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Case Report

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Evans Syndrome in a Patient with Auto Immune Thyroiditis – A Rare Association

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ABSTRACT

A 46-year-old woman, diagnosed with hypothyroidism, was on treatment with synthetic thyroxine 100 micrograms per day for one year. She complained of recent-onset exertional dyspnoea, and had malaise, lethargy, and pica. Investigations revealed significant anaemia and severe thrombocytopenia, necessitating blood transfusion. She had Coombs-positive autoimmune haemolytic anaemia and immune thrombocytopenic purpura, confirming a diagnosis of Evans syndrome. She also had a positive antinuclear antibody test but had no other notable findings of autoimmune disease, suggesting a diagnosis of primary Evans syndrome. The patient was treated with intravenous dexamethasone for four days, followed by oral prednisolone at 1mg/kg/day, with supplemental calcium and vitamin D. Thyroperoxidase antibody was positive and there was reduced uptake in thyroid scintigraphy, confirming a diagnosis of autoimmune thyroiditis.

Hashimoto's thyroiditis frequently coexists with non-endocrine autoimmune disorders. Presence of antithyroid antibodies is sometimes observed in Evans syndrome, a condition where there is simultaneous occurrence of autoimmune Haemolytic Anaemia, Cytopoenia and immune thrombocytopenic purpura. However, the development of Evans syndrome in patients with overt hypothyroidism and Hashimoto's thyroiditis is rare. This case implies the potential existence of a shared immunogenetic pathway among three distinct autoimmune diseases, namely autoimmune haemolytic anemia, immune thrombocytopenic purpura, and Hashimoto's thyroiditis, in the pathogenesis.

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Introduction

Evans syndrome is an uncommon autoimmune disorder characterized by the simultaneous presence of two or more cytopoenia. The most frequently observed cytopoenia are warm autoimmune haemolytic anaemia (AIHA) and immune thrombocytopenic purpura (ITP), with immune neutropoenia being a less frequent occurrence [1]. Evans syndrome may have connections to other illnesses or conditions, including systemic lupus erythematosus, lymphoproliferative disorders, primary immunodeficiencies, and viral infections such as hepatitis C, cytomegalovirus, varicella-zoster, and Epstein-Barr [2]. Autoimmune thyroid diseases (AITD) are the most common organ-specific autoimmune disorders and impact 2-5% of the population [3]. AITD include Graves' Disease (GD) and Hashimoto's Thyroiditis (HT), among others. HT and GD are the primary causes of hypothyroidism and hyperthyroidism, respectively[4]. However, association between Evans syndrome and auto immune thyroiditis is rarely reported .

Case Report

A 46-year-old woman presented with a one-week history of exertional dyspnoea. She also complained of malaise, lethargy, and pica for one month. She had no chest pain, palpitations, or other symptoms of heart failure. She was experiencing menorrhagia for the past few months but there were no other bleeding manifestations. She had a prior diagnosis of hypothyroidism but was not attending follow-up. There was no family history of bleeding disorders. She was not a vegan and was taking a mixed diet.

On examination, she was pale and icteric. There was no dyspnoea or lymphadenopathy. There were no features of connective tissue disorder, or peripheral stigmata of chronic liver or kidney disease. She did not have a goiter or features of Graves' ophthalmopathy. The pulse rate was 68 beats per minute with good volume and regular rhythm, blood pressure was 130/80mmHg and no cardiac murmurs were audible. Lung examination revealed clear breath sounds with equal bilateral air entry. Mild splenomegaly was noted. Neurological examination was normal.

Since the patient presented with symptoms of anaemia with a recent history of menorrhagia, iron deficiency anemia was suspected

initially. However, the blood count revealed bicytopoenia and the blood picture showed partially treated iron deficiency anaemia with thrombocytopenia,(refer to table 1) raising the possibility of immune thrombocytopenic purpura. Although LDH and serum bilirubin were normal the reticulocyte count was high and the direct antiglobulin test was positive, confirming the diagnosis of autoimmune haemolytic anaemia. Bone marrow examination confirmed the diagnosis of ITP. With the simultaneous presence of both autoimmune haemolytic anemia and ITP a diagnosis of Evans syndrome was made.

Table 1: Summary of investigations

Investigations	Value	Reference range
White cell count Haemoglobin Platelets	6970 ➡ 8420 ➡ 9880 6.7 ➡ 8 2000 ➡ 4000 ➡88000	4000-10000/µl 13.2-16.5 g/dl 150000-450000/µl
Erythrocyte sedimentation rate (ESR)	120	<30mm/hour
Aspartate transaminase(AST)	14	0-35 U/L
Alanine transaminase(ALT)	15	0-40 U/L
Total Protein	6.7	6-8.5 g/dl
Serum Albumin	3.5	3.5-5.3 g/dl
Serum Potassium	3.8	3.5-5.1 mmol/l
Serum Sodium	140	137-145 mmol/l
Serum Globulin	3.4	2.5-3.5 g/dl
Total Bilirubin	6.7	5-19 µmol/l
Direct Bilirubin	2.8	0-5 µmol/l
Indirect Bilirubin	3.9	
Serum Creatinine	94	70-115 µmol/l
Anti-Nuclear Antibody(ANA)	Positive	
Thyroid stimulating hormone (TSH)	>100	0.3-4.2 Miu/L
FT4	9.41	12-16.1 µmol/l
Ultrasound scan Abdomen	Splenomegaly	
Lactate dehydrogenase	223	0-240 U/L
C-Reactive protein	1.3	0-5 mg/L
Pus cells -1-3/high power field ,Red cells -1-2/high power field		
Iron	2	6.6-30.4 µmol/l
Transferrin saturation	2.4%	15-50- %
Fasting blood sugar	85	70-99 mg/dl
Direct antiglobulin test	Positive	
CXR-PA	Normal	
Retroviral screening	Negative	
VDRL	Non-reactive	
Blood picture	Partially treated iron deficiency anaemia with thrombocytopenia . ?ITP	
Bone marrow Aspiration	Erythroid hyperplasia and megakaryocytes seen.	

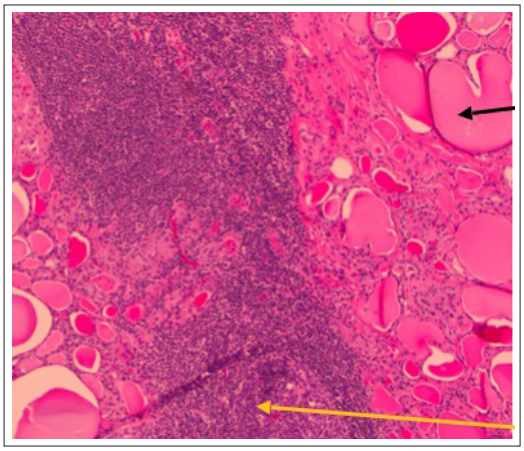

Figure A: Showing cytology of Auto immune thyroiditis in the patient. Black arrow -thyroid tissue,Yellow arow -lymphocytic infiltration

Discussion

Evans syndrome is characterized by the presence of two or more cytopoenia classically, which can occur either concomitantly or sequentially. The most common cytopoenia associated with Evans syndrome are autoimmune haemolytic anemia and immune thrombocytopenic purpura, typically occurring in the absence of an underlying cause such as malignancy or an offending medication [1]. Evans syndrome is a rare condition, diagnosed in only 0.8%–3.7% of all patients with either ITP or autoimmune haemolytic anemia. Specifically, the type of AIHA observed in Evans syndrome is warm AIHA, characterized by the reaction of IgG antibodies with red blood cell surface antigens at body temperature, as opposed to cold AIHA [2]. In ITP, the immune system targets GPIIb/IIIa on the platelets [2]. The pathogenesis of Evans syndrome remains complex and not fully understood, but it is believed to involve immune system dysregulation, leading to the destruction of red blood cells and platelets by autoantibodies [5].

Evans syndrome in patients with auto immune thyroiditis is infrequently described in literature [4,10,11]. When a patient presents with Evans syndrome together with autoimmune thyroiditis an autoimmune polyglandular syndrome (APS) becomes a possibility. These syndromes involve clusters of endocrine abnormalities that manifest in specific patterns in individuals with immune dysregulation, leading to the recognition and management of associated systemic or hormonal deficiencies. There are three primary types of APS; APS1, APS2, and APS3 [6]. APS1 is characterized by chronic muco-cutaneous candidiasis, hypoparathyroidism, primary adrenal insufficiency, ectodermal dystrophy, and various other autoimmune destructive processes affecting both endocrine and non-endocrine tissues [6]. APS2 is typified by type 1 diabetes mellitus, Addison disease, and hypothyroidism; APS3 is similar but without Addison disease [6]. If the autoimmune poly endocrinopathies do not meet the criteria of APS 1-3 they are categorized as autoimmune polyendocrine syndrome type 4 [7].

As Evans syndrome can be either primary or secondary to an autoimmune or lymphoproliferative disorder further investigations were undertaken. ANA was positive but further investigations for systemic lupus erythematosus (ds-DNA, C3 and C4) were negative. There was no clinical or imaging evidence to suggest a lymphoproliferative disorder. A diagnosis of primary Evans syndrome seemed likely. Hypothyroidism was confirmed with thyroid functions tests. Thyroid peroxidase antibody was positive and thyroid scintigraphy revealed reduced uptake confirming auto immune thyroiditis.

The patient received blood and platelet transfusions to relieve symptoms. She was given intravenous dexamethasone 10 mg six hourly for four days and was switched to oral prednisolone 1mg/kg/day thereafter with supplemental calcium, vitamin D and alendronate for bone protection. The patient responded remarkably well to prednisolone, with a rise of the platelet count from 4000/µl to 172000/µl over four days. Hematology follow-up was arranged, and the patient was discharged on a tapering regimen of prednisolone over four months. She did not experience any relapses during the tapering process.

Hashimoto's thyroiditis, also known as chronic autoimmune thyroiditis or chronic lymphocytic thyroiditis, is an autoimmune disorder characterized by the destruction of thyroid cells through a cell and antibody-mediated immune process [8]. When Evans syndrome occurs together with autoimmune thyroiditis the potential for multiple autoimmune disorders to coexist in a single individual is highlighted. As this patient had no clinical features or investigation results suggestive of Addison disease or diabetes, she was classified as APS 4. This case is a reminder to physicians to check the thyroid status and consider autoimmune thyroiditis in a patient with Evans syndrome.

The simultaneous occurrence of these autoimmune disorders may be due to shared genetic susceptibility factors and irregularities in immune regulation [8]. Emerging evidence from several studies indicates that specific genetic polymorphisms, particularly those within genes associated with immune response and self-tolerance, might increase an individual's susceptibility to developing multiple autoimmune disorders. Nevertheless, further studies are needed to unravel the exact genetic and immunological mechanisms responsible for this phenomenon [8].

The management of a patient with both Evans syndrome and autoimmune thyroiditis requires a multidisciplinary approach [9]. The treatment strategies should address the autoimmune response, alleviate cytopoenia, and manage thyroid dysfunction. Corticosteroids are frequently the initial therapy for both conditions, as they reduce inflammation by suppressing the immune system [9]. In certain cases, additional immunosuppressive agents such as rituximab or cyclosporine may be needed to achieve disease control. Autoimmune thyroiditis often requires thyroid hormone replacement therapy to ensure the maintenance of normal thyroid function [9].

Hye Jin Oh et al reported a case where the patient was successfully treated with intravenous rituximab [4]. Mi Yeon Kang et al reported a patient who was resistant to steroids and had to undergo splenectomy [10]. Koti et al also reported a case where Evans syndrome was successfully treated with corticosteroids [11]. Our patient was effectively treated with intravenous dexamethasone followed by a tapering dose of prednisolone. Evans syndrome and autoimmune thyroiditis can be successfully treated with steroids alone, as evidenced by these case reports.

Regular monitoring of the patient's blood counts, thyroid function, and overall clinical status is essential to assess treatment response and detect potential complications [12]. Long term follow up is crucial, as patients with Evans syndrome and autoimmune thyroiditis may require immunosuppressive therapy and thyroid hormone replacement over a long period [12].

Conclusion

The coexistence of autoimmune thyroiditis and Evans syndrome in this patient highlights the intricate interplay between autoimmune disorders and the need for a comprehensive diagnostic and therapeutic approach. This case underscores the importance of a thorough clinical evaluation and a wide-ranging haematological and thyroid assessment to identify and manage these concurrent conditions effectively. The successful treatment of our patient with a tailored regimen of corticosteroids demonstrates the potential for favorable outcomes. Multidisciplinary care and follow up are essential in the long-term management, to ensure patient well-being and optimal therapeutic outcomes. This case is a reminder of the intricate nature of autoimmune diseases and the critical role of healthcare professionals in providing holistic and personalized care to individuals with these conditions.

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