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CASE REPORT

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# Successful treatment of heparin-induced thrombocytopenia with apixaban in a patient with chronic kidney disease requiring hemodialysis

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**Key Clinical Message**

Heparin-induced thrombocytopenia (HIT) is a prothrombotic state that can affect patients with chronic kidney disease (CKD) on hemodialysis (HD). This case highlights the potential usefulness of apixaban therapy for patients with HIT and CKD on HD.

**KEYWORDS**

apixaban, hemodialysis, heparin, thrombocytopenia, thrombosis

## 1 | BACKGROUND

Heparin-induced thrombocytopenia (HIT) is a prothrombotic state that affects roughly 1 in 5000 hospitalized patients and is caused by antibodies directed against platelet factor 4–heparin complexes.[1] The diagnosis of HIT is based on a combination of clinical criteria and laboratory tests. Treatment involves suspension of all forms of heparin and institution of an alternative anticoagulant.[2] HIT is more commonly seen after exposure to unfractionated heparin (UFH) than after exposure to other heparin formulations, so patients with chronic kidney disease (CKD) on hemodialysis (HD) are at risk of developing this condition.[1] Argatroban is the recommended therapy for individuals with HIT and renal failure. Unfortunately, this medication must be administered as a continuous infusion and is not widely available everywhere.[1,2] Hence, treatment options for patients with diminished renal function and HIT are limited.

## 2 | REPORT OF A CASE

A 71-year-old former smoker with a previous history of hypertension, hypothyroidism, CKD, psoriasis, and primary myelofibrosis presented with pain in his right leg and productive cough. Relevant laboratory results can be found in Table 1. Acute limb ischemia of the right leg secondary to an occlusive thrombus of the femoral artery was diagnosed, a surgical embolectomy was performed, which was not successful and UFH was initiated in the postoperative period. In addition, an abscess was found on the right lung base. Bronchoscopy was performed, and microbiologic samples were obtained. However, no etiologic agent was found. Piperacillin tazobactam and vancomycin were initiated as empirical treatment. By the 10th inpatient day, a drop in the platelet count was evident, and anticoagulation was withheld. Five days later, renal function deteriorated, and intermittent HD was started. Despite optimal medical therapy, limb salvage was not successful and right leg amputation was performed. Thrombocytopenia persisted despite antibiotic therapy modification and multiple thrombotic events ensued; initially in the upper extremities, later in the HD access and finally in the pulmonary arteries. Testing for anti-phospholipid antibodies, paroxysmal nocturnal hemoglobinuria, thrombotic microangiopathy and human immunodeficiency virus infection was negative. A bone marrow biopsy was performed, it confirmed the previous diagnosis

**TABLE 1** Laboratory data

| Variable | Hospital admission | Inpatient, days 10-15 | Outpatient, follow-up visit | Reference range |
|---|---|---|---|---|
| Hemoglobin (g/dL) | 13.4 | 8.9 | 10.3 | 13.5-17.5 |
| White-cell count (per $mm^3$) | 46 600 | 47 800 | 44 300 | 4500-11 000 |
| Platelet count (per $mm^3$) | 385 000 | 54 000 | 315 000 | 150 000-400 000 |
| Creatinine (mg/dL) | 1.7 | 7.0 | 2.0 | 0.60-1.50 |
| Urea nitrogen (mg/dL) | 42 | 70 | 28 | 8-25 |
| Peripheral blood smear | Leukocytosis with a left shift; anisocytosis +; dacryocytes +; erythroblasts +, no schistocytes | Leukocytosis with a left shift; anisocytosis +; erythroblasts +, rare schistocytes | Leukocytosis with a left shift; anisocytosis +; dacryocytes +; erythroblasts +, no schistocytes | |
| Antiplatelet factor 4 antibodies, immuno-assay (U/mL) | | 1.9 | | <1.0 |

of myelofibrosis, JAK 2 V617F was not present. Eventually, during a HD session, the patient had facial flushing, hypotension, and fever. Heparin was used as an anticoagulant for the dialysis circuit. This systemic reaction recurred further on two other occasions. At that time, the clinical likelihood of HIT was estimated as high (8 points according to the 4T′s score) and testing for antiplatelet factor 4 antibodies was performed. Since argatroban is not readily available in our country, fondaparinux was begun at a dose of 2.5 mg SC every other day after HD. Also, a request for heparin-free anticoagulation of the HD circuit was made to the nephrology service. Despite these measures, the platelet count failed to improve after 5 days on fondaparinux, so this medication was stopped and apixaban was initiated at a dose of 2.5 mg PO bid. A sustained platelet elevation was seen and by the 10th day on apixaban the count was normal. No additional thrombotic episodes were observed, kidney function improved and eventually HD was suspended. No hemorrhagic complications were observed during anticoagulant therapy.

## 3 | DISCUSSION

Direct oral anticoagulants (DOACs) are being used increasingly in patients with HIT. A recent literature review suggested that DOACs are highly efficacious in this scenario, although most patients included in the report were treated with rivaroxaban.[3] Among DOACs, apixaban is the least dependent on renal clearance of the direct factor Xa inhibitors and might be the one with the smallest bleeding risk.[4] As a matter of fact, there is some pharmacokinetic evidence to support the use of an adjusted dose of apixaban

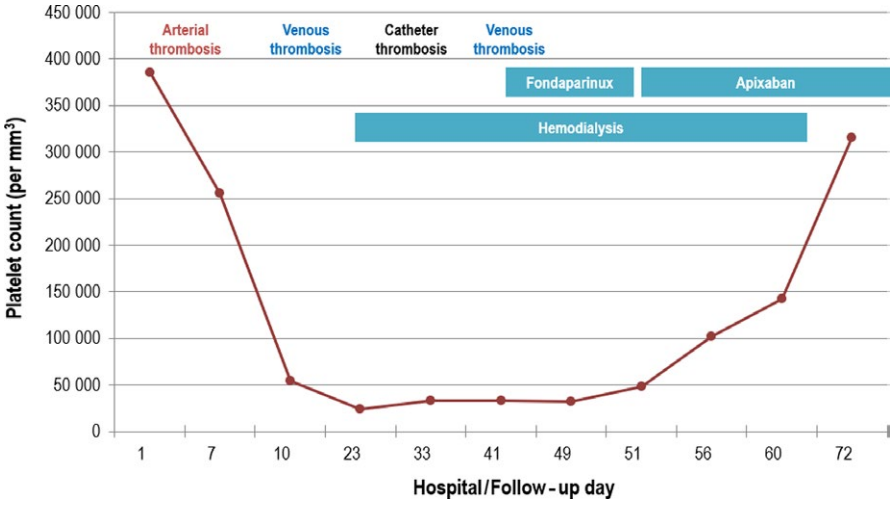


**FIGURE 1** Clinically relevant events

in patients on HD.[5] However, individuals with severely impaired kidney function and concomitant HIT are underrepresented in the medical literature. Fueled by the lack of platelet improvement in our patient, and in line with the aforementioned observations, we decided to switch from fondaparinux to apixaban. Although we acknowledge that fondaparinux is not a standard therapy for HIT among individuals with a creatinine clearance below 30 mL/min, it was used as first-line therapy in this patient because of the restricted access to argatroban in a resource-limited country such as ours. After switching to apixaban a prompt normalization of the platelet count followed, which is the strongest clinical indicator of recovery among patients with HIT.[1] Furthermore, the patient did not experience any bleeding events and no further thrombotic episodes took place. Platelet count trend and clinically relevant events can be found in Figure 1. In summary, this report helps expand the role of DOACs in novel clinical scenarios and specifically provides some support for the use of apixaban in patients with HIT and reduced renal function.

## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTION

DTA, JDRQ, and MAB: collected the information, reviewed the medical literature, and wrote the final draft.

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