, 2020). Hematological abnormalities are a significant component of SLE, with autoimmune hemolytic anemia (AIHA) being a common complication (Suzuki et al., 2023). AIHA is a disorder in which antibodies target erythrocyte cells, causing erythrocytes to lyse readily and shortening their lifespan. Although the lifespan of erythrocytes in adults ranges from 120 days, it is generally agreed that a shortened erythrocyte lifespan is defined as less than 100 days. Therefore, the occurrence of AIHA requires both the presence of antibodies and the process of erythrocyte destruction (Michalak et al., 2020). AIHA can be divided into two types, namely warm type and cold type. Approximately 70% of AIHA cases are of the warm type, in which

autoantibodies react optimally at a temperature of 37°C (Murakhovskaya, 2020). However, AIHA is a relatively rare disorder, affecting 1–3 out of 100,000 individuals per year, with a prevalence ratio of 17:100,000 (Suzuki et al., 2023).

The prevalence of AIHA in SLE patients varies, but is generally reported in 10–20% of SLE cases, dominated by warm-type AIHA (Crawford & Neparidze, 2022). Approximately 49% of patients with warm-type AIHA are accompanied by other diseases, such as SLE (Tranekær et al., 2021). In North America, the incidence of SLE patients with AIHA is 23.2 per 100,000 population per year (Rees et al., 2017). SLE with AIHA is associated with high morbidity and mortality, as both conditions pose a significant risk to the patient's health due to complications such as renal damage, cardiovascular disease, and infection. SLE patients with AIHA have a higher mortality rate than the general population, with a five-year survival rate of approximately 90% (Barber et al., 2023). In Indonesia, the prevalence of SLE and AIHA is increasing, but data on specific cases of AIHA in SLE remain very limited. This lack of information hinders the development of effective treatment strategies and management protocols for these patients (Oktafany & Natasha, 2017).

Systemic lupus erythematosus (SLE) is a complex autoimmune disease affecting multiple organ systems worldwide, with hematologic complications being among the most significant. Autoimmune hemolytic anemia (AIHA), particularly the warm type, is a common but often underreported manifestation of SLE, characterized by the premature destruction of red blood cells due to autoantibodies. Epidemiological data suggest that AIHA affects approximately 1–3 per 100,000 individuals annually, with a prevalence of 10–20% among SLE patients, and 49% of warm-type AIHA cases are associated with SLE itself. Despite this, detailed global statistics on AIHA in SLE remain limited, particularly in Southeast Asia, highlighting the need for focused clinical research.

The clinical burden of SLE with concurrent AIHA is substantial, as patients exhibit elevated morbidity and mortality risks due to complications such as renal dysfunction, cardiovascular disease, and increased susceptibility to infections. North American studies report an incidence of 23.2 per 100,000 population per year for SLE patients with AIHA, with a five-year survival rate of only 90%. In Indonesia, while the prevalence of SLE and AIHA is rising, data remain sparse, constraining the development of effective management protocols.

These figures underscore the global and regional relevance of studying AIHA in SLE patients. Previous research has explored various therapeutic approaches for AIHA in SLE, including corticosteroids, immunosuppressants, and transfusion strategies. Studies by Jäger et al. (2020) and Thiagarajan et al. (2021) emphasize that severe hemolysis can rapidly lead to life-threatening anemia, hepatosplenomegaly, and hemodynamic instability. However, existing literature often provides limited insights into severe warm AIHA cases in chronic SLE, especially in young adult populations, and lacks comprehensive longitudinal observations of treatment response.

A critical research gap persists in understanding the optimal diagnostic and therapeutic pathways for managing severe warm AIHA in SLE. Many studies focus on either pediatric or adult cohorts separately, and few address the integration of immunomodulatory therapies, blood transfusions, and adjunctive measures such as vitamin D supplementation. Moreover, there is limited qualitative documentation of clinical progression in severe cases, leaving clinicians without detailed case-based evidence for decision-making.

The urgency of this research lies in the potential for severe AIHA to exacerbate SLE morbidity and mortality if not promptly recognized and treated. Early identification of clinical signs, coupled with a structured management approach, is crucial to preventing organ damage and improving survival outcomes. By documenting detailed patient case studies, this research seeks to provide actionable insights for clinicians managing complex SLE presentations, especially in resource-limited settings.

This study introduces novelty by employing a qualitative case report methodology to examine the clinical trajectory, diagnostic evaluation, and therapeutic interventions in severe warm AIHA within chronic SLE. Unlike large-scale epidemiological studies, this approach allows for in-depth observation of disease manifestation, treatment response, and complications over time. Additionally, the inclusion of combined medical and non-medical management strategies, encompassing immunosuppressants, corticosteroids, transfusion techniques, and vitamin D supplementation, provides a holistic view of patient care.

The purpose of the research is to elucidate the clinical management strategies that can effectively stabilize hemoglobin levels, mitigate autoimmune activity, and improve quality of life in SLE patients with severe warm AIHA. By synthesizing laboratory findings, imaging studies, and therapeutic interventions, the study aims to identify best practices and potential pitfalls in the treatment of complex autoimmune hematologic disorders.

The research contributes to the field by bridging gaps in current clinical knowledge on severe warm AIHA in SLE, particularly in adult populations with relapsed or chronic disease. It offers practical insights into case-based management, demonstrating the effectiveness of integrated therapy approaches including packed red cell (PRC) transfusions, methylprednisolone, hydroxychloroquine, and vitamin D supplementation. These findings may inform clinical guidelines and support evidence-based decision-making in similar healthcare contexts.

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METHOD

This study uses a qualitative approach with a case report design to describe in depth the diagnosis, management, and clinical development process of patients with warm-type autoimmune hemolytic anemia (AIHA) in chronic systemic lupus erythematosus (SLE). Data were obtained through anamnesis, clinical observation, physical examination, medical record review, laboratory test results, supporting examinations, and documentation during the patient's treatment at the hospital. Data analysis was carried out in a qualitative descriptive manner by interpreting the relationship between clinical manifestations, diagnostic test results, therapy administered, and patient response to treatment to provide a comprehensive picture of the management of AIHA in chronic SLE patients.

CASE STUDY

A 28-year-old female patient came to the emergency room of Buleleng Hospital with complaints of weakness since three days before admission. The weakness was described as a feeling of powerlessness, rapid fatigue, and lethargy. The complaint was aggravated by physical activity and did not resolve with rest. This was also accompanied by blurred vision, which rendered the patient unable to get out of bed. The patient also complained of fever since three days before admission. The fever was felt to be high, though the patient had not measured it. She had taken antipyretic medications, but the fever recurred after each dose. The patient additionally complained of generalized jaundice since three months before admission, accompanied by tea-colored urine. The jaundice was initially noticed in the patient's hands and eyes, subsequently spreading to almost the entire body. The patient also complained of joint pain since three months before admission, felt in almost all limbs bilaterally, and always occurring simultaneously. The patient further reported easy hair loss upon gentle pulling, photosensitivity, and avoidance of sunlight since three months prior. She also reported that the skin on her face had felt sore three months before admission, for which she had only applied traditional oil.

On autoamnesis, it was established that the patient had been diagnosed with SLE seven months prior and had a history of a blood transfusion incompatibility reaction one month before admission. On physical examination, the patient's general condition appeared weak with a composite level of consciousness, GCS E4V5M6. Vital signs were as follows: blood pressure 100/60 mmHg, pulse rate 107 times/minute with regular rhythm and adequate tension, respiratory rate 20 times/minute, axillary temperature 38°C, and body weight 58 kg.

Figure 1 Condition of jaundice in patients

On the thorax examination, it was found that the chest wall was symmetrical, there were no abnormalities and retraction. From palpation, symmetrical vocal phremitus on both sides was obtained, and tactile ictus cordis. From the percussion, a sonor sound was obtained in the entire lung field and there were no signs of organ enlargement. From auscultation, vesicular breath sound, there is no additional breathing sound, such as rhonkhi or wheezing. Heart sounds I and II are single, regular, without murmurs.

On the abdominal examination, a normal impression was obtained during the inspection. From auscultation, intestinal noise is normal. On palpation, pressure pain was found in the left hypochondrial region, and grade II schuffner splenomegaly was found. From percussion it is obtained within normal limits.

On examination of the extremities, it was found that the patient's entire joint was compressive, as well as limited range of motion due to pain. The patient's entire body also has a jaundice condition.

On the patient's skin, a clear picture of discoid lesion was also found on the 5th day of treatment, as seen in figure 2, with typical characteristics in the form of disc-shaped lesions, firm borders, and accompanied by scales on the surface.

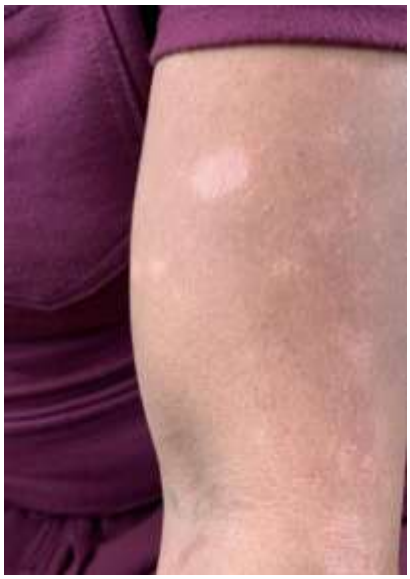

Figure 2 Condition of discoid lesion in the patient's body

A complete blood test showed a decrease in hemoglobin (4.5 g/dL), with an increase in MCV (96.4 fL) and MCH (32.2 pg), indicating severe normochromic-normositer anemia. White blood cells and platelets are within normal limits. An increase in total bilirubin (5.11 mg/dL), dirical bilirubin (0.63 mg/dL), and indilinear bilirubin (4.48 mg/dL) indicated the presence of pre-hepatic jaundice.

Peripheral blood tests showed normochrome erythrocytes with a positive rouleaux reaction. Direct and indirect Coombs tests are positive. Abdominal ultrasound revealed the presence of splenomegaly with a size of 13.78 cm (figure 3).

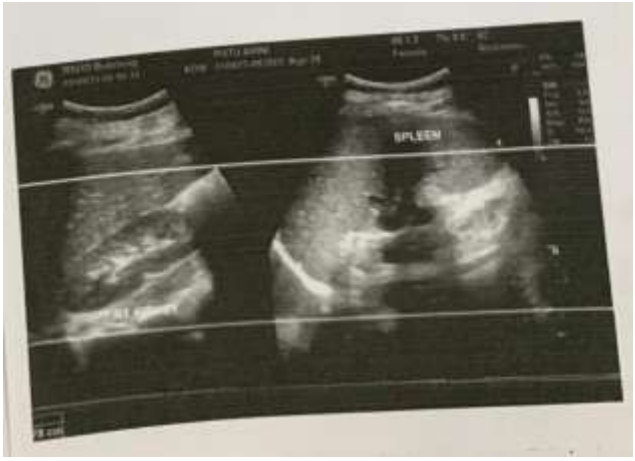

Figure 3 Splenomegaly on Ultrasound Examination of the Abdomen with a size of 13.78 cm

The ANA IF examination also showed a titer of 1:320 in favor of the diagnosis of SLE. Other tests such as blood glucose levels, kidney function, day function, and electrolytes are within normal limits.

Patients are given medical and non-medical management. Regarding non-medical therapy, patients are asked to rest in bed, use skin moisturizer, and be given education related to the diseases suffered by patients and their families. The medicamentous therapy given was 0.5 grams of methylprednisolone pulse/induction therapy in 100 cc of normal saline (in 30 minutes) for 3 consecutive days. After a full response, the dose was lowered to 62.5 mg every 12 hours IV. In addition, patients were also given a washed red cell transfusion of 1 colf/day up to Hb levels of 10 g/dL. Patients are also given symptomatic therapy such as paracetamol 500 mg every 8 hours of PO.

The patient was monitored for five days in the inpatient room. On the second day of treatment, the patient still complained of weakness, fever, and pain in the joints. Physical examination still found signs of anemis, jaundice, and splenomegaly. The patient is still on induction therapy plus a PRC 1 colf transfusion. On the third day, complaints of weakness and fever began to improve, but joint pain was still present. The patient was also transfused PRC 1 colf and was closely monitored for general conditions and vital signs. By the fourth day, the complaints of joint pain had decreased. The patient begins to be able to move more actively, such as getting up and walking. On the fifth day, the patient's condition improved, there were no complaints. The patient was discharged on day 5 after showing improvement in general condition and laboratory value results, with methylprednisolone 16 mg/PO every 8 hours, Hydroxychloroquine 200 mg/PO every 24 hours, and Vitamin D3 1000 IU/PO every 24 hours. Patients are asked for control to the Internal Medicine Polyclinic the following week.

RESULT AND DISCUSSION

SLE is a multi-organ autoimmune disease. One of its possible manifestations is AIHA (Aringer et al., 2019), which is caused by autoimmune antibodies that target red blood cells. The mechanism is thought to be caused by the damage of red blood cells through warm or cold antibodies (Jäger et al., 2020). Erythrocytes coated with immunoglobulin G antibodies undergo membrane changes as they pass through the spleen, and the resulting spherocytes are

expelled through phagocytosis which will be destroyed in the reticulo-endothelial system, especially in the spleen and cause extravascular hemolysis (Thiagarajan et al., 2021). Clinically, AIHA can range from mild hemolysis with compensatory reticulocytosis to life-threatening rapid hemolysis resulting in hemodynamic disorders (Lu & Huang, 2022).

Patients with AIHA can come with symptoms of anemia or hemolysis. Severe hemolysis can lead to hepatosplenomegaly, hemoglobinuria, and signs of heart failure (Hill et al., 2017). The diagnosis of AIHA is determined through a positive Direct Antiglobulin Test (DAT) or Coombs Test examination and laboratory evidence of hemolysis, namely anemia, an increase in indirect bilirubin, and an increase in the number of reticulocytes. Hemolytic anemia can occur years before or after an SLE diagnosis is established, and there are rarely early symptoms of SLE. This occurs as part of a recurrent onslaught of SLE that can occur with or without the conditions leukopenia and thrombocytopenia (Velo-García et al., 2016). Treatment varies based on severity, usually starting with corticosteroids and considering other immunosuppressive agents as well as supportive care for severe cases (Neely & von Scheven, 2018).

Based on the results of the anamnesis, the patient has met the criteria of the SLE condition where there is a young woman's condition with several systemic symptoms involving 2 or more organs without a clear cause. The patient also has a chronic SLE category because there is a discoid lesion condition on the patient's skin (Sumariyono et al., 2019). The patient also met the criteria for anemia with symptoms of weakness, fatigue, and lethargy, as well as loss of stamina to the point of being unable to get out of bed (Weckmann et al., 2023).

On physical examination, jaundice conditions on the face and the whole body were found which can indicate liver problems and problems outside the liver which can be confirmed by a bilirubin status supporting examination. In patients, there is also an enlargement of the spleen with schuffner grade II which indicates the involvement of organs that function in the reticuloendothelial system (RES) in patients who often occur in patients with Hemolytic Anemia (Thiagarajan et al., 2021).

On supporting examination, severe anemia was found with a hemoglobin level of 4.5 g/dL (World Health Organization, 2024) with normal MCV and MCH levels which indicates Normochromic-Normositer conditions which are a sign of hemolytic anemia (Baldwin et al., 2023). In bilirubin examination, an increase in total, indirect and direct bilirubin was found which indicates pre-hepatic jaundice which means that a hemolytic condition occurs due to aggressive red blood cell breakdown that is common in hemolytic anemia (Singh et al., 2023). In the ANA Test examination, a positive result has been obtained which indicates a positive in SLE screening but the ANA Test is not a gold standard examination of SLE where the ANA Test functions as an initial screening only. The specific test of SLE is the anti-dsDNA test (Sumariyono et al., 2019). Patients with suspected hemolytic anemia were strengthened by positive results on the direct/indirect coombs test. Ultrasound imaging of the abdomen has confirmed that there is an enlargement of the RES organ, namely splenomegaly (Thiagarajan et al., 2021).

This case is a patient with exacerbated and relapsed SLE conditions because they have been suffering since 7 months ago, the severity of SLE in patients uses the Mexican SLE Disease Activity Index (MEX-SLEDAI) criteria which received a score of 8 which indicates severe SLE conditions (Sumariyono et al., 2019). Therefore, based on the anamnesis, physical

examination, and supporting examinations, the patient was diagnosed with Normochromic-Normositer Severe Anemia (4.5 g/dL) et causa Autoimmune Hemolytic Anemia (AIHA) et causa Systemic Lupus Erythematous (SLE) degree of Weight MEX-SLEDAI 8.

In the patient, a packed red cell (PRC) transfusion has also been carried out which is indicated due to a life-threatening condition with a strict blood serum examination (Hill et al., 2017). The use of leukodepletion PRC transfusions in patients with refractory autoimmune hemolytic anemia (AIHA) has shown effectiveness in increasing hemoglobin levels and decreasing autoimmune antibody levels (William et al., 2021). However, in the case it is not explained whether the transfusion used the leukodepletion technique or not. In patients, autoimmune management has been carried out in accordance with the guidelines of the Indonesian Rheumatology Association in the form of providing immunosuppressants, namely hydroxychloroquine, and also giving steroids that are anti-inflammatory and have immunosuppressant effects, namely methylprednisolone (Sumariyono et al., 2019). Patients were also given D3 supplementation which has a role as an immunomodulator in SLE by suppressing effector T cell activity and increasing regulatory T cells. In addition, vitamin D reduces the production of pro-inflammatory cytokines such as IL-6 and IFN-α, which contribute to chronic inflammation. Other effects include controlling B cell activity, thereby reducing the production of autoantibodies that worsen SLE (Magro et al., 2021).

CONCLUSION

The findings of this study indicate that severe warm AIHA is a critical hematologic complication in chronic SLE, requiring prompt and integrated management to prevent morbidity and mortality. Through detailed qualitative case analysis, it was observed that a combination of immunosuppressive therapy, corticosteroids, packed red cell transfusions, and supportive care — including vitamin D supplementation — can effectively stabilize hemoglobin levels, reduce autoimmune activity, and improve overall patient outcomes. Clinical monitoring of organ involvement, laboratory parameters, and patient symptoms is essential for timely adjustments in treatment strategies. This research underscores the importance of individualized care plans, as each patient's disease trajectory and response to therapy may vary, highlighting the complexity of managing autoimmune hematologic disorders in chronic SLE.

For future research, it is recommended to conduct larger cohort studies and multi-center trials to validate the effectiveness of integrated treatment protocols for severe warm AIHA in SLE across diverse populations. Further investigation into the role of adjunctive therapies, such as immunomodulatory agents and vitamin D supplementation, in relation to long-term outcomes and relapse prevention is warranted. Additionally, studies exploring early diagnostic markers and predictive factors for severe hemolysis could enhance clinical decision-making and allow for more proactive interventions. These efforts will contribute to the development of standardized guidelines and evidence-based best practices for the management of severe hematologic complications in patients with chronic SLE.

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