Graves disease – induced immune thrombocytopenic purpura in an african female: a case report

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Case Report

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Abstract

Background

Immune thrombocytopenic purpura (ITP) is a condition associated with an unusual, unexplained, and sometimes very severe reduction in the level of platelets in the blood. Its association with Graves' disease, though documented, is not very common and can easily be missed or misdiagnosed, leading to excessive bleeding and mortality. Treatment with steroids and anti-thyroid medications has been shown to be beneficial in correcting thrombocytopenia in these patients, although the response is varied. We report on a patient with Graves' disease who presents with ITP.

Case presentation

The patient is a 37-year-old Ghanaian female who presented to our hospital's emergency department with a complaint of palpitations, difficulty breathing, easy fatigue, and headaches. She had been referred from a peripheral hospital as a case of thrombocytopenia, severe anemia, and anterior neck swelling. She was diagnosed with Graves' disease 2 years ago, became euthyroid in the course of treatment, but defaulted. On further examination and investigation, she was diagnosed with immune thrombocytopenic purpura and was also found to have elevated free T3, T4 and suppressed TSH. She also had high thyroid autoantibodies. She was initially started on oral prednisolone but there was no stabilisation of platelets until methimazole was introduced, which improved and normalised her platelet count.

Conclusion

The association of Graves' disease with immune thrombocytopenic purpura, though documented, is uncommon and very few cases have been reported thus far. There has not been any reported cases in Ghana or sub-Saharan Africa and hence, clinicians should be aware of this association when investigating for ITP and should consider graves' disease as a possible cause. From this study, we observed that there was no improvement in platelet count following the use of corticosteroid therapy until methimazole was started.

Introduction

Immune thrombocytopenic purpura (ITP) has been associated with autoimmune diseases such as Systemic lupus erythematosus (SLE), antiphospholipid syndrome and infections with hepatitis C infection, H pylori infection, and SARS-CoV-2 [1]. Graves' disease being autoimmune in etiology, is no exception even though there is a paucity of data in this area. Clinically, Graves' disease is characterized by a diffusely enlarged thyroid gland with associated symptoms of thyroid hormone overactivity, including palpitations, heat intolerance, diarrhea, and oligomenorrhea [2]. Additionally, there is evidence of platelet-related autoantibody production in some patients with Graves' disease [3], specifically CD4 T cell-mediated signalling of B cells to produce autoantibodies against platelet membrane GP11b111a ITP [4]. Other in vitro studies suggest mechanisms including megakaryocyte suppression by autoantibodies [5].

The diagnosis of ITP, especially in association with other conditions, requires a high index of suspicion considering the lack of specific diagnostic tests. Subsequent management involves the use of glucocorticoids and antithyroid medications with varying responses to the platelet count.

Case Presentation

We describe the case of a 37-year-old Ghanaian female who presented to the emergency department of our hospital with a complaint of palpitations, difficulty breathing, easy fatigue, and headaches. She had been referred from a peripheral hospital as a case of thrombocytopenia, severe anemia, and anterior neck swelling.

Relevant history included a diagnosis of Graves' disease 2 years prior to this admission, for which she was put on antithyroid medication. She became euthyroid during the course of treatment, but subsequently defaulted on her medications and long-term follow up. In the 4 months preceding her current admission, she had noticed heavy menstrual bleeding with progressive weight loss. Four days prior to presentation, the patient experienced dizziness, easy fatigue, profuse sweating, and tremors. At the referring hospital where she was initially presented, she was transfused with whole blood after laboratory results showed a hemoglobin (Hb) of 3.2g/dl (normal: 11.5–16.5) with Mean Corpuscular Volume (MCV) of 79fL (normal: 76–99), White blood cell (WBC) count of 8.3 x 109/L (normal: 4–10) and platelet (PLT) count of 1x109/L (normal: 150–450). Physical examination showed bruising and ecchymosis all over her body and petechiae on her lower lips with gum bleeding. She had an anterior neck swelling which moved on swallowing, was diffuse, non-tender, measured 3x3 cm, with no thyroid bruit. There was exophthalmos demonstrated by Naffziger sign. She had a blood-soaked diaper with significant amounts of clots. All other examination systems were unremarkable.

In the emergency room, her blood pressure was 121/68 mmHg. She had a heart rate of 175 beats per minute with a weak and thready pulse, a respiratory rate of 40 cycles per minute, and peripheral oxygen saturation of 97% on oxygen via face mask at 6L/min. On primary assessment, she was in severe respiratory distress and restless, severely pale, and had cold extremities with an axillary temperature of 36.5oC. She was noted to be bleeding per vaginum. Based on her laboratory results from the referral center (Hb:3.2g/dl and PLT:1x109/l), she was immediately scheduled to receive fresh frozen plasma and packed cells. However, within minutes after her arrival and initial assessment at the emergency room, the patient went into cardiac arrest. Cardiopulmonary resuscitation (CPR) was commenced and return of spontaneous circulation (ROSC) was achieved. She was subsequently sent to the High Dependency Unit (HDU).

A repeat complete blood count (CBC) showed an Hb of 5.4g/dl, MCV of 82.5fL, WBC count of 6.56 x 10^9/L and PLT of 4.0 x 10^9/L. On admission day 2, her post-transfusion peripheral film comment indicated 2 populations of cells: microcytic hypochromic and normocytic normochromic red blood cells. Additionally, neutrophilia and markedly reduced platelets without clumping were seen. These findings were suggestive of multiple blood transfusions and probable autoimmune disease, and a diagnosis of

ITP was considered. She was initially started on oral prednisolone 60mg daily for 5 days with a plan to gradually taper over a period of 4 weeks, and supported with parenteral esomeprazole 40mg 12hrly, and tranexamic acid 1g 8 hourly for 48 hours, whilst we awaited her remaining laboratory investigation results. Hepatitis B and C virus, and HIV serology were negative. Thyroid function testing revealed a Thyroid stimulating hormone (TSH) of 0.006 IU/ml (normal: 0.38–5.33), serum-free T3 of 9.2pmol/l (normal: 3.5–7.8) and serum-free T4 of 42.1pmol/l (7.9–18.5). The thyroid autoantibodies demonstrated thyroperoxidase antibodies (TPOAb) of 58.91 IU/ml (normal: <30 IU/ml), TSH receptor autoantibodies (TRAb) of 14.91 IU/L (normal: <1.80), and thyroglobulin antibodies (TgAb) of 32.51 IU/ml (normal; <4.11). Thyroid ultrasound revealed heterogenous and hyperechoic thyroid glands of average size, with a mild increase in vascularity but no nodularity. A diagnosis of Graves' disease-induced ITP was therefore made, and she was commenced on oral propranolol 40mg twice daily and oral methimazole 20mg daily. The patient was followed up at the endocrine and hematology clinics. Three weeks following admission, her thyroid function tests, Hb and platelet results were all within normal limits. A summary of the patient's CBC results from admission to her most recent review is shown in Table 1.

Table 1
Summary of patient's complete blood count results from admission to most recent review.

CBC parameter	Date (dd/mm) from admission to last review								
	17/01	18/01	21/01	22/01	25/01	29/01	31/01	03/02	05/02
Hb (g/dl)	3.2	5.4	3.0	4.6	4.3	6.6	7.2	9.0	12.5
WBC ($x10^9$/L)	7.85	6.56	5.0	28.6	8.3	11.7	12.7	5.7	6.0
Platelet ($x10^9$/L)	1.0	4.0	7.0	10.0	6.0	5.0	27	88	235
CBC: Complete blood count, Hb: Hemoglobin, WBC: white blood cell									

Discussion

As many as 80% of cases of hyperthyroidism are due to Graves' disease, with the overall prevalence of hyperthyroidism in the United States being 1.2% and the incidence being 20 per 100,000 to 50 per 100,000 population. Graves' disease is more common in females between the ages of 20 and 50 years [7]. Manifestations of ophthalmopathy, which vary in severity and have a course that is typically independent of the thyroid disease, may include proptosis, periorbital edema, exposure keratitis, extraocular muscle infiltration, lid lag, and lid retraction. A thyroid function test reveals a suppressed TSH and a raised free T3 (FT3) and free T4 (FT4) [6]. Our patient presented with exophthalmos and an enlarged thyroid gland with both FT3 and FT4 levels raised above normal. Diagnosis can also be made with antibody titers to the thyroid gland. About 95% of patients have antibodies to thyroid peroxidase (TPO) and about 50% to thyroglobulin (TG). Antibodies to the TSH receptor strongly support Graves'

disease [7]. The diagnosis of Graves' disease in our patient was supported by the presence of elevated autoantibodies.

Immune thrombocytopenic purpura is an acquired haematological disorder caused by autoimmune destruction of platelets with values below 100 x 109/L in the absence of other causes of thrombocytopenia, such as viral infections, rheumatic diseases, or drugs. A diligent search for other causes of thrombocytopenia, such as HIV, Hepatitis B and C viruses, drugs, or rheumatologic diseases, such as SLE and antiphospholipid syndrome, is therefore imperative prior to making this diagnosis [8]. ITP can vary from being asymptomatic to causing severe, life-threatening bleeding. In severe cases, treatment options include platelet transfusion, intravenous immunoglobulin (IVIG), and glucocorticoids, with the main aim of maintaining platelets at a level to prevent spontaneous bleeding [9].

The association between thyroid disease pharmacotherapy and ITP is controversial. There are several case studies which report complete reversal of thrombocytopenia after the use of antithyroid medications, whereas others report no improvement in platelet count after achieving euthyroidism [8]. There have been case reports of ITP induced by Graves' disease where patients were treated with IVIG or oral prednisolone but with little or no improvement until carbimazole was started [10]. Our patient was started on prednisolone, but there was no improvement in platelet levels until methimazole was started, which normalized the platelet count and the Hb.

From this case report, we observed that there was no improvement in platelet count following the use of corticosteroid therapy until a thionamide was started. In all cases of ITP with Graves' disease, we suggest thyroid function and autoantibody tests be conducted and appropriate treatment commenced, especially in the setting of poor response to standard ITP treatment protocols.

Conclusion

There has not been any case study reported on the association between Graves' disease and ITP in Ghana and sub-Saharan Africa, possibly due to underdiagnosis or late referrals to centres where a multidisciplinary team can institute care. In the treatment of ITP with underlying Graves' disease, there are different approaches and, consequently, responses. In some cases, glucocorticoids reverse thrombocytopenia, and those that yield no effect. In this case study, glucocorticoids did not reverse thrombocytopenia; however, anti-thyroid therapy reversed thrombocytopenia and normalized the Hb.

Declarations

Ethical approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

All data generated or analysed during this study are included in this published article (and its supplementary information files).

Competing interests

The authors declare that they have no competing interests

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KOA contributed to examining the patient, following up the patient, planning, writing up the manuscript, discussion, and reviewing the literature. AF contributed to the introduction and abstract. SAB CKS, KF, MT, HF, and RW worked manuscript revision, and final approval. All authors read and approved the final manuscript

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