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Skin necrosis: An uncommon side effect of warfarin therapy

Varfarin tedavisinde nadiren gözlenen yan etki: Deri nekrozu

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Abstract

Warfarin is commonly used in the treatment and prevention of thromboembolic events. However, it is known to undesirably cause hypercoagulable conditions, including warfarin-induced skin necrosis (WISN). This report describes a 70-year-old man presented with an extensive WISN while an inpatient for treatment of a left deep femoral vein thrombosis. He had a background of colon adenocarcinoma and multiple metastatic foci in the liver.

Keywords: Warfarin, skin necrosis, anticoagulants, therapeutic complication.

Öz

Varfarin yaygın olarak tromboembolik hastalıkların önlenmesinde ve tedavisinde kullanılmaktadır. Bununla birlikte varfarin kullanımının, istenmeyen şekilde, varfarin kaynaklı cilt nekrozunun (WISN) da dahil olduğu aşırı-pıhtılaşma koşullarına neden olduğu bilinmektedir. Bu olgu sunumunda, sol kalp yetmezliği sonucu gelişen femoral ven trombozunun tedavisi sebebiyle hastanede yatan ve WISN gözlenen 70 yaşındaki bir erkek hasta tanımlamaktadır. Hastanın öyküsünde ayrıca kolon adenokarsinomu ve karaciğerde çoklu metastatik odaklar bildirilmiştir.

Anahtar Sözcükler: *Varfarin, deri nekrozu, antikoagülanlar, tedavi komplikasyonu.*

Introduction

Warfarin-induced skin necrosis (WISN) is a rare dermatologic complication of vitamin K antagonist anticoagulant therapy. This pathological condition requires immediate drug cessation due to a highly associated morbidity and mortality. WISN cases occur by a small percentage (0.01 to 0.1) of warfarin induced patients. Emerging dermatopathological symptoms progress to ecchymoses and hemorrhagic bullae. Dermatologically pervasive microthrombi with endothelial damage and red cell extravasation with progression to full thickness coagulative necrosis are typical symptoms. Early recognition of WISN is very important for immediate intervention. The macroscopic view of WISN may be hard to distinguish from mimickers, therefore evaluating clinical history, time of onset, skin biopsy, cutaneous distribution of the lesions, and laboratory findings are essential for correct diagnosis and appropriate treatment (1).

Case Report

With the informed consent of the patient, we present the case of a 70-year-old man who had been given chemotherapy because of colon adenocarcinoma and multiple metastatic foci in the liver 6 months ago. The patient has not received chemotherapy for five months. Warfarin treatment was initiated due to left deep femoral vein thrombosis 1 month ago. Purple and some of which were ulcerated plaques have emerged on the skin of the feet, abdomen, and calves (Figure-1A-1B). WISN was diagnosed histopathologically due to the detection of ischemic full thickness epidermal necrosis as well as micro-thrombi within dermal capillaries, and focal red blood cell extravasation in skin punch biopsy material of the patient (Figure-1C-1D).

Written informed consent was obtained from the patient for publishing the individual medical records.

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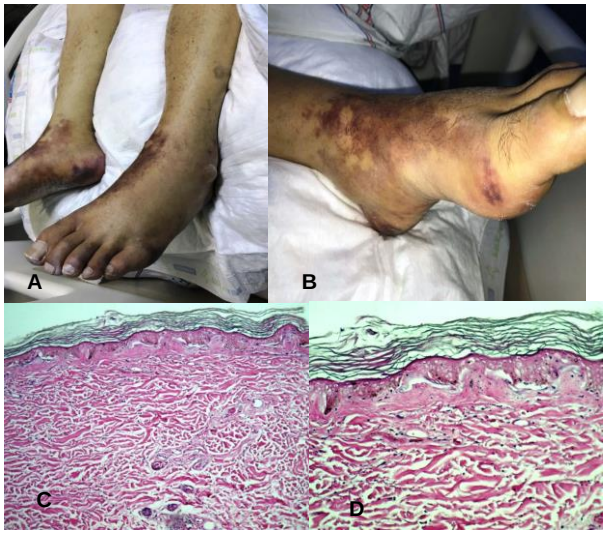

Figure-1. A. Purple plaques of WISN on the skin of the feet. **B.** Close-up view of the feet lesions. **C.** Coagulative epidermal necrosis and dermal non-inflammatory microthrombi (Hematoxylin-eosin stain; original magnification: X100). **D.** Full thickness coagulative epidermal necrosis (Hematoxylin-eosin stain; original magnification: X200).

Discussion

Warfarin associated skin reactions usually emerge 3 to 5 days after initiating of treatment. Due to the reduced blood supply to adipose tissue; lesions commonly occur on breasts, buttocks, abdomen, and calves. Rapid progression of skin lesions to WISN increases morbidity (2). WISN is a relatively hyper-coagulable state produced by the side effect of warfarin therapy. Warfarin therapy with high loading doses or without preliminary accompanying heparinization, are common clues in the clinical history, as in the patient presented herein.

Viral infections, obesity, hepatic disease, and drug interactions are some of the common predisposing factors. Deficiency of protein C, protein S or Factor V Leiden, antithrombin III, hyperhomocysteinaemia, and antiphospholipid antibodies are risk factors (2,3). Calciphylaxis, heparin-induced skin necrosis, micro-embolization (septic emboli, cholesterol emboli), DIC, cryoglobulinemia, purpura fulminans, inflammatory breast cancer, necrotizing fasciitis, and decubitus ulcers were reported as the mimickers of WISN (4,5). WISN should be suspected in all patients who undergo aggressive warfarinization, even with an initially normal clotting profile. Rapid diagnosis and drug withdrawal are critical for the prognosis (2).

WISN infrequently emerges on the trunk within 3-10 days after the initiation of oral warfarin. Hamada et al. (2017) reported the case of a patient with cutaneous arteritis treated with oral warfarin. They argued that soon after induction of the warfarin therapy, WISN had improved mainly in the lower legs, where the cutaneous arteritis had primarily influenced (6). The lesions presented in this study were thought to constitute more severe WISN lesions than our case. It was concluded that the difference in lesion severity between the two studies may be due to cutaneous arteritis.

In conclusion, it is difficult to distinguish the lesions of WISN, only with histopathological examinations. Skin biopsy as well as careful assessment of the clinical information, including time of onset and cutaneous spreading of the lesions is crucial for the accurate diagnosis and treatment of these cases.

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