A 65-year-old Caucasian man was diagnosed with immune thrombocytopenia in 2022 after presenting to the emergency department with a 2-day history of progressive, diffuse petechiae and a 1-day history of gross hematuria without clots, ecchymosis, and mucosal bleeding secondary to oral blisters. His past medical history is significant for atrial fibrillation on rivaroxaban for the last 4 months and hypertension on metoprolol succinate 25 mg and olmesartan 20 mg daily. He denies any personal or family history of autoimmune disorders, bleeding disorders, transfusions, or tick exposure. His granddaughter had nephrotic secondary to the Coxsackie virus 6-8 weeks before his symptoms, however, he denies any personal proctode of infection. A complete blood count showed a platelet count of 1,000/μL decreased from his baseline of 415,000/μL in 2016. Schistocytes were not visualized on his peripheral smear. Band form neutrophils demonstrated a BN of 24 mg/dL and CR of 0.9 mg/dL. His liver panel was within normal limits. Coagulation studies demonstrated a PT of 24 seconds, INR of 2, and fibrinogen of 538 mg/dL. Hepatitis C and HIV antibodies were negative. Hepatitis B core antibody (HBcAb) was positive, indicating a past exposure. His ANA titer was >1:640. Rivaroxaban was stopped due to severe thrombocytopenia. IVIG 1 mg/kg for 2 days and desmopressin 40 mg for 4 days were given with an increase of platelet count to 47,000/μL along with significant improvement of the petechial rash and with complete resolution of hematuria and mucosal bleeding.

He was discharged on prednisone of 0.5 mg/kg/day. However, he was readmitted 4 days later to moderate hematuria, oral gingival bleeding, flank pain, and a platelet count of 5,000/μL. Again, IVIG 1 mg/kg and desmopressin 40 mg for 4 days were given. Second-line therapy was considered due to the refractoriness of the first-line treatment including IVIG. Rituximab infusions were then started after intensive anticoagulation. 0.5 mg daily to prevent the risk of hepatitis B activation and were planned to continue until one year after rituximab is discontinued. Platelet counts increased to 68,000/μL on day 6 of admission and he was discharged with prednisone of 1 mg/kg/day. Given positive autoantibodies including high titer ANA and anti-SSA, autoimmune disease history was revised which was non-contributory.

**INTRODUCTION**

Immune thrombocytopenic purpura (ITP) is an autoimmune, hematological disorder resulting from the immune-mediated destruction of platelets. It is characterized by isolated thrombocytopenia (<100,000/μL) with normal white blood cells and hemoglobin that leads to generalized mucocutaneous manifestations, including petechiae, purpura, easy bruising, and oral mucosal bleeding [1]. ITP can be classified based on an underlying etiology as primary (idiopathic) and secondary with the onset of symptoms as acute (<6 months) and chronic (>6 months). Acute ITP is generally seen in childhood secondary to an acute infection with the resolution of symptoms in 2 months whereas chronic ITP is generally seen in adults without a specific cause [2-4]. While the exact molecular mechanism(s) of ITP remains elusive, the most favorable proposed mechanism is that antibodies against foreign antigens such as viruses, medications, and other autoimmune disorders may cross-react with host platelet antigens specifically platelet glycoprotein IIb/IIIa, Ib/IIa, and VI through molecular mimicry. Autoimmune destruction of immunoglobulin G (IgG) coated platelets by splenic sequestration and phagocytosis by macrophages results in a shortened half-life of platelets, leading to thrombocytopenia [2,5].

The incidence of ITP in adults is approximately 66 cases per 1,000,000 per year with female to male ratio of 2.6:1. The most common reason for mortality is cerebral hemorrhage which occurs in almost 5% of adults warranting the need for urgent treatment. As investigation for any underlying etiology is underway, clinical guidelines recommend initiating therapy in patients whose platelets are below 50,000/μL or at any platelet level when significant, active bleeding is present. First-line therapy for ITP includes corticosteroids and intravenous immunoglobulin (IVIG). Corticosteroids reduce antibody production, thereby preventing autoantibody-platelet complex destruction by splenic macrophages. IVIG is thought to saturate receptors in the reticuloendothelial system, decreasing splenic destruction of platelets bound for autoantibodies [6]. Secondary causes for chronic or refractory ITP include splenectomy and Rituximab, an anti-CD20 cytolytic monoclonal antibody that inhibits B cell production of autoantibodies [6].

In this article, we present a case of refractory ITP of unknown etiology in a 65-year-old man with positive antinuclear antibodies (ANA) titer, anti-Sjögren’s syndrome-related antigens A antibody (Anti-SSA), and positive Hepatitis B core antibody.

**CASE PRESENTATION**

ITP is a relatively common hematological disorder that affects adults with a peak age of 20-50 with female predominance. While ITP is generally acute and secondary to an identifiable reason such as viral illness or medications during illness, ITP is generally chronic and idiopathic in adults. Severe thrombocytopenia with normal other cell lineages is the first and most of the time solely laboratory finding causing petechia and mucosal bleeding [6]. A platelet count of less than 50,000/μL increases the risk of dangerous bleeding. Patients with ITP don’t typically start showing signs of thrombocytopenia, e.g., bruising, petechiae, epistaxis, and bleeding gums until the platelet count is less than 20,000/μL [7]. Our patient presented with just a 2-day history of petechiae which then progressed to hematuria and oral mucosal bleeding with a platelet count of 1,000/μL at the age of 65 with no identifiable underlying etiology.

A peripheral smear is a simple, cheap however indispensable test to rule out any other causes of thrombocytopenia such as pseudothrombocytopenia, leukemia, or hemolytic anemia [9]. Thrombocytopenia occurs as a clinical manifestation in 7 to 50 % of patients with SLE [9]. Our patient had an ANA titer of 1/1640 with a positive titer for Anti-SSA. While Anti-SSA is often associated with SLE and Sjögren’s syndrome [SS], it can rarely be seen in other systemic autoimmune disorders such as mixed connective tissue disease, rheumatoid arthritis, systemic sclerosis, and polymyositis/diaphragmopathy [10]. Our patient did not have any complaints of the typical symptoms of SS or any other clinical manifestations of SLE. Although the diagnosis of SLE typically needs to have 4 of 11 clinical land laboratory findings, patients can be diagnosed with SLE with SLE with one single organ involvement such as lupus nephritis. Positive ANA and anti-SSA may indicate an autoimmune process.

Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Once the patient’s hepatitis B was controlled, a hepatitis B vaccination was initiated. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started. Due to the refractory nature of his ITP, we preferred to start second-line treatment with the monoclonal antibody targeted against CD20, rituximab. Although rituximab depletes autoantibody-producing B-cell lymphocytes, it also increases the risk of hepatitis B reactivation [11]. Since he had positive serology for hepatitis B core antibody, suggesting a past exposure, prophylactic treatment with entecavir was started.