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Case Report

SYMPTOMATIC THROMBOCYTOPENIA FROM APIXABAN IN PATIENT WITH DEEP VEIN THROMBOSIS: A CASE REPORT

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ABSTRACT

Introduction: The Non-Vitamin K Antagonist Oral Anticoagulants (NOACs) is the main treatment of venous thrombosis. A review of use for rare adverse reaction of these drugs are still needed. The use of Apixaban related thrombocytopenia has been reported previously, but its clinical significance remains still under-reported. We report a case of 63-year-old Asian woman who suffered from severe and symptomatic thrombocytopenia with mild bleeding manifestation after taking Apixaban

Case Summary: A 63‑year‑old Asian woman was admitted for neurological clinical due to severe asthenia for 1 week ago accompanied by multiple ecchymoses. The initial presentation was left arm and leg oedema. This patient was previously treated with Apixaban, Furosemide, Vitamin D, and Metamizole for deep vein thrombosis in the femoral, popliteal, and subclavian veins. Apixaban had been used by the patient for 2 months at a dose of 5 mg per day. The test results showed that the patient had mild anemia and a significantly low platelet count.

Discussion: Potential mechanisms of Apixaban-induced thrombocytopenia may involve immune-mediated reactions through drug-dependent antibodies, or bone marrow suppression pathway. This rapid increase in platelet count supports the immune-mediated hypothesis, as bone marrow recovery generally takes more than 7 days.

Conclusion: We report on a patient who developed severe and symptomatic thrombocytopenia due to Apixaban. The other possible causes of thrombocytopenia were ruled out.

Keywords: apixaban; thrombocytopenia-induced; NOAC

INTRODUCTION

Apixaban acts by directly inhibition factor Xa in the coagulation pathways by preventing the formation of thrombin from prothrombin. This pathway mechanism is required for inhibiting the conversion of fibrinogen to fibrin. Previous clinical trials have shown that Apixaban is equally effective as warfarin in avoiding systemic embolism or stroke. Apixaban is also associated with a decreased risk of bleeding compared to warfarin. This fact enhances the use of Apixaban in current daily clinical practice.

The adverse events related to very low platelet count after Apixaban administration were very rare. This rare manifestation of adverse events has been previously reported. We report a case of 63-year-old Asian woman who suffered from severe and symptomatic thrombocytopenia

with mild bleeding manifestation after the use of Apixaban.

CASE REPORT

A 63-year-old Asian woman was brought in for neurological clinical due to severe asthenia for 1 week ago. The initial presentation was left arm and leg oedema. This patient was previously treated with Apixaban, Furosemide, Vitamin D, and Metamizole for deep vein thrombosis in the femoral, popliteal, and subclavian veins. Apixaban had been used by the patient for 2 months at a dose of 5 mg per day. The previous D-dime examination showed a high result (1,4 g/L, normal value < 0,5 g/L), but after using Apixaban for 30 days, the D-dimer value returned to near normal (0,6 g/L). Leg oedema associated with deep vein thrombosis also improved significantly. Apixaban was then continued with vitamin D supplementation.

The patient visited our clinic due to severe asthenia accompanied by multiple ecchymoses. Complete blood tests, and blood glucose levels were performed to identify the cause of asthenia. The test results showed that the patient had mild anemia (9,8 g/dL, normal value 12-14 g/dL) and a significantly low platelet count (32.000, normal value 150.000-450.000 platelets per microliter). Other test results were unremarkable. The cause of the low platelet count was also sought by testing for dengue fever and sepsis, but the results were normal. CRP, procalcitonin, ECG, Thrombophilia tests (CEA, Ca-125, Ca 15-3) were also performed and found to be normal.

We discontinued Apixaban and the patient was treated with high folic acid supplementation and steroids. The platelet count was also closely monitored and after 6 days in the hospital, the patient’s platelet count returned to near normal values of 124.000 platelets per microliter. The patient’s condition was stable, and the clinical presentation of deep vein thrombosis also improved.

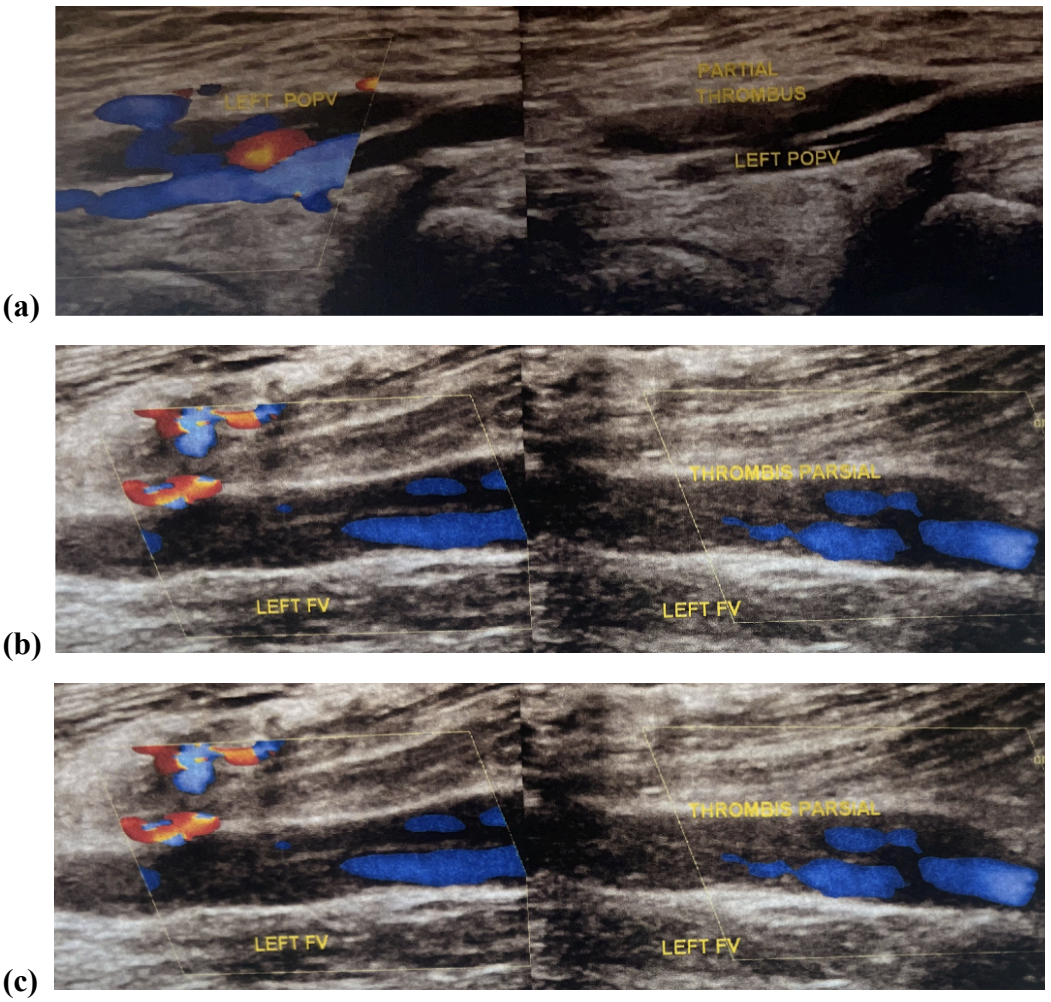

Figure 1. (a) Partial thrombus in left popliteal vein; (b) Partial thrombus in left femoral vein); (c) Large thrombus in left femoral vein.

DISCUSSION

We report a case of symptomatic thrombocytopenia that induced by Apixaban. After taking a history, physical examination, laboratory examination, and consideration of concomitant medications, food, or other disease, we conclude that the possible thrombocytopenia in this patient was induced by the drug Apixaban. However, there are only a few reported cases with possible apixaban-induced thrombocytopenia. In our case, this condition appeared to be caused because of apixaban. The timing of its occurrence also coincided with apixaban exposure. The other possibilities have been considered, especially other drugs.

The use of apixaban in this patient had started 1-2 months prior to hospitalization, and was discontinued at the time of hospitalization, followed by a gradual significant increase in platelet count. This is consistent with the concept of temporality between exposure and outcome. Other common conditions typically associated with thrombocytopenia, such as dengue infection or sepsis, were neither confirmed nor proven and treated in this patient. Additionally, laboratory results showed no evidence of DIC, TTP, or neutropenia. This approach should be considered in all patients suspected of having drug-induces thrombocytopenia. In our patient, thrombocyte count improved after cassation of the medication. This is consistent with the concept of challenge and de-challenge. Previous case studies have suggested that potential mechanisms for Apixaban-induced thrombocytopenia may involve immune-mediated reactions through drug-dependent antibodies, or bone marrow suppression pathway. This rapid increase in platelet count supports the immune-mediated hypothesis, as bone marrow recovery generally takes more than 7 days. This rare but clinically significant case study should increase our clinical alertness. Apixaban has demonstrated superior efficacy in preventing stroke or systemic embolism compared to warfarin. Apixaban has also been used as an alternative to oral anticoagulation in patients with heparin-induced thrombocytopenia (HIT). Direct oral anticoagulants (DOACs) are being explored for HIT treatment and may address the challenges of current therapeutic approaches. Apixaban is prescribed

in patients to prevent stroke with atrial fibrillation, the risk of thrombocytopenia should be considered as a potential side effect.

Thus, it is imperative for clinicians to be aware of these potential side effects. This case report is one of the very few known case reports that has strongly documented this cause. The use of an agent with close clinical and laboratory monitoring is necessary. These rare side effects should be closely monitored and reported, especially given the growing use of Apixaban in the treatment of HIT.

CONCLUSION

We report a patient who developed severe and symptomatic thrombocytopenia due to Apixaban. The other possible causes of thrombocytopenia were ruled out.

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