An Idiopathic Thrombocytopenic Purpura Responding to the Antithyroid Treatment in a Patient with Graves Ophthalmopathy: A Case Report

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Authors’ contributions
This work was carried out in collaboration between all authors. Author MO wrote the draft of the manuscript and supervised the work. Author AE managed the literature searches. Author IU designed the figures. Authors HK and FB managed literature searches and contributed to the correction of the draft. Author CG provided the case and the figures. All authors read and approved the final manuscript.

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ABSTRACT
Autoimmune diseases may be related with the development of a secondary autoimmune disorder. We, herein, report a case (31 years old female) of idiopathic thrombocytopenic purpura responding to antithyroid treatment in a patient with Graves Ophthalmopathy (GO). The relation between Idiopathic Thrombocytopenic Purpura (ITP) and Graves Disease (GD) is not well known. In the current case, recovery from hyperthyroidism by propylthiouracil (PTU) coincided with the platelet count improvement to a tolerable level. To the literature, this is the first case of GD-GO associated with ITP responding to antithyroid-PTU therapy.

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ABBREVIATIONS

GO : Graves Ophthalmopathy
IT : Idiopathic Thrombocytopenic Purpura
GD : Grave’s Disease
PTU : Propylthiouracil
TSH : Thyroid Stimulating Hormone
CAS : Clinical Activity Score
RA : Radioactive Iodine Therapy
CTLA-4 : Cytotoxic T lymphocyte-associated molecule-4

1. INTRODUCTION

Development of a secondary autoimmune disease may be noticed in the course of primary autoimmune disorder. We, herein, report a case of idiopathic thrombocytopenic purpura (ITP) responding to antithyroid treatment in a patient with Graves Ophthalmopathy (GO). The relation between ITP and Grave’s disease (GD) is not well known. The immunologic relationship between these two disorders is reported, but poorly mentioned in the literature. According to our knowledge, this is the first case involved with ophthalmopathy investigating the relationship between GO and ITP.

2. PRESENTATION OF CASE

A 31 years old female was referred to the outpatient clinic due to petechiae for 3 days. She had no known history of any systemic disorder. Physical examination revealed petechiae on the upper and lower extremities. No palpable lymphadenopathy or hepatosplenomegaly was detected and the other systems were normal. In the laboratory assessment, hemoglobin and white blood cell count were in normal range, but thrombocytopenia was detected with platelet count of 38X10^9/L. Thyroid function test was also in normal range. [TSH:1.05 (normal 0.4-4) μIU/mL, free T3: 3.10 (normal 1.7-4.9) pg/mL, free T4:0.95 (normal 0.7-2.0) ng/dL]. The peripheral blood smear was consistent with thrombocytopenia. A detailed differential diagnosis had been done in terms of any secondary thrombocytopenia etiology and all secondary causes were ruled out including the drugs. Bone marrow biopsy and aspiration confirmed the diagnosis as ITP and there was no disorder involving the bone marrow. The patient was administrated prednisolone with a daily dose of 1 mg/kg initially. A mild improvement in the platelet count was seen after the mentioned drug treatment. The case was discharged after 7 days when the platelets count increased to the level of 50X10^9/L, and the follow up had been performed periodically for four years due to chronic ITP. During this period, peripheral blood staining and complete blood count routinely checked. She had had no hemorrhagic symptoms and signs and her platelet count ranged between 50-100X10^9/L.

The case was admitted to the endocrinology outpatient clinic because of the symptoms of tachycardia and nervousness four years later after the diagnosis. Physical examination was unremarkable except palpable thyroid glands. Thyroid glands were diffusely palpable and voluminous. Laboratory results were consistent with hyperthyroidism: TSH was<0.005 (normal 0.4-4) μIU/mL, free T3 was 19.12 (normal 1.7-4.9) ng/dL free T4 was 4.75 (normal 0.7-2) ng/dL and. Mild thrombocytopenia (60X10^9/L) was found and the case had no complaint regarding chronic ITP. Parenchymal heterogeneity and bilateral hyperplasia was displayed at thyroid sonography (Fig. 1a-b). Thyroid scan displayed diffuse, homogeneous iodine uptake, suspecting the diagnosis of GD (Fig. 2). TSH receptor antibody (TSI) was positive >13.4 IU/mL (normal <1) confirming the diagnosis. She had no finding in case of GO. Hence, the patient was diagnosed as GD associated with ITP. It was suggested that there may be some causative immunological relationship. An antithyroid therapy was started as propylthiouracil (PTU) with a dosage of 300 mg/day. Four months later without any additional therapy other than PTU, her platelet count dramatically increased to 200X10^9/L. Thyroid function test was TSH 0.10 μIU/mL, free T4 of 0.8 ng/dL and free T3 of 3.47 ng/dL and the patient had no clinical symptoms due to hyperthyroidism. Two months later, the patient was euthyroid, and had radioactive iodine (RAI) therapy. Two years later, she had hyperthyroidism again (TSH 0.01 μIU/mL, free T4 2.2 ng/dL and free T3 5.8 ng/dL) and also GO without thrombocytopenia. Activity score for GO by clinical activity score (CAS) was 4-5 and the severity score by NO SPECS was Class III [1]. Because of GO antithyroid therapy (PTU 5-40 mg/day) was preferred as an initial therapy for the patient. PTU and glucocorticoid therapy were given for the management of hyperthyroidism and GO. Her GO by CAS was 2 and NO SPECS was Class II after glucocorticoid therapy. After completing therapy for 5 months, she became
euthyroid and a total thyroidectomy was performed. We had not observed any complications due to the surgical therapy. A Levothyroxine replacement therapy was started after thyroidectomy. The case has been following up every 4 to 6 months at the outpatient clinic for the thyroid hormone replacement and chronic ITP. We have done radiological imaging in our Endocrine Clinic by thyroid US. Nodule formation was not detected. A signed informed consent has been obtained from the patient.

3. DISCUSSION

The relationship between ITP and GD is not well known. The immunologic relation between these two disorders: Activation of reticuloendothelial system by thyroid hormone, and the existence of autoimmunity which leads to both diseases [2]. Although hyperthyroidism is shown to decrease the platelet survival by increasing reticuloendothelial activity, the resultant degree of thrombocytopenia is usually mild to moderate [3].

In the literature, there are different cases of GD associated with ITP. In some reports, GD or ITP started initially. In the other report, GD decreased the platelet counts in the patient with ITP and it may be due to the common autoimmune pathway [5-7]. In the present case, firstly ITP presented before GD and GO. Also GO may be related with RAI therapy.

PTU is an antithyroid drug, as well as having the immunomodulatory- immunosuppressive and antioxidant effects [8,9]. The immunosuppressive effects might have favorable impact on autoimmune diseases such as ITP, GD or GO.
The existence of GO in our patient after the discontinuation of PTU may be explained because of the immunological effects of the drug. However, GO development after 2 years may also be due to RAI therapy. It is well known that Cytotoxic T lymphocyte-associated molecule-4 (CTLA4) is associated with thyroid autoimmunity such as GD. In the literature, the polymorphism at CTLA4 gene is associated with hyperthyroidism relapse in GD after PTU discontinuation [10]. Therefore, GO is an also autoimmune disorder and may be related to Graves exacerbations in terms of autoimmunity.

It should be kept in mind that early diagnosis and treatment of the hyperthyroidism with antithyroid drugs can result in significant improvement of platelet count in ITP patients, especially those who are persistent ITP like the current patient not maintaining complete response off therapy [11]. In the current case, recovery from hyperthyroidism by PTU coincided with the platelet count recovery to 50x10⁹/L. In addition, GO developed after RAI therapy, and it might also be related with the immunological interactions regarding ITP apart from GD or RAI therapy. To the literature, this is the first case of GD and GO associated with ITP responded to antithyroid-PTU therapy.

4. CONCLUSION

Autoimmune disorders may be related with the development of a secondary autoimmune disorder. Here we report a case of ITP responding to antithyroid treatment in a patient with GO. The relation between ITP and GD is not well known. In the current case, recovery from hyperthyroidism by PTU coincided with the platelet count improvement to a tolerable level. To the best of our knowledge, the involvement with GO are firstly mentioned in an ITP patient associated with GD in the current report. Therefore, autoimmune disorders should be closely followed up in terms of the development of the other secondary autoimmune diseases.

CONSENT

The authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

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