

with “normal” P waves on ECG. P-wave morphology is usually similar or identical to sinus rhythm. In general, IST is a diagnosis made by exclusion. The treatment for IST has been limited to calcium channel blockers, beta-blockers, antiarrhythmic drugs, and sometimes, radiofrequency ablation. Although metoprolol, verapamil, and digoxin were used in maximum doses in our patient, the control of HR was not achieved and LVEF deteriorated each day, which led to the development of symptomatic HF.

The most popular choice for patients with drug-refractory IST is sinus node modification using radiofrequency ablation (2, 3). However, our patient did not agree to undergo the procedure because of risks such as ionizing radiation, phrenic nerve injury, requirement for permanent pacing, and pericarditis.

A specific HR reducing agent (through the inhibition of pacemaker If current), ivabradine has been documented to be effective for treating angina pectoris and HF (4, 5). The benefit of ivabradine in patients with drug-refractory IST has been described (3–6). There is no information regarding the safety of ivabradine use during pregnancy. In the literature, there is only one study by Babic et al. (7) that demonstrates the administration of ivabradine to a first-trimester pregnant patient presenting with myocardial infarction.

The success of ivabradine treatment for IST-associated cardiomyopathy has been reported in 2 patients in the literature (8, 9). With the improvement of tachycardia, the patients’ clinical symptoms and LVEF also improved, and reduction in MR was observed.

In rats, ivabradine has been shown to pass to the breast milk, but its effect is unknown (10). In our patient, the baby was only fed breast milk and neither bradycardia nor cardiac dysfunction was observed. Therefore, we concluded that ivabradine did not pass to breast milk in amounts that affect the baby’s HR.

## Conclusion

We have shown that ivabradine treatment improved tachycardia and HF in a pregnant patient with IST-induced cardiomyopathy. In addition, no maternal and fetal side effects were observed. However, further studies are still needed to evaluate the use of ivabradine treatment during pregnancy and breastfeeding.

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## A rare side effect seen due to the use of apixaban: Palmoplantar psoriasiform drug eruption

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### Introduction

Psoriasiform drug eruptions are very rare and generally characterized as erythematous, thick, dry, squamous, and demarcated plaques, resembling those of idiopathic psoriasis (1). Drugs may result in the exacerbation of pre-existing psoriasis or initiation of de novo psoriatic lesions (2). Apixaban, a reversible direct inhibitor factor Xa, is a novel anticoagulant, and its side effects mainly include clinically relevant major and non-major bleeding. Although <1% of patients receiving apixaban develop hypersensitivity reactions (including skin rash and anaphylactic reactions such as allergic edema) (3), there is no published case report demonstrating a psoriasiform drug eruption associated with apixaban. We report a psoriasiform drug eruption induced by apixaban.

## Case Report

A 78-year-old female patient who was being followed for hypertension and atrial fibrillation was referred to our department due to a pruritic skin eruption. She had been operated on due to a fracture on the left arm after the discontinuation of warfarin. After being discharged from hospital, warfarin was switched with apixaban due to the advanced age of the patient and challenges faced by arriving at the hospital. The dermatological complaints started approximately 3 days after receiving apixaban therapy. Her physical examination revealed thick, scaly, hyperkeratotic, erythematous, and desquamative plaques of various sizes on the palmoplantar areas, suggestive of a psoriasiform eruption (Fig. 1a, b). She had no personal or family history of psoriasis. Routine laboratory test results were within normal limits. A skin biopsy specimen taken from the plantar lesion revealed mild keratosis, acanthosis, focal parakeratosis, neutrophilic exudate, psoriasiform hyperplasia, necrotic keratinocytes at all levels of the epidermis, a reduction in the granular layer, and superficial perivascular dermatitis (mainly lymphocytes), which might be consistent with a psoriasiform drug eruption. She had been taking oral diltiazem and perindopril since 2009, which were not suspected as provocative agents for a psoriasiform drug eruption, and they were continued. Apixaban was withdrawn, and enoxaparin was subcutaneously administered (1 mg/kg twice daily). Further, treatment with topical corticosteroids (clobetasol propionate ointment USP, 0.05% daily) was used until the lesions disappeared. After discontinuation of apixaban, the psoriasiform eruptions began to gradually improve within 3 weeks, and the patient was asymptomatic (Fig. 1c, d). The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 4, and HAS-BLED score was 3. After 1 month, warfarin treatment was initiated again as the INR level within the therapeutic level.

On the basis of the findings, the diagnosis of psoriasiform drug eruptions induced by apixaban was made.

## Discussion

Cutaneous drug eruptions have been considered as a common adverse reaction, with an overall incidence rate of 2–3% (4, 5). Some cardiovascular drugs such as beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitor, digoxin, quinidine, and chlorthalidone have been found to be possible offenders for psoriasiform drug eruptions (6, 7). In contrast, anticoagulant drugs are rarely associated. Although adverse skin effects of dabigatran (8) and rivaroxaban (9) have been reported, there is no reported case report related to apixaban.

Drug-related psoriasiform eruptions closely resemble those of idiopathic psoriasis clinically. Therefore, a histopathological examination of the skin biopsy plays an important role in the differential diagnosis of the former from the latter. Psoriasiform hyperplasia, thinning of the granular layer on the epidermis, and neutrophilic accumulation in parakeratosis may be observed,



**Figure 1. Clinical features of psoriasiform lesions. (a) Squamous plaques of the palm. (b) Thick hyperkeratotic yellow-colored plaques of the sole. Recovery after drug cessation. Palmoplantar lesions began to improve 3 weeks after discontinuing the drug, without any additional treatment (c, d)**

both in the psoriasiform drug eruptions and idiopathic psoriasis (6, 10). However, suprapapillary thinning, absence of corrugated capillaries among dermal capillaries, interstitial eosinophils in the upper dermis, delayed hypersensitivity, impaired lymphocyte transformation, and decreases in epidermal cyclic adenosine monophosphate levels are in favor of psoriasiform drug eruptions (6, 10). Further, a temporal relationship accompanying the prompt and complete disappearance of lesions after drug cessation al-

lowed us to diagnose the drug-related psoriasiform eruption.

Our patient did not have a history of psoriasis or any possible causative medication usage. Lesions developed de novo 3 days after starting apixaban therapy and improved within weeks of ceasing the medication. The histopathological features of skin biopsy were consistent with those of drug-related psoriasiform eruptions. Thus, we have agreed that apixaban should be considered a possible causative agent of the psoriasiform drug eruption in our patient. To the best of our knowledge, this is the first report of an apixaban-induced psoriasiform drug eruption.

## Conclusion

It is important for physicians to recognize that apixaban might produce, though rarely, psoriasiform drug eruptions or aggravate the pre-existing psoriasis.

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A stamp published in Austria in 1937 for the memory of physician Leopold Auenbrugger (From Dr. Ahmet Doğan Ataman's collections)