

Idiopathic Thrombocytopenic Purpura (ITP) and Hyperthyroidism: An Unusual But Critical Association for Clinicians

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The connection between idiopathic thrombocytopenic purpura (ITP) and Grave's disease is not well known in the Western hemisphere. The immunologic relationship between these 2 conditions is well reported^{1–5} but poorly defined in the literature. New-onset hyperthyroidism in the setting of preexisting ITP can be overlooked and, if untreated, lead to worsening of the ITP, rendering it refractory to standard therapy. Early recognition and treatment of the hyperthyroid state with antithyroid medications can lead to significant improvement in the platelet count.^{1,8} We report this rare but critical clinical relationship.

CASE REPORT

A 35-year-old Asian woman with a known history of stable ITP for 12 years (baseline platelet count of 40,000/mL) presented to her outpatient provider with a diffuse petechial rash, easy bruisability, and heavy menorrhagia for 2 weeks. Her new platelet count was 7000/mL. She was immediately started on prednisone at a dose of 1 mg/kg without any improvement in her platelet count. At the end of 4 weeks on prednisone, she developed fever, intractable nausea and vomiting, severe headache, hypotension, and tachycardia. She was subsequently hospitalized with the presumptive diagnosis of meningitis and sepsis syndrome. Her clinical syndrome was consistent with systemic inflammatory response syndrome. She was treated aggressively with intravenous fluids and a broad-spectrum empirical antimicrobial regimen consisting of ceftriaxone, vancomycin, and acyclovir. Lumbar puncture was deferred because of her low platelet count. The sepsis workup, which included viral, fungal, and bacterial blood cultures, remained negative. Her peripheral smear did not show evidence of microangiopathic hemolytic anemia, therefore ruling out thrombotic thrombocytopenic purpura and disseminated intravascular coagulation. HIV and tuberculosis were also ruled out. After the initial sepsis workup turned out negative, she was started on solumedrol 125 mg IV every 6 hours. Over the next 2 weeks, she received an average of 4–6 units of platelets per day

and multiple blood transfusions to maintain her hemoglobin and platelet counts. The latter remained in the 1000-5000 platelets/mL range throughout her hospitalization without any significant improvement. Her clinical course was further complicated by multiple small intracranial hemorrhages without major focal neurological deficits. A bone marrow biopsy was eventually done. It showed early dysplastic cells but no definite features of myelodysplasia and few large megakaryocytes. She received 1 dose of vincristine without response in the bone marrow after 2 weeks, and consideration was given to treatment with rituximab for refractory ITP. At that point, she informed her hematologist that 10 years ago, she had been treated for hyperthyroidism with antithyroid medications for 6 months, without further follow-up. A thyroid panel was then ordered, and she was found to be hyperthyroid, with thyroid-stimulating hormone (TSH) < 0.01 mU/mL and free T4 of 3.1 ng/dL. She was subsequently started on propylthiouracil at 300 mg per day. Her platelet count dramatically improved and went up to the 50,000/mm³ range without further intervention over the next few months. After her discharge, an outpatient thyroid scan showed diffuse, homogeneous uptake of iodine, thereby confirming the diagnosis of Grave's disease. Retrospectively, her initial clinical syndrome of fever, hypotension, and tachycardia may have been the result of thyrotoxicosis or worsened by it.

DISCUSSION

The association between ITP and Grave's disease is poorly understood. Many hypotheses from observational data have been given in the literature. The leading theory to explain the coexistence of these 2 disorders is the presence of a common autoimmune pathway with production of 2 kinds of antibodies against platelets and TSH receptors. Indeed, autoimmune disorders tend to occur concurrently in individuals or families. Bizzaro et al. reported the coexistence of ITP and Grave's in 4 members of the same family.⁶ Hymes et al. found elevated levels of platelet-bound IgG in 44% of 25 study patients with Grave's thyrotoxicosis.⁷ Most of these patients had easy bruising and/or bleeding, and 12% were thrombocytopenic. Panzer et al. reported the presence of antiplatelet IgG in patients with Grave's as well as improved platelet counts and increased mean platelet volume after successful antithyroid therapy.⁸

In addition to the coexistence of thyroid-stimulating immunoglobulins (TSIs) and anti-platelet antibodies as a potential mechanism for Grave's-associated thrombocytopenia, some have postulated that in Grave's patients, TSIs and other thyroid antibodies might actually bind to the platelets themselves. The postulated site for binding would be a truncated actin-binding protein on the platelets that would link the high-affinity Fc receptor of immunoglobulin G to the platelets' cytoskeleton, thereby accelerating their destruction.⁹

Another plausible mechanism is activation of the reticuloendothelial system by thyroid hormones, with increased clearance of platelets by the spleen in thyrotoxic states. This may explain the restoration of the platelet count when euthyroidism is reached.

Finally, thyrotoxicosis seems to alter platelet aggregation, partially by inhibition of myosin light-chain kinase, and that also improves with restoration of euthyroidism.¹⁰

The coexistence of severe hyperthyroidism and thrombocytopenia can mimic severe sepsis in critically ill patients, and the hyperthyroid state in itself can worsen the thrombocytopenia of ITP. We suspect this patient's "severe sepsis" may actually have been an unrecognized severe thyrotoxicosis, with bone marrow dysfunction secondary to the hyperthyroidism, which might partially explain her lack of response to standard therapy.

CONCLUSIONS

This case underscores the importance of screening for and treating hyperthyroidism in patients with ITP, especially those resistant to steroid therapy, because the literature seems to indicate that treatment of the hyperthyroid state improves platelet count. This might help to prevent devastating clinical complications. Further research is necessary to define this empirical finding.

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