The association of hyperthyroidism and immune thrombocytopenia: Are we still missing something?

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ABSTRACT

Though the American society of hematology Guidelines and British guidelines do not recommend screening of thyroid diseases in cases of immune thrombocytopenia (ITP), more than 160 cases of hyperthyroidism associated with ITP have been reported. Numerous case reports would suggest that patients with ITP and concurrent hyperthyroidism would respond to control of thyroid disease rather than the standard ITP treatment. Although this issue is still debatable, we report a case of a young female with a previous diagnosis of hyperthyroidism which was not well controlled, had presented with severe thrombocytopenia. Initially, all work-up had been done to find out the cause of thrombocytopenia. After all normal reports except deranged thyroid function tests, the patient was labeled as ITP and started on steroids. Even after a few months of steroid treatment, platelet counts had not improved. However, after starting antithyroid drugs, platelet counts had become normalized.

KEYWORDS: Antithyroid drugs, Autoimmune disease, Platelet counts, Steroids

INTRODUCTION

Though guidelines do not recommend the screening of thyroid diseases in cases of Immune thrombocytopenia (ITP), numerous case reports would suggest that patients with ITP and concurrent hyperthyroidism, would respond to control of thyroid disease rather than the standard ITP treatment.

CASE REPORT

We report a case of ITP in a known case of hyperthyroidism in a 36-year-old female of Indian origin. She initially presented to the outpatient department with asymptomatic thrombocytopenia. However, she had a history of bleeding gums, menorrhagia, and ecchymotic patches on all over body 4 months back. These complaints were associated with weakness and easy fatigability for which she had consulted a private physician. Laboratory reports were suggestive of serum thyroid-stimulating hormone (TSH): 0.001 microIU/mL (normal range: 0.35–5.5 microIU/mL), hemoglobin: 4.8 g%, white blood cells 5000/µL, and platelet: 36,000/µL. Considering anemia due to an acute bleeding episode, she was given 2-pack cell volume. After a week, she underwent investigations for thrombocytopenia. All investigations turned out to be negative (serum lactate dehydrogenase, specific antigen 1, Ig-G, and Ig-M were negative. Human Immunodeficiency Virus (HIV), HbsAg, hepatitis C virus were negative. Peripheral smear did not show malarial parasite. Dengue non-specific antigen 1, Ig-G, and Ig-M were negative. Human Immunodeficiency Virus (HIV), HbsAg, hepatitis C virus were also negative. On admission, laboratory investigations revealed: hemoglobin 13.6 g/dL, total leukocyte count 7800/µL, platelet count 21,000/µL. Serum TSH 0.01 mIU/L (normal range: 0.35–5.5 mIU/L), serum free T3 8.48 pmol/L (normal range: 3.542–6.468 pmol/L), and serum free T4 37.97 pmol/L (normal range 11.5–22.7 pmol/L). Urine routine examination, liver function test, and renal function test were within normal limits. Abdominal examination spleen and liver were not palpable and the rest of systemic examinations were unremarkable.

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negative. Antinuclear antibody profile was negative ruling out autoimmune causes. Bone marrow examination revealed normal functioning marrow. However, we restarted carbimazole 10 mg three times a day which had been kept on hold, and steroids were tapered off. After starting antithyroid medications, her platelet counts gradually improved. During subsequent follow-up, her thyroid function tests and platelet counts became normal. The trend of her platelet counts and thyroid function tests is summarized in [Tables 1 and 2].

**DISCUSSION**

Coexistence of ITP and hyperthyroidism is a well-documented but not a well-understood association. The association of these two diseases can be explained by the theory of the production of two kinds of antibodies (platelet-associated IgG, antithyroid antibodies [Microsomal and thyroglobulin antibodies]) against platelets and TSH receptor [1]. In addition to this, shorter platelet lifespan, which is metabolic in nature rather than immunogenic, in patients with hyperthyroidism and increased reticuloendothelial phagocytic activity are also postulated as a mechanism for thrombocytopenia in a case of hyperthyroidism [2,3]. The presentation of this association varies from case to case. It can present with a new onset of thrombocytopenia without life-threatening symptoms in a patient with preexisting hyperthyroidism, or it can present with a life-threatening thyrotoxic crisis which mimics sepsis in a known case of stable ITP [4,5]. In fact, studies show that autoimmune thrombocytopenia, in the course of thyroid disease, is far more prevalent than vice versa [1].

Although hyperthyroidism is known to shorten the platelet survival by enhancing reticuloendothelial activity, the resultant thrombocytopenia is usually mild-to-moderate [3]. Therefore, this mechanism cannot explain the severe thrombocytopenia of the present case. The severity of the thrombocytopenia and its responsiveness to antithyroid medication strongly support the first view that both disorders stemmed from a common autoimmunity. A similar response was seen in a case of ITP with Graves, whereby dose adjustment of methimazole normalized the thyroid function as well as spontaneous recovery of platelet count which had fallen due to irregular adherence to antithyroid medication [4]. However, in our case-patient was already prescribed steroids for ITP for 2 months, but the failure of the standard therapy to improve platelet counts prompted us to look for other therapeutic options. After correcting thyroid function with antithyroid medication, platelet count raised without concurrent steroid supplementation. This suggests that in a patient of hyperthyroidism with ITP, correction of the hyperthyroidism plays a role in correcting the immune system imbalance which impairs not only the thyroid function but also the platelet antigen response. Despite more than 160 cases of hyperthyroidism associated with ITP that have been reported, the American society of hematology Guidelines and British guidelines do not recommend screening of thyroid diseases in cases of ITP [6-8]. This is might be because of lack of clarity of the exact mechanism and association.

**Declaration of patient consent**

The author certifies that the patient has obtained appropriate patient consent form. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initial will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

### Table 1: Trend of thyroid function test and platelet counts before starting antithyroid therapy

| Date       | Serum TSH (normal range: 0.35-5.5 mIU/L) | Free T3 (normal range: 3.542-6.468 pmol/L) | Free T4 (normal range: 11.5-22.7 pmol/L) | Platelet counts (normal range: 150,000-450,000/µL) | Treatment received | Steroid dose |
|------------|----------------------------------------|---------------------------------------------|----------------------------------------|-------------------------------------------------|-------------------|--------------|
| March 08, 2016 | 0.001                                  | 7.3                                         | 29.5                                   | 36,000                                           | FFP, PCV, steroids | Methylprednisolone 1 g/day for 3 days then prednisolone 70 mg/day (1 mg/kg/day) for 1st month then tapered. 5 mg reduced every week |
| March 16, 2016 | 0.06                                   | 8.12                                        | 30.1                                   | 12,000                                           | Steroids          | Steroids     |
| April 08, 2016 | -                                      | -                                           | -                                      | 73,000                                           | Steroids          | Steroids     |
| May 05, 2016  | 0.08                                   | -                                           | -                                      | 45,000                                           | Steroids          | Steroids     |
| June 01, 2016 | -                                      | -                                           | -                                      | 121,000                                          | Steroids          | Steroids     |
| July 08, 2016 | 0.05                                   | 12.2                                        | 35.3                                   | 34,000                                           | Steroids          | Steroids     |
| July 14, 2016 | 0.01                                   | 8.48                                        | 37.97                                  | 21,000                                           | Carbimazole       | Carbimazole  |

TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Thyroxine, FFP: Fresh frozen plasma, PCV: Pack cell volume

### Table 2: Trend of thyroid function test and platelet counts after starting antithyroid therapy

| Date       | Serum TSH (normal range: 0.35-5.5 mIU/L) | Free T3 (normal range: 3.542-6.468 pmol/L) | Free T4 (normal range: 11.5-22.7 pmol/L) | Platelet counts (normal range: 150,000-450,000/µL) | Treatment received | Dose of carbimazole |
|------------|----------------------------------------|---------------------------------------------|----------------------------------------|-------------------------------------------------|-------------------|---------------------|
| July 17, 2016 | -                                      | -                                           | -                                      | 30,000                                           | Carbimazole       | 30 mg               |
| August 08, 2016 | 0.02                                   | 3.90                                        | 13.53                                  | 292,000                                          | Carbimazole       | Carbimazole         |
| September 19, 2016 | 0.13                                   | 4.32                                        | 14.33                                  | 308,000                                          | Carbimazole       | Carbimazole         |
| October 25, 2016 | 0.6                                    | 5.01                                        | 18.25                                  | 210,000                                          | Carbimazole       | Carbimazole         |
| December 05, 2016 | 0.7                                    | 5.4                                         | 20.72                                  | 249,000                                          | Carbimazole       | Carbimazole         |
| January 06, 2017 | -                                      | 4.3                                         | 17.85                                  | 297,000                                          | Carbimazole       | Carbimazole         |
| February 13, 2017 | -                                      | -                                           | 22.45                                  | 271,000                                          | Carbimazole       | Carbimazole         |

TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Thyroxine
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Conflicts of interest
There are no conflicts of interest.

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