Case Report

Acquired Thrombotic Thrombocytopenic Purpura in a Patient with Pernicious Anemia

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Introduction. Acquired thrombotic thrombocytopenic purpura (TTP) has been associated with different autoimmune disorders. However, its association with pernicious anemia is rarely reported.

Case Report. A 46-year-old male presented with blood in sputum and urine for one day. The vitals were stable. The physical examination was significant for icterus. Lab tests' results revealed leukocytosis, macrocytic anemia, severe thrombocytopenia, renal dysfunction, and unconjugated hyperbilirubinemia. He had an elevated LDH, low haptoglobin levels with many schistocytes, nucleated RBCs, and reticulocytes on peripheral smear. Low ADAMTS13 activity (<10%) with elevated ADAMTS13 antibody clinched the diagnosis of severe acquired TTP, and plasmapheresis was started. There was an initial improvement in his hematological markers, which were however not sustained on discontinuation of plasmapheresis. For his refractory TTP, he was resumed on daily plasmapheresis and Rituximab was started. Furthermore, the initial serum Vitamin B12 and reticulocyte index were low in the presence of anti-intrinsic factor antibody. So with the concomitant diagnosis of pernicious anemia, Vitamin B12 was supplemented. The rest of the immunological workups were negative. Subsequently, his symptoms resolved and his hematological parameters improved. Discussion. While pernicious anemia can masquerade as TTP, an actual association between the two can also occur and needs further evaluation and characterization.
episode in the past and no family history of any bleeding disorder or malignancy. The vitals were stable with a temperature of 98.2°F, pulse rate of 72, respiratory rate of 18, and blood pressure of 140/94 mm Hg. Physical examination was significant for icterus and absence of any petechial rash, lymphadenopathy, or hepatosplenomegaly. Lab test results were significant for leukocyte of 15,000/μL (normal 4,500–11,000/μL), hemoglobin (Hb) of 10.7 g/dL (normal 13.5–17.5 g/dL), hematocrit (Hct) of 32% (normal 41–53%), mean corpuscular volume of 102 fL (normal 80–100 fL), mean corpuscular hemoglobin of 34.2 pg (normal 26–34 pg), platelet of 13,000/μL (normal 130,000–400,000/μL), blood urea nitrogen of 41 mg/dL (normal 8–20 mg/dL), serum creatinine of 1.9 mg/dL (normal 0.4–1.3 mg/dL), and total bilirubin of 3.1 mg/dL (normal 0.3–1.2 mg/dL) with unconjugated bilirubin of 2.6 mg/dL (normal 0.2–1.1 mg/dL). Subsequent tests showed an elevated LDH (1499 IU/L, normal 98–192 IU/L) and low haptoglobin levels (<10 mg/dL, normal 34–200 mg/dL) with many schistocytes, nucleated RBCs, and reticulocytes (2.3%, normal 0.5–1.5%) on peripheral smear. ADAMTS13 activity of less than 10% (normal > 66%) with elevated ADAMTS13 antibody (>140 u/mL, normal < 12 u/mL) clinched the diagnosis of severe acquired TTP, and the patient was started on plasmapheresis.

Furthermore, in the background of macrocytic anemia and a reticulocyte index of 1.04 at presentation, which worsened to Hb of 6.9 mg/dL and Hct of 20.6% on the third day of presentation, the initial serum Vitamin B12 returned to low level (202 pg/mL, normal 211–946 pg/mL) with normal serum folate (5.9 ng/mL, normal > 3.0 ng/mL) in the presence of anti-intrinsic factor (IF) antibody. Antiparietal cell antibodies were, however, negative. So with the concomitant diagnosis of pernicious anemia, the patient was supplemented with 1000 μg of intramuscular Vitamin B12 for 7 days, beginning on the third day. The rest of the immunological workups, including antibodies against double stranded DNA, Smith antigen, thyroid peroxidase, myeloperoxidase, and proteinase-3, were negative. Thyroid function test was normal with free T4 of 1.07 ng/dL (normal 0.82–1.77 ng/dL) and thyroid stimulating hormone level of 2.38 uIU/mL (normal 0.450–4.500 uIU/mL). Daily plasmapheresis and Vitamin B12 supplementation improved the hematological markers over the subsequent days. The platelet count rose to 204,000/μL and Hb and Hct stabilized at 9 mg/dL and 27%, respectively, with a reticulocyte count of 5.38% and a reticulocyte index of 2.36, while the serum LDH (302 IU/L), serum creatinine (1.4 mg/dL), and serum bilirubin (1.2 mg/dL) continued to fall. So a decision to taper the frequency of plasmapheresis was made. However, a day after skipping a session of plasmapheresis, the platelet count dropped to 67,000/μL which further dropped to 22,000/μL over the next few days. So a diagnosis of refractory TTP was made, and the patient was put back on daily plasmapheresis schedule. His platelet counts improved steadily to 148,000/μL at which point it was decided to start the patient on Rituximab, while tapering down the frequency of plasmapheresis. He received two doses of Rituximab at a dose of 375 mg/m² body surface area every week in the hospital and two more doses were planned after discharge from the hospital. Over the subsequent days, his symptoms resolved and there was significant improvement in his platelet count, hemoglobin, hematocrit, LDH, serum creatinine, and bilirubin. So after a total of 31 sessions of plasmapheresis with 24 units of fresh frozen plasma per session, the frequency of plasmapheresis was slowly tapered off, and he continued to remain asymptomatic while his hematological parameters stabilized with a platelet count of 257,000/μL at discharge.

3. Discussion

Autoimmunity, with the development of antibodies against ADAMTS13 and the subsequent deficiency of ADAMTS13, is the driving process behind acquired TTP [7, 8]. Our patient had a very low ADAMTS13 level with elevated titers of ADAMTS13 antibodies, making it a severe form of acquired TTP. Autoimmune diseases tend to cooccur in individuals and families [19]. Cooccurrences of TTP with other autoimmune diseases have been reported. Multiple case reports have described the development of TTP in the background of SLE [9–11, 20, 21]. Similarly, there are cases of cooccurrence of Sjögren’s syndrome and TTP [12, 22–24]. One particular study investigated the prevalence of concurrent autoimmune disorders in 76 patients with TTP [13]. They found a statistically significant higher occurrence of Hashimoto’s thyroiditis, SLE, idiopathic thrombocytopenia purpura, psoriasis, and celiac disease in patients with TTP as compared to the general population. Our patient was simultaneously diagnosed with TTP and pernicious anemia, but this association has rarely been reported before [12].

Pernicious anemia is an autoimmune disorder that impairs the secretion and function of intrinsic factors secreted from the gastric parietal cells. The subsequent Vitamin B12 deficiency impairs DNA synthesis without affecting synthesis of cytoplasmic components [25]. The classic hematological finding in pernicious anemia consists of megaloblastic anemia, characterized by macroglossia and hypersegmented neutrophils on peripheral smear [26–28]. However, myriad of other hematological presentations including pancytopenia and hemolytic anemia are seen [29].
Vitamin B12 deficiency results in ineffective erythropoiesis and causes intramedullary destruction of RBCs, which manifests as hemolytic anemia with indirect hyperbilirubinemia and elevated LDH. Moreover, elevated levels of homocysteine in Vitamin B12 deficiency promotes hemolysis besides causing endothelial dysfunction with microvascular thrombi formation and results in peripheral hemolysis and thrombocytopenia [30–33]. In fact, multiple cases of pernicious anemia and the resulting Vitamin B12 deficiency presenting with MAHA and thrombocytopenia with schistocytosis have been described [14–18]. These cases of isolated pernicious anemia, thus, may masquerade as TTP and pose initial therapeutic dilemma. In contrast to these previously reported cases where pernicious anemia was mistaken for TTP, our patient had concomitant pernicious anemia and TTP showing a possible association between these two autoimmune conditions. Furthermore, our patient needed a two-pronged treatment strategy as each entity had the potential to feed into the pathogenesis of another. TTP with its massive hemolysis and stimulation of erythropoiesis could worsen the Vitamin B12 deficiency of pernicious anemia, while pernicious anemia with its propensity for microvascular thrombi formation could worsen the MAHA and thrombocytopenia of TTP. Rituximab along with plasmapheresis treated the TTP in our patient, while Vitamin B12 injections treated the pernicious anemia.

4. Conclusion

Acquired TTP is immunologically mediated and has been associated with several autoimmune disorders like systemic lupus erythematosus (SLE) and Hashimoto’s thyroiditis. While several cases of TTP-like features in patients with pernicious anemia have been reported, actual TTP in such patients is rarely reported. This association between TTP and pernicious anemia needs further evaluation given the reported overlap in features of the two entities and the potential of each entity to feed into the pathogenesis of another.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors’ Contributions

Ramesh Kumar Pandey and Sumit Dahal contributed equally to this work.

References


