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Lupus Presenting with Evans Syndrome: Two Adult Cases

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ABSTRACT

Evans syndrome (ES) is a rare autoimmune disorder defined by the coexistence of autoimmune hemolytic anemia and immune thrombocytopenia. Secondary ES, particularly in association with systemic lupus erythematosus (SLE), is uncommon and presents diagnostic and therapeutic challenges. We report two adult women with ES secondary to SLE who presented to a tertiary care hospital in Pakistan. Both patients developed simultaneous cytopenias. One responded well to corticosteroids and azathioprine, while the other had refractory thrombocytopenia and suffered a non-ST elevation myocardial infarction (NSTEMI), but she then stabilized on mycophenolate mofetil. These cases underscore the heterogeneity of ES in adults, highlight the risks of treatment-related complications, and reflect challenges in low- and middle-income countries where access to diagnostics and advanced therapies is limited.

Highlights:

1. Evans syndrome (ES) combines autoimmune hemolytic anemia and immune thrombocytopenia.
2. Secondary ES may complicate systemic lupus erythematosus (SLE) and worsen prognosis.
3. We describe two adult women with SLE-associated ES presenting with profound cytopenias.
4. Case 1 stabilized on corticosteroids and azathioprine, while Case 2 required mycophenolate after relapse.
5. Limited resources in low- and middle-income countries contribute to delayed recognition and poorer outcomes.

Introduction

Evans syndrome (ES) is a rare cause of thrombocytopenia, first described in 1951 as the co-occurrence or sequential development of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenic purpura (ITP). In 10-15% of cases, neutropenia may also occur [1]. When no underlying cause is identified, the condition is referred to as primary ES. Increasingly, however, ES has been recognized as secondary to other conditions including systemic lupus erythematosus (SLE), common variable immunodeficiency (CVID), non-Hodgkin lymphoma, viral infections (HCV, HIV), and autoimmune lymphoproliferative syndrome (ALPS) [2]. Secondary ES is often characterized by more severe cytopenias, worse outcomes, and a need for more aggressive treatment [3].

Pathogenesis involves autoimmune dysregulation, chronic T-cell activation, and B-cell maturation defects, with genetic abnormalities detected in up to 40% of patients [4,5]. First-line therapy remains corticosteroids, with IVIG, conventional immunosuppressants (azathioprine, cyclophosphamide), and rituximab increasingly used as second-line options [6-8].

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Most reports focus on pediatric populations. In adults, the average age of onset is ~55 years, with a slight female predominance consistent with other autoimmune diseases [2]. Danish registry data estimate a prevalence of 10–20 per million, with mortality highest in the first year after diagnosis [3]. Among SLE patients, ~2.7% may develop ES, usually with systemic involvement, and over half present with hematological manifestations at disease onset [9].

Despite advances, there are no standardized diagnostic or treatment algorithms. Here we describe two adult female patients presenting to a tertiary care hospital in Karachi, Pakistan, with ES secondary to SLE.

Case 1

A 54-year-old woman presented to the emergency department (ED) with a 3-month history of fatigue, easy bruising, a single episode of epistaxis, and oral ulcers. Past history included bilateral knee osteoarthritis treated with meloxicam. She denied fever, weight loss, night sweats, smoking, or substance use. On exam, BMI was 26.7 kg/m^2, blood pressure 150/90 mmHg, and pallor was noted.

Labs revealed Hb 3.9 g/dL and platelets < 4 ×10^9/L. Reticulocyte count was elevated. Peripheral smear showed anisopoikilocytosis, nucleated

RBCs, and reactive lymphocytes. LDH was raised. A direct Coombs test was positive (2+ C3d). Autoimmune serologies are shown in Table 1.

Table 1: Autoimmune workup, Case 1.

Test	Result	Test	Result
ANA	1:640 (+), homogeneous	U1-RNP	2.51 (–)
Anti-dsDNA	80.09 (+)	Anticardiolipin IgM/IgG	Negative
SSA (Ro)	13.10 (+)	β2-GPI IgM/IgG	Negative
SSB (La)	49.91 (+)	Lupus anticoagulant	Negative
Sm	<0.2 (–)	C3	1.69 (normal)
Scl-70	<0.2 (–)	C4	0.45 (normal)

She received 3 days of pulse methylprednisolone, 8 units of platelets, and 4 units of PRBCs. She improved clinically and hematologically, and was discharged on prednisone 60 mg/day, azathioprine 150 mg/day, hydroxychloroquine (later added), folate, B12, and PPIs. Hepatitis B/C screens were negative. PET scan and bone marrow biopsy ruled out malignancy.

At 3-month follow-up, she remained stable (Hb ~10 g/dL, platelets ~100 $\times 10^9$/L) without new lupus features.

Case 2

A 42-year-old woman presented with 3 months of heavy and intermenstrual bleeding, plus 1 day of gum bleeding, dizziness, and lethargy. Past history included hyperthyroidism. She reported a viral URI a week prior, 3 kg weight loss, arthralgias, alopecia, and one prior miscarriage.

On exam, she was pale, BMI 27 kg/m^2, vitals stable.

Labs: Hb 5.5 g/dL, platelets 4 $\times 10^9$/L, normal WBCs/MCV, INR 2.3, ferritin 21.1 ng/mL, TSH 4.9. Peripheral smear showed anisopoikilocytosis, polychromasia, nucleated RBCs, reactive lymphocytes. Direct Coombs test was strongly positive. Autoimmune workup is shown in Table 2.

Table 2: Autoimmune workup, Case 2.

Test	Result	Test	Result
ANA	1:2560 (+), homogeneous	U1-RNP	1.12 (–)
Anti-dsDNA	209.89 (+)	Anticardiolipin IgM/IgG	Negative
SSA (Ro)	44.99 (+)	β2-GPI IgM/IgG	Negative
SSB (La)	48.60 (+)	Lupus anticoagulant	Positive
Sm	0.27 (–)	C3	0.44 (low)
Scl-70	0.89 (–)	C4	<0.02 (low)
Anti-TPO	548 (+)	—	—

She received 3 days of pulse methylprednisolone followed by oral prednisolone 60 mg/day, azathioprine 50 mg/day, HCQ 400 mg/day, norethisterone, tranexamic acid, and insulin for steroid-induced hyperglycemia. She required FFP transfusion for factor II deficiency.

Bone marrow biopsy showed dysplasia but normal cytogenetics. Viral studies (HCV, HIV) were negative. Two weeks post-discharge, platelets fell to 16 $\times 10^9$/L; eltrombopag was started but discontinued after NSTEMI. Azathioprine was switched to Mycophenolate mofetil. She responded well to this regimen and at follow-up, Hb and platelets stabilized.

Discussion

Both patients presented with severe cytopenias and were diagnosed with ES secondary to SLE. While many cases of ES are first identified as ITP with later AIHA,[3] both our cases demonstrated simultaneous onset.

Case 2 was more complex, with additional autoimmune features (alopecia, arthralgia, miscarriage, hyperthyroidism, remote type 1 renal tubular acidosis) and coagulopathy (factor II deficiency, positive lupus anticoagulant). This likely represented lupus anticoagulant-hypoprothrombinemia syndrome [10].

Poor prognostic factors in ES include later age, severe bleeding, refractory cytopenias, and poor steroid response [3]. Both patients had Hb and platelet nadirs lower than typical averages (Hb ~6 g/dL, platelets ~6 $\times 10^9$/L), but Case 1 had a smoother course despite older age, whereas Case 2 developed resistant thrombocytopenia and complications.

Sociocultural context may have contributed: subtle SLE features in Case 2 were overlooked for around 1 year, reflecting common diagnostic delays in Pakistan due to financial constraints, limited resources, and low awareness [11,12]. Delays in SLE diagnosis stem from a multitude of reasons in LMIC settings. These include but are not limited to financial barriers, limited diagnostic infrastructure, shortage of specialists and low health education. These delays mean that the disease at presentation is more severe and harder to manage.

Therapeutically, Case 1 responded well to corticosteroids and azathioprine. Case 2 required escalation to mycophenolate, and rituximab was considered. Eltrombopag, though reported in pediatric ES [13,14], may have contributed to thrombosis in our adult SLE patient, highlighting the need for caution [15].

Conclusion: Although uncommon, Evans syndrome may complicate SLE with simultaneous ITP and AIHA. These cases underscore diagnostic and therapeutic challenges, highlight prognostic factors, and stress the importance of individualized treatment approaches. Further studies are needed to optimize management strategies for secondary ES in lupus.

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References

1. Evans RS, Duane RT. ACQUIRED HEMOLYTIC ANEMIA: I. The Relation of Erythrocyte Antibody Production to Activity of the Disease. II. The Significance of Thrombocytopenia and Leukopenia. *Blood*. 1949;4(11):1196-1213. doi:10.1182/blood.V4.11.1196.1196
2. Michel M, Chanet V, Dechartres A, et al. The spectrum of Evans syndrome in adults: new insight into the disease based on the analysis of 68 cases. *Blood*. 2009;114(15):3167-3172. doi:10.1182/blood-2009-04-215368
3. Hansen DL, Möller S, Andersen K, Gaist D, Frederiksen H. Evans syndrome in adults - incidence, prevalence, and survival in a nationwide cohort. *Am J Hematol*. 2019;94(10):1081-1090. doi:10.1002/ajh.25574
4. Rao VK. Evans syndrome: pathology and genomic hubris. *Blood*. 2022;139(3):312-313. doi:10.1182/blood.2021013636
5. Kumar D, Prince C, Bennett CM, et al. T-follicular helper cell expansion and chronic T-cell activation are characteristic immune anomalies in Evans syndrome. *Blood*. 2022;139(3):369-383. doi:10.1182/blood.2021012924
6. Audia S, Grienay N, Mounier M, Michel M, Bonnotte B. Evans' Syndrome: From Diagnosis to Treatment. *J Clin Med*. 2020;9(12):3851. doi:10.3390/jcm9123851
7. Kashif M, Qureshi A, Adil SN, Khurshid M. Successful use of rituximab in Evans syndrome and refractory immune thrombocytopenic purpura. *J Pak Med Assoc*. 2010;60(1):64-65.
8. Birgens H, Frederiksen H, Hasselbalch HC, et al. A phase III randomized trial comparing glucocorticoid monotherapy versus glucocorticoid and rituximab in patients with autoimmune haemolytic anaemia. *Br J Haematol*. 2013;163(3):393-399. doi:10.1111/bjh.12541
9. Costallat GL, Appenzeller S, Costallat LTL. Evans syndrome and Systemic Lupus Erythematosus: Clinical presentation and outcome. *Joint Bone Spine*. 2012;79(4):362-364. doi:10.1016/j.jbspin.2011.07.004
10. Mulliez SMN, De Keyser F, Verbist C, et al. Lupus anticoagulant-hypoprothrombinemia syndrome: report of two cases and review of the literature. *Lupus*. 2015;24(7):736-745. doi:10.1177/0961203314558859
11. Rabbani MA, Siddiqui BK, Tahir MH, et al. Systemic lupus erythematosus in Pakistan. *Lupus*. 2004;13(10):820-825. doi:10.1191/0961203303lu1077xx

12. Paruk F, Dey D, Mosam A, Amira Christina O, Tikly M. Challenges in Diagnosis and Management of SLE in Africa: An Online Survey. *ACR Open Rheumatol*. 2024;7(1):e11749. doi:10.1002/acr2.11749

13. Blanco BP, Garanito MP. Pediatric Evans Syndrome: A 20-year experience from a tertiary center in Brazil. *Hematol Transfus Cell Ther*. 2023;45(2):196-203. doi:10.1016/j.htct.2022.01.011

14. Shah SJ, Etzl MM. Eltrombopag in long-term management of pediatric thrombocytopenia. *Clin Case Rep*. 2018;7(1):196-201. doi:10.1002/ccr3.1916

15. Samuelsson I, Parodis I, Gunnarsson I, et al. Myocardial infarctions, subtypes and coronary atherosclerosis in SLE: a case–control study. *Lupus Sci Med*. 2021;8(1). doi:10.1136/lupus-2021-000515