

CASE REPORT

Evans Syndrome and Systemic Lupus Erythematosus (SLE): A Case Report

Cheifia Krissanti Sasono^{1*}, Myrna Saphira Fulca¹, Yahya Haryo Nugroho², Sarah Yunara²

¹Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

²Department of Internal Medicine, RSUD dr. Mohammad Soewandhie, Surabaya, Indonesia

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ORCID ID:

Cheifia Krissanti Sasono

<https://orcid.org/0009-0006-0530-2421>

Myrna Fulca

<https://orcid.org/0000-0001-8118-6334>

ABSTRACT

Background: Evans syndrome is a condition characterized by the simultaneous occurrence of immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA). The diagnosis of Evans syndrome presents a significant challenge due to its overlapping features with other autoimmune disorders. **Objective:** This case report aims to identify a diverse range of symptoms, including hematological and dermatological manifestations to provide a comprehensive diagnosis. In this case, the coexistence of fatigue, jaundice, pigmented macules, and papules led to the diagnosis of systemic lupus erythematosus (SLE) and Evans syndrome. **Case:** This case report presents a case of Evans syndrome in a 16-year-old female, delving into the intricate interplay of clinical manifestations and the potential association with SLE. The patient exhibited fatigue, pallor, jaundice, and dark-colored urine, along with the concurrent symptoms of dry cough and runny nose. A dermatological examination revealed hyperpigmented macules and papules on the face and extremities. Laboratory findings indicated severe anemia, thrombocytopenia, abnormal liver function, hyponatremia, and hypokalemia. The positive direct Coombs test and urinalysis findings supported the diagnoses of both Evans syndrome and SLE. The patient responded positively to systemic corticosteroid therapy and supportive care. **Conclusion:** This case underscores the diagnostic challenges associated with Evans syndrome, especially when overlapping with SLE. A multidisciplinary approach is crucial for accurate diagnosis and effective therapeutic interventions. Further research is necessary to unravel the complex relationships between these autoimmune diseases in cases of coexistence or overlap.



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*Corresponding Author:

Cheifia Krissanti Sasono. Faculty of Medicine Universitas Airlangga, Jl. Mayjen Prof. Dr. Moestopo no. 46, Surabaya, Indonesia. Email: cheifiaks@gmail.com

Highlights

1. Evans syndrome is an autoimmune disease characterized by the coexistence of immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA).



2. The collaboration of specialists, including rheumatologists, hematologists, and dermatologists, was crucial for the accurate diagnosis of SLE and Evans syndrome, which present with similar symptoms.
3. Successful corticosteroid therapy underscores the importance of prompt intervention. Regular monitoring of hematological parameters and symptoms during follow-up is essential for ensuring sustained improvement and allowing for necessary treatment adjustments.

INTRODUCTION

Evans syndrome is named after Robert Evans who first identified this autoimmune disease in 1951 (Audia et al., 2020; Jaime-Pérez et al., 2018). It is more commonly observed in pediatric patients rather than adults (Couri and Kandula, 2020). This disease is a combination of immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA) with clinical manifestations including anemia, thrombocytopenia, fatigue, jaundice, petechiae, and epistaxis (Aladjidi et al., 2023; Audia et al., 2020; Jaime-Pérez et al., 2018). Laboratory investigations unveiled a severe hematological profile, with anemia, thrombocytopenia, and abnormal liver function. The positive direct Coombs test and urinalysis findings further supported the diagnosis of Evans syndrome (Jaime-Pérez et al., 2018). Evans syndrome is a rare disease, with the prevalence of 0.8% to 3.7% (Michel et al., 2009). It is more commonly observed in children and has been associated with connective tissue disease, immune deficiency disorders, lymphoproliferative disorders, and malignancy of the immune system (Couri and Kandula, 2020). Due to the association with the connective tissue disease and immune disease, Evans syndrome is classified as primary or secondary (Audia et al., 2020). The etiology of Evans syndrome remains unknown, although it is known to result in alterations of the immune system. Evans syndrome has been associated with connective tissue disorders due to alterations of the cellular and humoral immunity, with systemic lupus erythematosus (SLE) representing one of the main conditions associated with it (Cojocar et al., 2011).

Systemic lupus erythematosus (SLE) is a prototypical autoimmune disorder, characterized by a dysregulated immune response targeting various organs and tissues. Cases of SLE predominantly affect females, with a widely reported female-to-male ratio ranging from 9:1 to 15:1 (Lao et al., 2023). It often manifests during the reproductive years, underscoring the influence of hormonal and genetic factors. The hallmark of SLE is the production of autoantibodies against nuclear antigens, leading to a myriad of clinical manifestations, including arthritis, rash, nephritis, and hematological abnormalities (Liu and Ahearn, 2009). However, this disease poses diagnostic challenges due to its heterogeneous clinical presentation and potential overlap with other autoimmune conditions.

OBJECTIVE

This case report presents a compelling case study of a 16-year-old female admitted to the Emergency Department of dr. Mohammad Soewandhie Regional General Hospital with symptoms suggestive of Evans syndrome. The patient's clinical journey unravels not only the complexities associated with Evans syndrome, but also suggests the potential combination with SLE.

CASE

A 16-year-old female patient presented with symptoms of fatigue, pallor, and jaundice, along with a one-month history of yellowing of the eyes and dark-colored urine. The patient denied experiencing nausea, vomiting, epistaxis, or gum bleeding. Concurrently, she reported a recent onset of dry cough and runny nose one day prior to admission. Notably, the patient acknowledged the gradual appearance of pigmented macules on her face and arms over the past year. She had no history of diabetes, hypertension, cardiovascular diseases, or other chronic illnesses, and her family medical history was unremarkable.

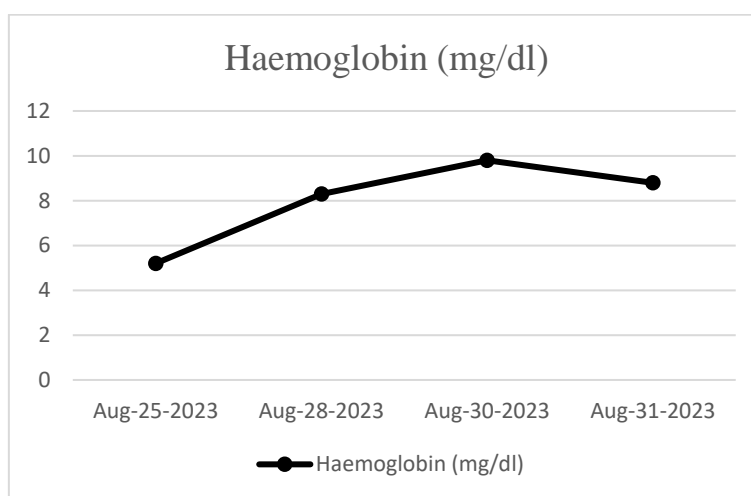
Upon physical examination, the patient exhibited signs of illness with stable vital signs. Conjunctival pallor was noted, while a general physical examination revealed no significant abnormalities. A dermatological examination revealed multiple hyperpigmented macules of varying sizes on the facial

region and symmetrical papules on both upper extremities. Some lesions exhibited mild scaling, were circumscribed, and discretely distributed.



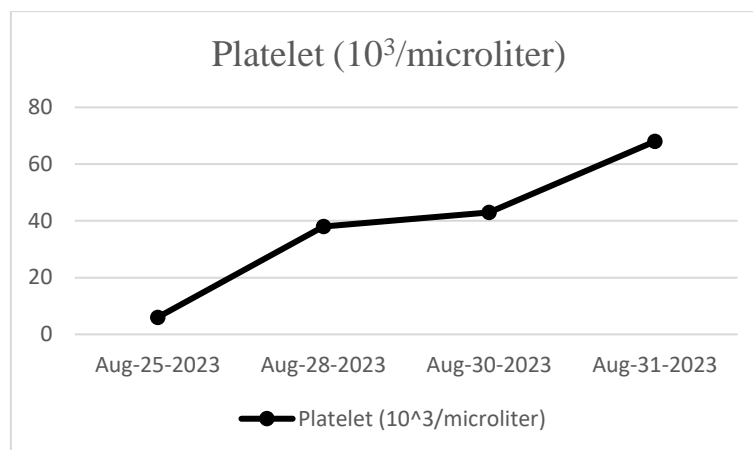
Figure 1. Dermatological manifestation found in patient

Laboratory investigations revealed a hemoglobin level of 5.2 mg/dl, elevated mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH), thrombocytopenia (PLT: 6×10^3), leukopenia (white blood cell or WBC: 4.89×10^3), and abnormal liver function (SGOT: 107, SGPT: 41). Hyponatremia (Na: 126) and hypokalemia (K: 2.8) were also observed. The direct Coombs test was positive, and urinalysis indicated dark-colored urine with positive urobilinogen and erythrocytes. The ANA test was conducted, showing a positive result with a decrease in complement components of C3 and C4. The chest X-ray results were within the normal range. Based on the comprehensive clinical history, physical examination, and laboratory findings, the patient was diagnosed with SLE and Evans syndrome.



Graphic 1. Laboratory results of hemoglobin during hospitalization

The patient received systemic corticosteroid therapy with methylprednisolone (100 mg/day) along with supportive care, including fluid therapy, blood transfusions (packed red cells and thrombocyte concentrate), and electrolyte balance correction during hospitalization. The patient exhibited a positive response to the administered therapy, as evidenced by an increase in hemoglobin and platelet count (as shown in Figures 1 and 2), along with a reduction in symptoms. After a seven-day hospitalization, the patient was discharged with a prescription for ongoing oral corticosteroid therapy. One week after discharge, the patient showed continued improvement during a follow-up visit to the hospital.



Graphic 2. Laboratory results of platelet during hospitalization

DISCUSSION

The presented case presents a compelling narrative that underscores the potential interconnection between SLE and Evans syndrome, which is referred to as an overlap syndrome or an inflammatory rheumatic disease with clinical features of autoimmune rheumatic disease (Pope, 2002). The syndrome is characterized by multifaceted autoimmune that lead to organ dysfunction without any specific clinical criteria, which presents a challenge to the diagnosis and therapy for clinicians (LaBere et al., 2023). The convergence of clinical manifestations and laboratory findings prompts a thorough exploration of the complex relationship between these autoimmune disorders. Laboratory findings can distinguish the predominant autoinflammatory mechanisms, but the overlap syndrome shares similar mechanisms. As a result, the laboratory findings cannot be used as diagnostic approaches, including autoantibodies, histologic analysis of immune cell infiltrates, radiologic imaging, and genetic testing (LaBere et al., 2023).

The main characteristics of Evans syndrome include fatigue, pallor and jaundice (Jaime-Pérez et al., 2018). Other manifestations of the syndrome include weakness, lightheadedness, and easy bruising (Stolyar et al., 2019). Another notable observation is hyperpigmentation on the face and upper extremities. Hyperpigmentation in Evans syndrome or SLE is the result of an upregulation of melanin synthesis activity, which causes the development of darker skin patches. The melanin synthesis leads to the increment of melanocytes and decreased melanosome degradation. The synthesis of melanin involves the oxidation reaction that generates superoxide anions and hydrogen peroxide. Those two substances maintain the oxidative stress in the melanocytes (Flores-Terry et al., 2017).

The patient's profound anemia, thrombocytopenia, and positive direct Coombs test are consistent with the classical hematological abnormalities observed in Evans syndrome (Audia et al., 2020; Couri and Kandula, 2020). However, it is important to note that similar hematological abnormalities are commonly encountered in the spectrum of SLE, including anemia (involving 50% of the patients) (Giannouli et al., 2006), thrombocytopenia (the prevalence ranged from 0% to 45%) (Quintana-Ortega et al., 2022), and positive Coombs test or antiglobulin (Skare et al., 2017). The hematological manifestations are also key clinical indicators of SLE (Stolyar et al., 2019). The coexistence of these manifestations poses a diagnostic challenge, necessitating a meticulous evaluation to discern the primary autoimmune process. Nevertheless, the similar laboratory findings of SLE and Evans syndrome overlap in a 33-year-old man, including low levels of C3 and C4, and a positive ANA test (Stolyar et al., 2019). In addition, the patient exhibited positive anti dsDNA titer (Mendonca et al., 2016). It should be noted that the ANA test is not specific for SLE diagnosis.

The presence of hyperpigmented macules and papules on the face and extremities introduces a dermatological facet to the case. While Evans syndrome is recognized for cutaneous involvement, SLE is renowned for its extensive dermatological manifestations, including malar rash and discoid lupus lesions (Fava and Petri, 2019). The dermatological findings in this case suggest a range of potential

diagnoses, emphasizing the need for a comprehensive assessment to determine the contributions of SLE and Evans syndrome.

The multisystemic nature of the patient's complaints, ranging from constitutional symptoms, such as fatigue, pallor, and jaundice, to urological symptoms, such as tea-colored urine, signifies the potential involvement of multiple organs. SLE is known to affect various organ systems, and the confluence of symptoms raises the question of whether the patient might be experiencing an overlap syndrome involving both SLE and Evans syndrome (Audia et al., 2020; Fava and Petri, 2019). The tea-colored urine indicates the mixture of urine with red blood cells and hemoglobinuria (Mendonca et al., 2016).

The patient's history of a prior hospitalization with similar complaints and a substantial transfusion of packed red cells introduces a temporal dimension to the diagnostic dilemma. The recurrence of symptoms and the need for repeated interventions hint at the chronic and relapsing nature often associated with both SLE and Evans syndrome.

The favorable response to systemic corticosteroid therapy is a notable aspect of the case. While this aligns with the expected therapeutic outcome in Evans syndrome, it is also reflective of the immunosuppressive role of corticosteroids in managing SLE (Audia et al., 2020; Jaime-Pérez et al., 2018). Given the intricate interplay of clinical features, hematological abnormalities, and response to therapy, consideration should be given to the possibility of an overlap syndrome involving both SLE and Evans syndrome. This scenario necessitates a nuanced approach to treatment, considering the complexities inherent in managing multiple autoimmune conditions simultaneously.

Strengths and Limitations

The clinical manifestations of Evans syndrome can vary between individual cases, which presents a significant challenge in diagnosis. Multidisciplinary collaboration is needed for accurate diagnosis and effective therapeutic intervention. Further studies are needed to unravel the complex relationship between these autoimmune diseases.

CONCLUSION

In conclusion, the presented case exemplifies the potential for diagnostic intricacy, prompting consideration of the possibility of coexistence or overlap between SLE and Evans syndrome. The coexistence of hematological manifestations, cutaneous findings, and therapeutic response opens up an avenue for further exploration into the nuanced relationships between these autoimmune diseases. A multidisciplinary approach, involving rheumatologists, hematologists, and dermatologists, is imperative to unravel the diagnostic challenges and therapeutic interventions.

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Conflict of Interest

All authors have no conflict of interest to declare.

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Author Contribution

All authors contributed to all processes in this study, including preparation, data collection and analysis, drafting, and approval for the publication of the manuscript.

Patient Consent for Publication

This case report has been approved by the patient and her guardian.



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