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Case Report

Evans Syndrome with Secondary Hypogammaglobulinemia and Recurrent Infections in a Post-Splenectomy Patient: A Case Report Highlighting Diagnostic and Therapeutic Challenges

Pabitra T[1], Pratyusha Dutta[2], Mayugha V[3], Shaun Nevil[4], S Anton Charles[5*], Debdip Ghosh[6], Chaitra C S[7]

[1]*Kempegowda Institute of Medical Sciences, Karnataka, India*

[2]*Assam Medical College and Hospital, India*

[3]*Department of Internal Medicine, ESIC Medical College & PGIMSR, Karnataka, India*

[4]*Department of Internal Medicine, ESIC Medical College & PGIMSR, Karnataka, India*

[5]*Department of Internal Medicine, ESIC Medical College & PGIMSR, Karnataka, India*

[6]*Rajarajeshwari Medical College, Karnataka, India.*

[7]*Assistant Professor, Department of Internal Medicine, ESIC Medical College & PGIMSR, Karnataka, India*

***Corresponding author:** S. Anton Charles, Department of Neurology, 41st Cross, 2nd block Rajajinagar, Bengaluru-560010, Karnataka, India.

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Abstract

Evans syndrome is a rare autoimmune disorder characterized by the coexistence of multiple immune cytopenias, most commonly Autoimmune Haemolytic Anemia (AIHA) and Immune Thrombocytopenia (ITP), with a relapsing–remitting course and significant morbidity. We report a 45-year-old female with a long-standing history of recurrent infections, undifferentiated connective tissue disease, and prior splenectomy, who presented with fatigue and gastrointestinal symptoms. Evaluation revealed haemolysis with positive direct antiglobulin test, persistent thrombocytopenia, and hypogammaglobulinemia. The diagnosis of Evans syndrome was established by exclusion. Despite treatment with corticosteroids and intravenous immunoglobulin, the patient demonstrated a complicated clinical course marked by recurrent infections, including pneumonia and rhino-orbital mucormycosis. This case highlights the diagnostic complexity and therapeutic challenges of Evans syndrome, particularly in post-splenectomy patients with underlying immune dysregulation, and underscores the need for vigilant monitoring and individualized management strategies.

Introduction

First described by Robert Evans in 1951, Evans syndrome is a rare autoimmune disorder with an estimated incidence of 1–9 per million individuals worldwide, with its reported prevalence rising nearly six-fold in recent decades, largely due to improved clinical recognition [1,2]. The condition is defined by the simultaneous or sequential occurrence of at least two autoimmune cytopenias, most commonly Autoimmune Haemolytic Anaemia (AIHA) and Immune Thrombocytopenia (ITP), and less frequently immune neutropenia,

and is associated with a significantly increased mortality compared to the general population [3,4]. Clinical manifestations vary by the affected cell lineage: haemolysis presents with fatigue, pallor, icterus and exertional dyspnea, while thrombocytopenia leads to petechiae, purpura and bleeding tendencies, and neutropenia predisposes to recurrent severe infections [3]. The disease typically follows a relapsing–remitting course, and elderly patients may additionally develop thrombotic complications secondary to chronic haemolysis [4]. Etiologically, Evans syndrome is classified as primary (idiopathic) or secondary, occurring in association with systemic conditions such as Systemic Lupus Erythematosus (SLE), Common Variable Immunodeficiency (CVID), Autoimmune Lymphoproliferative Syndrome (ALPS), and haematological malignancies [1,2,3,4].

Diagnosis is by exclusion, as no single confirmatory test exists. It requires the demonstration of cytopenias with a positive Direct Antiglobulin Test (DAT), alongside systematic exclusion of mimicking conditions including thrombotic microangiopathy, myelodysplastic syndrome, paroxysmal nocturnal hemoglobinuria and drug-induced cytopenias [2]. Management is often challenging and frequently necessitates multiple lines of therapy; splenectomy is commonly employed as a second-line intervention to reduce peripheral destruction [1]. However, persistence or relapse following splenectomy significantly complicates both diagnostic evaluation and therapeutic decision-making, particularly as such patients are at heightened risk of severe intercurrent infections. Disease-related complications include uncontrolled haemorrhage, sepsis, thromboembolism and cardiac compromise, with haemorrhage and infection accounting for the majority of deaths [1]. A substantial proportion of patients require three or more therapeutic modalities, contributing to cumulative toxicity [5]. The unpredictable disease trajectory, prolonged immunosuppression, diagnostic delays and reduced functional productivity collectively impose a considerable burden on patients and healthcare systems. Herein, we report a rare presentation of Evans syndrome in a post-splenectomy patient, highlighting the unique diagnostic and therapeutic challenges in this surgically altered host.

Case Description

A 45-year-old female presented to the casualty with a 6-day history of loose stools, occurring 4–5 times daily, along with complaints of easy fatigability. There was no history of fever, abdominal pain, vomiting, haematochezia, or loss of consciousness. She had no known comorbidities, including diabetes mellitus, hypertension, or thyroid dysfunction. On examination, she was conscious, cooperative, and well-oriented, with a Glasgow Coma Scale (GCS) score of 15/15. General physical and systemic examinations were unremarkable, and her vital parameters were stable.

Her past medical history was significant for multiple hospital admissions over several years, during which she was found to have concurrent Immune Thrombocytopenia (ITP) and Autoimmune Haemolytic Anaemia (AIHA), although a definitive diagnosis had not been established at the time. She was also diagnosed with Undifferentiated Connective Tissue Disease (UCTD) based on positive Antinuclear Antibody (ANA) testing. Over the preceding 15 years, she experienced recurrent respiratory tract infections, febrile episodes, and pneumonias, suggestive of an underlying immune dysregulation. In November 2017, she presented with pneumonia and relapsed haemolytic anaemia; evaluation revealed severe thrombocytopenia (<10,000/mm^3) and anaemia (haemoglobin 7g/dL), with elevated indirect bilirubin and a positive direct antiglobulin (Coombs) test. Due to persistently low platelet counts, she underwent splenectomy in December 2017, following which she demonstrated transient clinical improvement.

Table 1: Laboratory findings at time of admission.

Test	Result	Normal Range	Unit
Hemoglobin	**6.5**	12.0-15.5	gm/dL
Red blood cells	**2.2**	4.0-6.0	million/mm^3
Mean corpuscular volume	**112**	78-100	fL
Mean corpuscular hemoglobin	31	27-32	pg
Mean corpuscular hemoglobin concentration	37	30-36	g/dL
Red cell distribution width	**20**	10-16	%
White blood cells	7,200	4,000-11,000	mm^3
Platelet count	**18,000**	150,000-450,000	mm^3
Erythrocyte sedimentation rate	**80**	0-20	mm
C-reactive protein	**75**	0-6	mg/L
Haptoglobin	**<30**	30-200	mg/dL
Reticulocyte count	**18**	0.5-2.5	%
Lactate dehydrogenase	**7000**	40-280	U/L

Serum iron	168	33-193	mcg/dL
Ferritin	**450**	30-400	ng/mL
Total iron-binding capacity	240	250-450	mcg/dL
Transferrin saturation	15	14-50	%
Total bilirubin	**5.8**	0.2-1.2	mg/dL
Direct bilirubin	0.7	0.10-0.40	mg/dL
Indirect bilirubin	**5.1**	0.10-1.00	mg/dL
Aspartate transaminase	**72**	5-40	IU/L
Alanine transaminase	**45**	5-40	IU/L
Alkaline phosphatase	115	40-125	IU/L
Serum creatinine	1	0.5-1.5	mg/dL
Blood urea nitrogen	14	8-21	mg/dL

Table 2: Laboratory findings after 7 days following start of treatment.

Test	Result	Normal Range	Unit
Hemoglobin	14.2	12.0-15.5	gm/dL
Red blood cells	**3.5**	4.0-6.0	million/mm^3
Mean corpuscular volume	**111**	78-100	fL
Mean corpuscular **hemoglobin**	28	27-32	pg
Mean corpuscular **hemoglobin** concentration	37	30-36	g/dL
Red cell distribution width	15.2	10-16	%
White blood cells	12,510	4,000-11,000	mm^3
Platelet count	2,00,000	150,000-450,000	mm^3
Erythrocyte sedimentation rate	**35**	0-20	mm
C-reactive protein	**30**	0-6	mg/L
Haptoglobin	<30	30-200	mg/dL
Reticulocyte count	1.74	0.5-2.5	%
Lactate dehydrogenase	241	40-280	U/L
Serum iron	80.6	33-193	mcg/dL
Ferritin	450	30-400	ng/mL
Total iron-binding capacity	306.7	250-450	mcg/dL
Transferrin saturation	26.28	14-50	%
Total bilirubin	0.35	0.2-1.2	mg/dL
Direct bilirubin	0.03	0.10-0.40	mg/dL
Indirect bilirubin	0.32	0.10-1.00	mg/dL
Aspartate transaminase	36.2	5-40	IU/L
Alanine transaminase	37.2	5-40	IU/L
Alkaline phosphatase	74	40-125	IU/L
Serum creatinine	0.9	0.5-1.5	mg/dL
Blood urea nitrogen	16	8-21	mg/dL

At the current presentation, relapse of haemolytic anaemia was suspected. Examination revealed pallor and icterus. Laboratory investigations (Table 1) supported ongoing haemolysis, and she was transfused with two units of packed red blood cells. Further immunological evaluation demonstrated marked hypogammaglobulinemia (IgG 331 mg/dL, IgA 22.4 mg/dL,

IgM 37.6 mg/dL). She was initiated on monthly intravenous immunoglobulin (IVIG) therapy (5 g per cycle, total of four cycles), along with hydroxychloroquine (200 mg), folic acid (5 mg), aspirin (75 mg), and prednisolone (50 mg). The laboratory investigations showed improvement after 7 days of medical therapy as seen in (Table 2).

Based on the relapsing–remitting course, coexistence of AIHA and ITP, and exclusion of alternative etiologies, a diagnosis of Evans syndrome was established. Despite treatment, she continued to experience recurrent infections, including three episodes of pneumonia and one episode of rhino-orbital mucormycosis over the following year. This case highlights the complex interplay of Evans syndrome, underlying connective tissue disease, and immunodeficiency, contributing to a highly morbid, relapsing clinical course that remains challenging to manage.

Discussion

Evans syndrome is a rare autoimmune disorder characterized by the coexistence of at least two immune cytopenias, most commonly Autoimmune Haemolytic Anaemia (AIHA) and Immune Thrombocytopenia (ITP), with or without autoimmune neutropenia. It accounts for a small proportion of cases of isolated AIHA or ITP and remains poorly understood in terms of pathophysiology. Recent advances have implicated immune dysregulation at a molecular level, including defects in immune checkpoint pathways such as CTLA-4 and LRBA, abnormalities in TPP2, and an altered CD4/CD8 ratio, suggesting a complex interplay of impaired immune tolerance and lymphocyte dysfunction [6].

Evans syndrome continues to pose significant diagnostic and therapeutic challenges due to its rarity, heterogeneous clinical presentation, and relapsing remitting course. In our case, the diagnosis was supported by the coexistence of autoimmune haemolysis and thrombocytopenia, evidenced by elevated lactate dehydrogenase, indirect hyperbilirubinemia, persistent thrombocytopenia, and positive direct and indirect Coombs tests. Notably, haemoglobin levels were relatively preserved during part of the clinical course, indicating a compensated phase of haemolysis, a recognized feature of the disease. The absence of identifiable secondary causes, including negative viral serology and lack of clinical evidence for systemic autoimmune or lymphoproliferative disorders such as Systemic Lupus Erythematosus (SLE) or lymphoma, further supported the diagnosis of primary Evans syndrome.

Epidemiologically, Evans syndrome is uncommon, representing less than 5% of cases of AIHA or ITP, with a predilection for adults and a slight female predominance [4]. The disease is associated with a poor prognosis, with studies reporting a median survival of approximately 7.2 years with outcomes notably worse in secondary Evans syndrome, where five-year survival rates may be as low as 38% [7]. Increased disease severity, reflected by the need for multiple second-line therapies and the occurrence of recurrent or severe infections has been consistently associated with higher mortality [8]. These factors contribute to repeated hospitalizations, prolonged treatment courses, and substantial healthcare burden, alongside indirect impacts such as reduced productivity and impaired quality of life.

Management remains challenging and often requires a stepwise, individualized approach. First-line therapy typically includes corticosteroids and Intravenous Immunoglobulin (IVIg), although responses are frequently transient with a high relapse rate [4]. Rituximab has emerged as a preferred second-line agent in refractory or steroid-dependent cases due to favourable response rates, while splenectomy is now less commonly performed given concerns regarding relapse and increased infection risk [4]. Additional immunosuppressive agents, such as cyclosporine and mycophenolate mofetil, may be required in resistant cases. Hematopoietic stem cell transplantation is reserved for severe, refractory disease, reflecting the absence of a definitive curative therapy [4,7].

Conflict of Interest

The authors declare no conflict of interest and no funding was received for the study.

Conclusion

Evans syndrome in post-splenectomy patients presents a uniquely challenging clinical scenario, with heightened susceptibility to infections and frequent relapses. Early recognition, exclusion of secondary causes, and tailored immunomodulatory therapy are critical to improving outcomes in this high-risk population.

References

1. Audia S, Grienay N, Mounier M, Michel M, Bonnotte B (2020) Evans' syndrome: from diagnosis to treatment. J Clin Med 9(12): 3851.
2. Fattizzo B, Carrai V, Crugnola M, Baldacci E, Bellini M, et al. (2024) Evans syndrome: disease awareness and clinical management in a nation-wide ITP-NET survey. Eur J Haematol 113(4): 472-6.
3. Jaime-Pérez JC, Aguilar-Calderón PE, Salazar-Cavazos L, Gómez-Almaguer D (2018) Evans syndrome: clinical perspectives, biological insights and treatment modalities. J Blood Med 9: 171-84.
4. Shaikh H, Mewawalla P (2026) Evans syndrome In: StatPearls [Internet] Treasure Island (FL): StatPearls Publishing.
5. Michel M, Chanet V, Dechartres A, Morin AS, Piette JC, et al. (2009) The spectrum of Evans syndrome in adults: new insight into the disease based on the analysis of 68 cases. Blood 114(15): 3167-72.
6. Ghebranious MA, Eseddi J, Galous H (2023) A woman with Sjogren's syndrome and a new diagnosis of Evans syndrome: a case report. AME Case Rep 7: 25.
7. Hansen DL, Möller S, Andersen K, Gaist D, Frederiksen H (2019) Evans syndrome in adults: incidence, prevalence, and survival in a nationwide cohort. Am J Hematol 94(10): 1081–90.
8. Pincez T, Fernandes H, Leblanc T, Michel G, Barlogis V, et al. (2022) Long-term follow-up of pediatric-onset Evans syndrome: broad immunopathological manifestations and high treatment burden. Haematologica 107(2): 457-466.