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Original Research Article

Autoimmune Hemolytic Anemia and Thrombocytopenia in Autoimmune Hypothyroidism: A Rare Case of Evans Syndrome

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Abstract: ***Background:*** Evans syndrome is a rare autoimmune disorder characterized by the coexistence or sequential occurrence of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP) in the absence of an underlying cause. It poses significant diagnostic and therapeutic challenges due to its variable clinical course and frequent association with other autoimmune diseases. The coexistence of Evans syndrome with autoimmune hypothyroidism is extremely uncommon and represents a unique manifestation of immune dysregulation. ***Case Presentation:*** A 32-year-old female with known autoimmune hypothyroidism on levothyroxine therapy presented with complaints of menorrhagia and generalized weakness. Clinical examination revealed hemodynamic stability without organomegaly or lymphadenopathy. Laboratory evaluation showed anemia (Hb 7.8 g/dL), thrombocytopenia (platelets 48,000/mm³), elevated reticulocyte count (12.4%), and peripheral smear suggestive of dimorphic anemia with thrombocytopenia. Bone marrow aspirate revealed megaloblastic changes with erythroid hyperplasia, while trephine biopsy showed a hyperplastic normoblastic marrow with megakaryocytic hyperplasia. Autoimmune workup demonstrated markedly elevated anti-TPO antibodies (>600 IU/mL) and borderline anti-Ro (SSA) positivity, with negative ANA. A positive Coombs test confirmed autoimmune hemolysis. After ruling out secondary causes such as lupus, infections, and malignancy, a diagnosis of Evans syndrome secondary to autoimmune hypothyroidism was made. ***Management and Outcome:*** The patient received intravenous methylprednisolone for three days followed by tapering oral corticosteroids, alongside thyroid hormone replacement, iron and folate supplementation, and supportive transfusions. Menorrhagia resolved, and hematologic parameters improved with hemoglobin rising to 11.7 g/dL and platelets to 235,000/mm³ within one week. She was discharged on a maintenance taper of prednisolone and remained stable at follow-up. Conclusion: This case underscores the importance of considering Evans syndrome in patients with autoimmune thyroid disorders presenting with unexplained cytopenias. The rare association reflects a shared autoimmune pathogenesis and highlights the need for early recognition, multidisciplinary management, and long-term follow-up to prevent relapses and complications.

Keywords: Evans syndrome, Autoimmune hemolytic anemia, Immune thrombocytopenia, Autoimmune hypothyroidism.

INTRODUCTION

Evans syndrome is an uncommon, chronic autoimmune hematologic disorder defined by the simultaneous or sequential occurrence of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP) without an identifiable secondary cause such as systemic lupus erythematosus, malignancy, or infection. First described by Evans and Duane in 1951, the syndrome represents a profound breakdown in immune tolerance, with autoantibodies directed against erythrocytes and platelets, leading to their premature destruction. In a subset of patients, autoimmune neutropenia may also

occur, adding further complexity to both diagnosis and management.[1]

The condition is rare, with an estimated incidence of fewer than 1 per 1,000,000 individuals and accounting for less than 7% of all AIHA cases. Although Evans syndrome can affect individuals of any age, a slight female predominance has been observed, particularly in cases associated with endocrine and connective tissue autoimmune diseases.[2] Secondary Evans syndrome is known to coexist with systemic lupus erythematosus, Sjögren's syndrome, autoimmune lymphoproliferative syndrome, common variable immunodeficiency, and autoimmune thyroid disorders such as Hashimoto's thyroiditis.

The coexistence of Evans syndrome with autoimmune hypothyroidism is extremely uncommon and has been infrequently documented in literature. Autoimmune thyroiditis, characterized by elevated anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies, may rarely progress into a broader autoimmune state involving hematologic cell lines, reflecting the phenomenon of "polyautoimmunity," wherein multiple autoimmune disorders coexist due to shared pathogenic mechanisms, including genetic predisposition, T-cell dysregulation, and aberrant cytokine networks.[3] Clinically, Evans syndrome typically manifests with features of both hemolytic anemia—fatigue, pallor, jaundice—and thrombocytopenia—mucocutaneous bleeding, petechiae, or menorrhagia. A positive direct Coombs test together with laboratory evidence of hemolysis confirms AIHA, whereas thrombocytopenia indicates ITP. Bone marrow examination generally shows preserved cellularity with erythroid hyperplasia and increased megakaryocytes, suggestive of compensatory marrow activity rather than primary marrow failure.[4] Corticosteroids remain the mainstay of initial therapy and often induce remission. However, the relapsing nature of Evans syndrome frequently necessitates second-line treatments such as intravenous immunoglobulin, rituximab, splenectomy, or immunosuppressive agents. Owing to its chronic course and variable prognosis, Evans syndrome requires vigilant long-term follow-up to monitor for relapse and treatment-related complications.[5]

The present case describes an unusually rare coexistence of Evans syndrome and autoimmune hypothyroidism in a young woman, emphasizing the need for heightened clinical suspicion in patients with autoimmune thyroid disease who present with unexplained cytopenias.

Case Description

A 32-year-old female, presented to KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, with complaints of heavy menstrual bleeding for two months. She reported using 6–8 pads per day with passage of clots and increasing fatigue. There was no history of fever, weight loss, hematuria, hematemesis, or melena. She denied any previous episodes of mucosal bleeding, epistaxis, or petechial rash. Her medical history was notable for autoimmune hypothyroidism for five years, managed with levothyroxine 100 µg daily. She had a full-term vaginal delivery four years ago, during which she developed postpartum anemia treated with parenteral iron therapy. Family history was negative for autoimmune or hematological disorders.

Clinical Examination: On examination, she was alert, afebrile, and hemodynamically stable (BP 110/90 mmHg, pulse 80 bpm). No pallor, petechiae, ecchymoses, lymphadenopathy, or hepatosplenomegaly were noted. Cardiovascular, respiratory, and abdominal examinations were unremarkable. Neurological and thyroid examinations were normal, with no evidence of goiter.

Initial Laboratory Evaluation:

- Hemoglobin: 8.3 g/dL (nadir 7.8 g/dL)
- Hematocrit: 29.5%
- Platelets: 48,000/mm³
- Total Leukocyte Count: 9,600/mm³
- Reticulocyte Count: 12.4% (elevated)
- Peripheral Smear: Dimorphic anemia with thrombocytopenia, neutrophilic leukocytosis
- MCV: 85.8 fL; MCH: 23.4 pg; MCHC: 27.2 g/dL
- ESR: 22 mm/hr

Biochemical Parameters:

- LDH: 647 U/L (elevated)
- Indirect Bilirubin: 0.27 mg/dL
- Direct Bilirubin: 0.01 mg/dL
- TSH: 20.5 µIU/mL (elevated)
- Anti-TPO: >600 IU/mL (positive)
- Anti-Ro (SSA): Borderline positive
- ANA: Negative
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Bone Marrow and Trephine Biopsy Findings:

- Bone marrow aspiration: Megaloblastic changes with erythroid hyperplasia and normoblastic maturation.
- Trephine biopsy: Hyperplastic normoblastic marrow with megakaryocytic hyperplasia.
- Impression: Suggestive of autoimmune thrombocytopenia; rule out Evans syndrome.

Additional Workup:

- Coombs Test: Positive (confirming autoimmune hemolysis)
- Viral serology (HIV, Hepatitis B/C, EBV, CMV): Negative
- Ultrasound abdomen: Normal spleen size, no hepatomegaly
- Gynecologic ultrasound: Simple right ovarian cyst, no structural uterine pathology

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Diagnosis:

Based on the coexistence of autoimmune hemolytic anemia and immune thrombocytopenia, elevated reticulocyte count, positive Coombs test, and exclusion of secondary causes, a final diagnosis of Evans syndrome secondary to autoimmune hypothyroidism (Hashimoto's thyroiditis) was made.

Treatment and Management: The patient was admitted and transfused with 2 units of packed red blood cells and 4 units of platelet concentrate. Intravenous methylprednisolone 1 g/day was initiated for 3 days, followed by oral prednisolone 1 mg/kg/day (Omnacortil 40 mg OD). Levothyroxine 50 µg/day was continued to optimize thyroid function. Additional medications included:

- Inj. Piptaz 4.5 g IV TID (empirical antibiotic coverage)
- Inj. Emeset 8 mg IV (antiemetic)
- Inj. Buscopan 20 mg IV (antispasmodic)
- Tab. Folic acid 5 mg OD
- Inj. Optineuron IM OD (vitamin supplementation)
- Tab. Pause 500 mg TID (to control menorrhagia)
- Tab. Mepareate 10 mg OD
- Tab. Calcium 500 mg OD
- Syp. Sucralfate 10 mL TID

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Over the next 7 days, her menstrual bleeding subsided and her laboratory values improved:

- Hemoglobin increased to 11.7 g/dL
- Platelet count rose to 235,000/mm³
- Reticulocyte count normalized to 3.7%

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Follow-up:

On discharge, the patient was advised to continue oral prednisolone tapering over 6 weeks, thyroid hormone replacement, and iron-folate supplementation. She was counselled regarding relapse risk and the need for periodic CBC and thyroid profile monitoring. At one-month follow-up, she remained clinically stable without recurrence of bleeding or cytopenia.

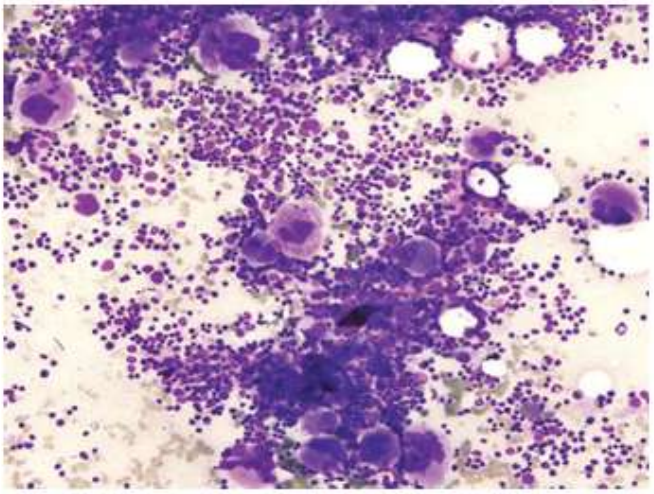

Figure 1: Bone marrow aspirate smear showing erythroid hyperplasia with megaloblastic maturation and increased megakaryocytes, consistent with hypercellular marrow suggestive of Evans syndrome secondary to autoimmune etiology (Leishman stain, 40×)

DISCUSSION

Evans syndrome (ES) is a rare, immune-mediated condition characterized by concurrent or sequential development of AIHA and ITP in the absence of an identifiable secondary pathology. Although first described decades ago, its pathogenesis remains incompletely understood. Evidence suggests that dysregulation of both humoral and cellular immunity plays a central role, involving impaired regulatory T-cell function, defective apoptosis of autoreactive B cells, and heightened cytokine-driven autoantibody production. This dysfunctional immune environment leads to simultaneous targeting of erythrocytes and platelets. Hanafy E et al.6 and Uddin SM et al.7 highlight the variability in clinical expression, which contributes to frequent diagnostic delays and challenges in long-term management.

Several mechanisms have been proposed to explain the pathogenesis, including genetic predisposition, molecular mimicry following infections, and associations with systemic autoimmune diseases. Calapkulu M et al.8 suggest that Evans syndrome represents a generalized state of immune dysregulation rather than isolated cytopenias. The rare coexistence of Evans syndrome with autoimmune thyroid disorders, as seen in the present patient, further supports this notion. Naji P et al.9 emphasize that thyroid autoimmunity may predispose patients to developing additional hematologic autoimmune conditions.

In our patient, markedly elevated anti-TPO

antibodies (>600 IU/mL) confirmed underlying autoimmune hypothyroidism, and the presence of severe anemia, thrombocytopenia, and elevated reticulocyte count was highly suggestive of peripheral destruction. Bone marrow studies revealed hypercellularity with erythroid and megakaryocytic hyperplasia, consistent with a compensated marrow response. The positive Coombs test and exclusion of secondary causes such as infections, malignancy, or systemic autoimmune disease aligned with the diagnostic criteria for Evans syndrome. Shanafelt TD et al.10 Secondary Evans syndrome associated with autoimmune thyroiditis remains rare. Gupta S et al.11 describe similar cases of autoimmune hypothyroidism with coexisting cytopenias, suggesting shared immunopathogenic mechanisms including HLA-linked susceptibility, Th1/Th17 immune activation, and antibody-mediated destruction. Noiwatanakul J et al.12 also highlighted the possibility of polyautoimmunity in such patients.
Clinically, Evans syndrome may present with symptoms of anemia (fatigue, pallor, jaundice) and thrombocytopenia (menorrhagia, petechiae, mucosal bleeding). In this case, menorrhagia served as the initial manifestation, illustrating how gynecologic presentations can obscure underlying systemic autoimmune pathology. The absence of organomegaly, normal leukocyte counts, and preserved marrow cellularity helped exclude infiltrative and myelodysplastic disorders. Yarali N et al.13 First-line therapy with corticosteroids remains the cornerstone of management. Our patient responded promptly to intravenous methylprednisolone followed by oral prednisolone, with normalization of hemoglobin and platelet counts within one week. This favorable early response is consistent with current literature. In relapsed or refractory cases, IVIG, rituximab, azathioprine, mycophenolate mofetil, cyclosporine, and splenectomy have been documented as effective options. Importantly, maintaining euthyroid status with levothyroxine was a critical adjunct, as thyroid dysfunction can exacerbate hematologic abnormalities. Supportive measures such as iron and folate supplementation helped optimize marrow recovery.

The diagnostic challenge in the present case stemmed from overlapping features with megaloblastic anemia and isolated ITP. However, erythroid hyperplasia, normal megakaryocyte morphology, and evidence of hemolysis directed the diagnosis toward Evans syndrome. Kang MY et al.4 emphasize the need for careful differentiation from other autoimmune cytopenias, especially in patients with underlying thyroid disease.

The long-term prognosis of Evans syndrome is variable. Relapses occur in up to 60–70% of cases, and prolonged immunosuppression may result in infections or steroid-related complications. Hence, ongoing follow-up with repeat hematologic and thyroid assessments is essential. Oh HJ et al.14

CONCLUSION

This case highlights a rare presentation of Evans syndrome occurring in association with autoimmune hypothyroidism in a young female. The coexistence of autoimmune hemolytic anemia and thrombocytopenia, along with elevated anti-TPO antibodies, underscores the significance of autoimmune overlap syndromes. Early diagnosis, exclusion of secondary causes, and prompt initiation of corticosteroid therapy led to rapid clinical improvement in this patient. However, due to the relapsing nature of the disease, long-term follow-up and multidisciplinary management are crucial. Awareness of such associations can facilitate early recognition and improve outcomes in patients presenting with otherwise unexplained cytopenias in the background of endocrine autoimmunity.

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