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Case Report

Internal Medicine Section

Bridging Immune Realms: A Striking Case Report on Autoimmune Thyroiditis Co-existing with Immune Thrombocytopenic Purpura

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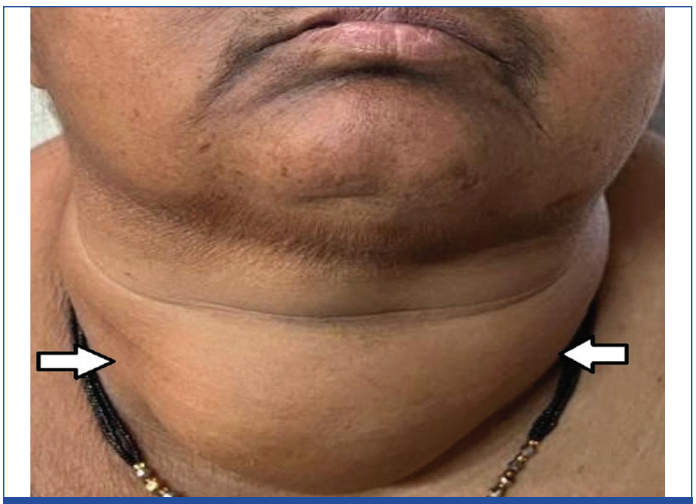
ABSTRACT

Immune Thrombocytopenic Purpura (ITP), an autoimmune disease, is characterised by isolated thrombocytopenia, with or without bleeding. Thyroid autoimmune illness can coexist with ITP. The specific clinical characteristics are still unknown. The length of ITP or the patients' response to treatment is not related to their thyroid condition. In patients with ITP, thyroid impairment is more common. In the present case report, a 60-year-old female patient, a known case of asthma, presented to the hospital with complaints of swelling in the neck along with transient episodes of breathlessness for 3-4 years. On local examination, a butterfly-shaped mass was seen in the neck, which moved upwards on deglutination but did not move on protrusion of the tongue. Pemberton's sign was also positive. On palpation, the thyroid measured around 8×6 cm in size, thyroid lobes were bosselated, consistency was firm, and no bruit was heard on auscultation. Based on routine laboratory findings, she was found to have refractory thrombocytopenia with a normal thyroid profile. Further investigations revealed that the patient had positive antithyroid stimulating hormone antibodies, and Fine Needle Aspiration Cytology (FNAC) showed colloid nodular goitre with haemorrhagic cystic changes. A bone marrow biopsy was performed in view of refractory thrombocytopenia, which was suggestive of ITP. The patient was advised to take tablet eltrombopag, after which the platelet counts improved drastically. Subsequently, the patient was advised to undergo thyroidectomy, but this could not be done due to haemodynamic instability.

Keywords: Bleeding, Colloid nodular goitre, Eltrombopag, Euthyroid, Refractory thrombocytopenia, Thyroid enlargement

CASE REPORT

A 60-year-old female presented to the medicine outpatient department with chief complaints of swelling in the neck and transient episodes of breathlessness for the past 3-4 years. The swelling in the neck was gradually progressive in nature [Table/Fig-1]. The patient also reported a significant weight gain of around 30-40 kg in the last 4-5 years. The thyroid profile was conducted 3-4 years ago, which was found to be normal. The patient was a known case of bronchial asthma for the last 5-6 years, for which she was using a formoterol and budesonide combination inhaler. There was no history of any co-morbidities such as systemic hypertension, diabetes mellitus, or tuberculosis in the past. Additionally, there was no significant family history, no previous hospitalisations, and no known drug allergies.



[Table/Fig-1]: A 60-year-old female patient presenting with swelling in the neck of around 8×6 cm shown by white arrows.

During the general physical examination, bilateral pitting pedal oedema was noted, along with facial puffiness. The patient did not exhibit pallor, icterus, cyanosis, lymphadenopathy, or clubbing. Her blood pressure was 130/70 mmHg measured in the right arm in a supine position, with a heart rate of 82 beats per minute. On local examination, a butterfly-shaped mass was observed in the neck, which moved upwards on deglutination but did not move on protrusion of the tongue.

Pemberton's sign was positive on palpation, the thyroid measured around 8×6 cm in size, and the thyroid lobes were bosselated. The consistency was firm, and no bruit was heard. Bilateral crepitations were present in the basal lung field on auscultation.

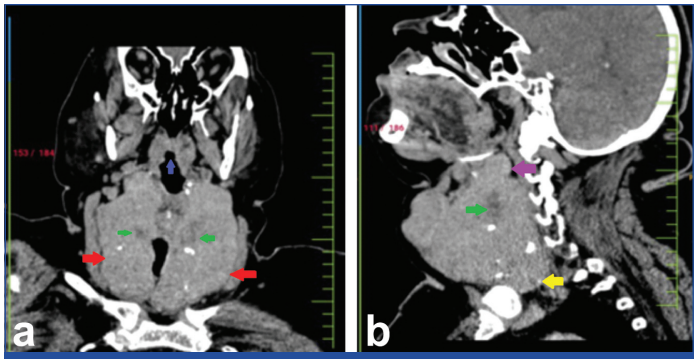
Upon evaluation of the blood investigations [Table/Fig-2], she was found to have thrombocytopenia with normal levels of leukocytes. However, the thyroid profile was normal despite the large thyroid swelling. Therefore, an antithyroid antibodies test was suggested. The antithyroid Peroxidase antibody was negative, but the antithyroid stimulating hormone receptor antibodies were elevated (4.9 IU/L) (normal range 0-1 IU/L), suggestive of autoimmune thyroiditis. [Table/Fig-2] displays the laboratory blood investigations.

The ultrasound of the neck indicated multiple solid cystic lesions in the bilateral enlarged thyroid lobes with the isthmus suggestive of Thyroid imaging Reporting and Data System (TIRADS). The Contrast-enhanced Computed Tomography (CECT) of the neck venous phase, coronal and sagittal images showed well-defined, lobulated, diffusely enlarged bilateral lobes of the thyroid gland and isthmus with a few non enhancing necrotic areas. The thyroid gland extended superiorly from behind the hyoid bone up to the suprasternal notch, as shown in [Table/Fig-3a,b].

The FNAC revealed multiple sheets of follicular cells and giant follicles with nuclei showing moderate anisonucleosis, along with a

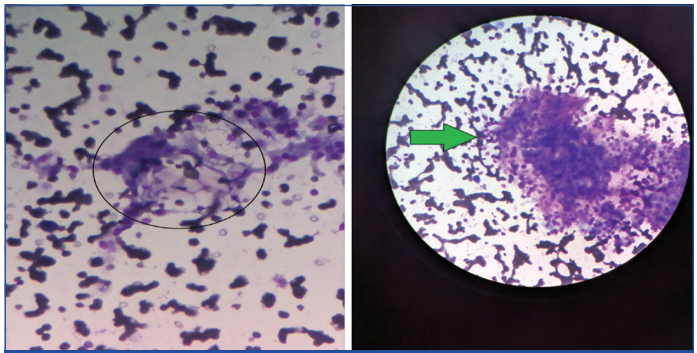
Parameters	Value	Normal value
Haemoglobin (gm%)	11.3	12-15
Total leukocyte count (cu. mm)	9000	4000-11000
Platelet count (lacs/ cu. mm)	0.40	1.5-4.1
Mean corpuscular volume (fL)	72	83-101
Alkaline phosphatase (U/L)	112	38-126
Alanine aminotransferase (U/L)	22	<35
Aspartate aminotransferase (U/L)	25	14-36
Urea (mg/dL)	17	15-36
Creatinine (mg/dL)	0.5	0.52-1.04
Potassium (meq/L)	4.6	3.5-5.1
Total bilirubin (mg/dL)	1.3	0.2-1.3
Conjugated bilirubin (mg/dL)	0.6	0- 0.3
Thyroid stimulating hormone (microIU/ mL)	0.501	0.465-4.68
Free T3 (pg/mL)	5.13	2.77-5.27
Free T4 (ng/dL)	1.98	0.78-2.19
Anti-thyroid peroxidase antibody (IU/mL: Negative >75 IU/mL: Positive)	12.3	<50
Antithyroid stimulating hormone receptor antibodies (IU/L)	4.9	0-1

[Table/Fig-2]: Laboratory blood investigations of the patient.



[Table/Fig-3]: Contrast-enhanced computed tomography (CECT) of neck venous phase coronal (a), and sagittal (b) images showing enhancing, well-defined, lobulated, diffusely enlarged bilateral lobes of thyroid gland (red arrows) and isthmus (blue arrows) with few non enhancing necrotic areas within (green arrows). The thyroid gland is seen extending superiorly from behind the hyoid bone (purple arrow) upto the suprasternal notch inferiorly (yellow arrow).

few colloidophages and haemosiderophages (TBS Category II) [1], as shown in [Table/Fig-4].

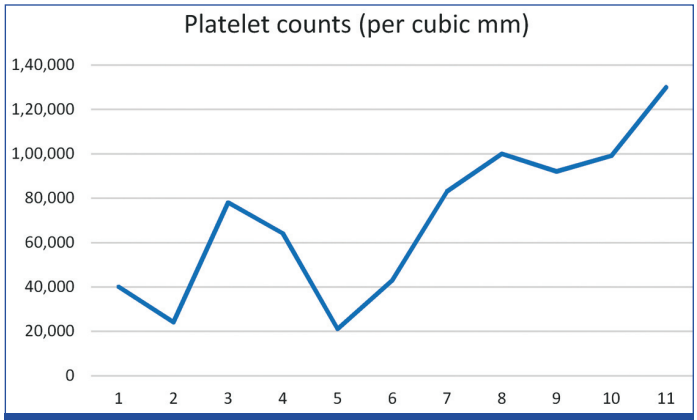


[Table/Fig-4]: Follicular cells with moderate anisonucleosis admixed in haemorrhagic stroma (Black circle) with multiple sheets of giant follicular cells placed in cohesion (Green arrow) (Giemsa stain, 40X).

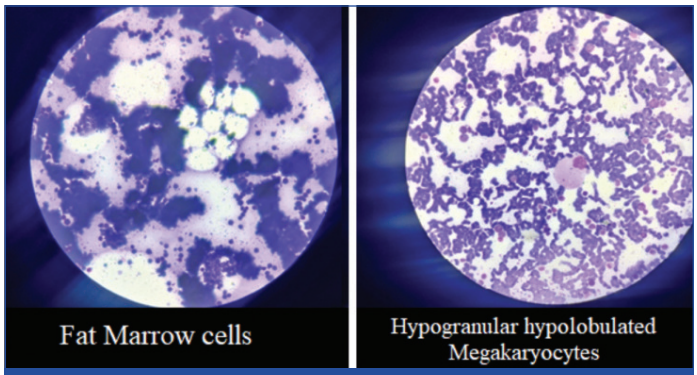
The ultrasound of the abdomen and pelvis suggested hepatomegaly with grade II fatty liver and non visualisation of bilateral ovaries.

A 2D echo indicated good biventricular systolic function with mild left ventricular hypertrophy and a left ventricular ejection fraction of 60% with grade II diastolic dysfunction. The patient was suspected to have secondary ITP.

Daily platelet counts were monitored, as shown in the line graph below [Table/Fig-5]. Due to persistent thrombocytopenia, a bone marrow biopsy was performed, and serum antinuclear antibodies were tested, which came back negative. The bone marrow biopsy revealed a moderate increase in the number of immature, large, and non lobulated megakaryocytes with single nuclei and hypogranularity, along with fibroadipose tissue suggestive of idiopathic thrombocytopenic purpura, as depicted in [Table/Fig-6].



[Table/Fig-5]: Line graph: Daily platelet monitoring (Platelets concentrates were given on day 2 and day 3, while eltrombopag was started on day 5).



[Table/Fig-6]: Bone marrow biopsy showing moderate increase in number of megakaryocytes which were immature, large, non lobulated with single nuclei with hypogranularity along with fibroadipose tissue suggestive of Idiopathic thrombocytopenic purpura (Leishmann stain, 400X).

Treatment for the patient commenced with injectable dexamethasone 6 mg once a day, two doses of injection romiplostim 250 mg, and capsule danazol [2] 100 mg once a day. Subsequently, the patient was started on tablet prednisolone 60 mg once daily. Despite receiving two doses of romiplostim and steroids, the patient's platelet count continued to fluctuate. Therefore, the patient was initiated on tab eltrombopag 50 mg once daily, after which her platelet count stabilised and remained consistently above one lakh/cubic millmetre.

While on steroids, the patient experienced deranged blood sugar levels and blood pressure, prompting the administration of insulin regular and insulin glargine for glycaemic control. Additionally, the patient received oral antihypertensive medications to manage her blood pressure.

Ultimately, the patient's platelet counts, blood sugar levels, and blood pressure were regulated, leading to her discharge from the hospital. She was scheduled for regular follow-up appointments every 15 days.

DISCUSSION

The ITP is described as isolated thrombocytopenia (platelet count 100,000/per microlitre) with normal white blood cells and normal haemoglobin in the context of a widespread purpuric rash by the American Society of Haematology [3]. The present report focuses on primary ITP, which is ITP without an underlying illness or secondary aetiology. ITP with an underlying ailment or aetiology, such as drug-induced or systemic illness-induced ITP, is known as secondary ITP {e.g.,Systemic Lupus Erythematosus (SLE), Human Immunodeficiency Virus (HIV), Common Variable Immunodeficiency (CVID), etc.} [4]. Treatment is necessary for

severe ITP, which often occurs when platelet counts are below 20,000/micro L [3].

The timing and persistence of symptoms are used to further divide primary ITP into three phases. ITP that has been less than three months since the diagnosis. Persistent ITP is the continuation of ITP after the initial diagnosis of 3 to 12 months, while chronic ITP is the continuation of ITP for more than 12 months. Refractory ITP is the failure of splenectomy [3].

Immunoglobulin G autoantibodies make the circulating platelets more vulnerable, speeding up their removal by the antigen-presenting cells (macrophages) of the spleen and occasionally the liver, as well as other components of the monocyte-macrophage system [4,5]. The bone marrow increases platelet production to compensate for platelet loss. ITP typically appears a few weeks following a viral infection in healthy children and adolescents.

With immunosuppressive treatment, ITP is typically treatable. SLE, infectious mononucleosis, lymphomas, chronic lymphocytic leukaemia, and other bacterial and viral diseases can all be linked to the same type of autoimmune thrombocytopenia [5]. ITP and autoimmune thyroid disorders can manifest at the same time when they are linked; however, the intervals between their onset might vary greatly from months to years [5].

Particularly in those with hyperthyroidism, patients with autoimmune thyroid disease may exhibit thrombocytopenia. Recent research indicates that thyroid hormone activation of the reticulo-endothelial phagocyte system or platelet immune destruction may be secondary causes of thrombocytopenia in thyroid disorders [6]. ITP is currently considered an acquired autoimmune disease that causes isolated thrombocytopenia and is one of the most common causes of thrombocytopenia in otherwise asymptomatic adults. Autoantibodies against platelet antigens are the cause of ITP, an acquired thrombocytopenia [4].

Infections, autoimmune diseases, and lymphoproliferative disorders are a few examples of concurrent diseases that might result in secondary ITP. Due to their different origins, secondary ITP has a different response to treatment than primary ITP. Therefore, a correct diagnosis is crucial [3,5].

Once all other possible causes of thrombocytopenia, such as infections with HIV, hepatitis C, or hepatitis B viruses, medications, or rheumatologic conditions including systemic lupus erythematosus and antiphospholipid antibody syndrome, have been ruled out, ITP is the only possible diagnosis. The pathophysiology of thrombocytopenia in ITP is explained by the destruction of the platelet-antibody complex by the reticuloendothelial system at a rate greater than the marrow's capacity for replacement. Recent data from the past few years suggest that patients with ITP may also have reduced platelet production [3].

In recent years, the co-existence of thyroid dysfunction (mainly hyperthyroidism) with ITP, particularly in adult chronic ITP patients, has received considerable attention; however, the pathophysiology is not fully understood. Although reports and research have shown the existence of ITP patients with positive antithyroid antibodies, thyroiditis as the underlying cause of newly diagnosed ITP is a relatively uncommon occurrence [5].

The activation of the reticuloendothelial system by thyroid hormones and the existence of an autoimmune mechanism that can cause both ITP and thyroiditis are the two hypothesised theories to explain the relationship between the two illnesses [5].

In 1931, Jackson was the first to identify a link between thrombocytopenia and hyperthyroidism. Although uncommon, this relationship has been shown in numerous investigations, particularly in relation to Graves' disease and Hashimoto's thyroiditis. ITP and autoimmune thyroid disorders can both manifest at the same time when they are linked; however, the intervals between their onsets can range from months to years [5]. Thyroid disorder can invariably be associated with neuropsychiatric manifestations, chronic kidney disease, myasthenia crisis, and may even present as multiorgan dysfunction syndrome [6-9].

In a case study by Yingchoncharoen P et al., where they discuss a patient presented with ITP and hyperthyroidism. The platelet count drastically improved on treating the patient's hyperthyroidism while no other treatment was given for ITP [10].

In another case study by Tahir H et al., they discuss a patient with ITP secondary to Hashimoto's Thyroiditis, in whom treatment of subclinical hypothyroidism with levothyroxine along with corticosteroids resulted in improved platelet counts [11].

During the emergency observation phase, the present patient's response to first-line ITP treatment was unsatisfactory, thus eltrombopag was added. For more than 10 years, individuals with chronic ITP have commonly taken the thrombopoietin receptor agonist eltrombopag, although it is rarely used in newly diagnosed ITP patients [6]. Elevated liver enzymes, headaches, upper respiratory tract infections, and diarrhoea are the most frequent adverse reactions to eltrombopag medication in children [5,6].

It is still debatable how thyroid illness and its therapy affect the clinical course of ITP. In contrast to hypothyroidism, most case reports of hyperthyroidism and ITP demonstrate complete remission of the thrombocytopenia or better management with the standard therapy approaches [5].

The finding of this instance strongly suggests that thyroid function interferes with corticosteroid's ability and reduces thrombocytes in ITP cases. Therefore, thyroid function assessment is recommended in cases that display resistance to the standard ITP therapy procedures [5].

However, no association has been found between the severity of thyroid function and the severity of ITP. This demands the need for more research in this aspect of medical science correlating the thyroid autoimmune disease and ITP.

CONCLUSION(S)

The present case report discusses a 60-year-old female who presented with thyroid swelling and refractory thrombocytopenia, which was found to be ITP on further evaluation. However, the patient's thyroid profile was found to be normal, but her antithyroid stimulating hormone receptor antibody was found to be elevated. This suggests the relationship between autoimmune thyroid illness and ITP, highlighting the significance of testing for thyroid disease in patients with profoundly isolated thrombocytopenia, especially those resistant to standard therapy. However, when managing and monitoring such individuals, it is also important to consider long-term improvement monitoring.

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