Rivaroxaban treatment failure: Adding a new case to the list

Sir,

Rivaroxaban is a factor Xa inhibitor, which is commonly used for the treatment of venous thromboembolism (VTE) as one of the novel oral anticoagulants found to have a safety and efficacy profile comparable to traditional anticoagulants. However, sporadic reports from some centers have shown a failure of treatment in patients with VTE.[1-3] In this report, we present the case of a woman who developed pulmonary embolism 12 days after receiving rivaroxaban for deep-vein thrombosis (DVT).

A 54-year-old woman with a history of left leg DVT, on rivaroxaban 15 mg twice daily for 12 days, presented to the emergency room with chest pain for 14 hours and increased swelling of left leg. The DVT occurred after a long flight trip, otherwise, her past medical history was unremarkable. Upon being questioned, she asserted strict compliance with rivaroxaban (with meal). On examination, she was alert, oriented, but dyspneic. The temperature was 36.8°C; blood pressure was 96/57 mmHg; heart rate was 64/min; respiratory rate was 20/min; and room air–oxygen saturation was 98%. Physical examination revealed erythema, warmth, tenderness, and swelling of the entire left leg, while the pulse was intact. The remainder of her examination was not significant.

Computed tomography angiogram–chest revealed a filling defect consistent with pulmonary embolism in the left main pulmonary artery and the segmental branches of the left lower pulmonary artery. Compared with the previous one, Doppler ultrasonography of the left leg showed an increase in the thrombosis in the common femoral and proximal superficial femoral veins. White blood cell count was $5.2 \times 10^9$/$\text{L}$; hemoglobin was 11.1 g/$\text{dL}$; and platelet count was $291 \times 10^9$/$\text{L}$. Coagulation profile and blood chemistry were within the normal range.

The patient was admitted to the medical ward and was treated with enoxaparin in therapeutic dose and warfarin. The swelling of the left leg reduced in a few days and the chest pain resolved. On day 5, the international normalized ratio was 2.5, therefore enoxaparin was discontinued and the patient was discharged on warfarin.

The mechanism for the possible failure of rivaroxaban therapy in the treatment of DVT is not well understood. It is known that the bioavailability of this drug is dose dependent, and therefore, patient compliance is mandatory to ensure the optimal bioavailability of this drug. Our patient repeatedly insisted on having taken rivaroxaban regularly with meals. However, owing to the lack of laboratory facilities to estimate the serum level of the drug, it was difficult to assess her compliance. The other proposed mechanism for treatment failure is based on the interaction of drugs that affects cytochrome (CYP) enzymes. The metabolism of rivaroxaban is mediated through CYP 3A4, therefore co-administration of CYP 3A4 inducer drugs may decrease the bioavailability of rivaroxaban, resulting in treatment failure. As our patient was not taking any medications that could interact with rivaroxaban, this was unlikely.

Therefore, providing laboratory facilities to estimate the level of rivaroxaban would be of great value in assessing the compliance of patients experiencing treatment failure. Owing to the lack of guidelines for treatment failure, anticoagulation with warfarin would be better in this group of patients.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published, and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest
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Letter to Editor

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References

1. Ahmed TS, Tewari P, Kaur J, Rizvi S, Nafsi T. Recurrence of pulmonary embolism while on rivaroxaban: Treatment failure. Chest 2016;149:A505.
2. Kaur J, Rizvi S, Tewari P, Tamer S, Nafsi T. Rivaroxaban treatment failure from possible drug interaction: A case report. Chest 2016;149:A501.
3. Rankin J, Nagar M, Crosby J, Toomari N, Pietras R, Ben-Zur UM. Possible failure of novel direct-acting oral anticoagulants in management of pulmonary embolism: A case report. J Med Case Rep 2016;10:346.