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CASE REPORT / OLGU SUNUMU

A Case Of Late-onset Warfarin Induced Skin Necrosis Resulting In Mortality

Mortaliteyle Sonuçlanan Geç Başlangıçlı Warfarin Kaynaklı Cilt Nekrozu Olgusu

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Abstract

Warfarin-induced skin necrosis is a rare complication of warfarin therapy and is associated with high mortality. Here, we present a case of warfarin-induced skin necrosis, that was fatal in a 53-year-old female patient who was started on warfarin treatment 5.5 years ago due to atrial fibrillation and previous mitral valve surgery. Patients using warfarin should be evaluated for warfarin-induced skin necrosis when they present with skin lesions. Early diagnosis, early discontinuation of the drug, early initiation of supportive treatment can be life-saving.

Öz

Warfarine bağlı cilt nekrozu, warfarin tedavisinin nadir görülen bir komplikasyonudur ve yüksek mortalite ile ilişkilidir. Burada 5,5 yıl önce atriyal fibrilasyon ve geçirilmiş mitral kapak cerrahisi nedeniyle warfarin tedavisine başlanan 53 yaşında kadın hastada ölümcül seyreden warfarine bağlı cilt nekrozu olgusu sunulmaktadır. Warfarin kullanan hastalar cilt lezyonları ile başvurduklarında warfarine bağlı cilt nekrozu açısından değerlendirilmelidir. Erken tanı, ilacın erken kesilmesi ve destek tedavisine erken başlanması hayat kurtarıcı olabilir.

INTRODUCTION

Warfarin is an anticoagulant that is taken orally and is used to prevent and treat thromboembolic events in patients with a variety of medical problems. Vitamin K-dependent coagulation factors II, VII, IX, and X, as well as anticoagulant proteins C and S, are all inhibited by warfarin. Hemorrhage, alopecia, urticaria, maculopapular eruptions, dermatitis, purple toe syndrome, and leukocytoclastic vasculitis are all possible side effects of warfarin. Cutaneous necrosis affects 0.01–0.1% of patients and can result in considerable morbidity and mortality (1).

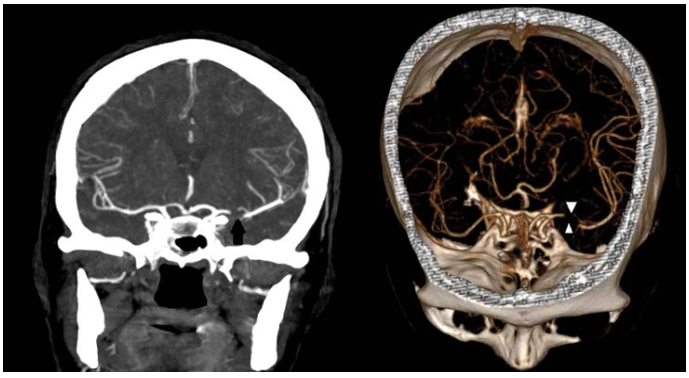
In warfarin-naive individuals, warfarin-induced skin necrosis (WISN) usually appears three to ten days after starting the drug. WISN cases, on the other hand, have been recorded in the literature even years after patients were started on warfarin medication (2). Here, we present a case of warfarin-induced skin necrosis in a patient who has been using anticoagulants for five and a half years without complications.

CASE REPORT

A 53-year-old obese female patient with a past medical history of hypertension, diabetes mellitus, atrial fibrillation, and mitral valve operation was admitted to the emergency department with complaints of dyspnea and chest pain. Findings compatible with pulmonary edema were detected in thoracic computed tomography, and the patient was hospitalized in the emergency critical care unit due to tachycardia and tachypnea. The warfarin 5 mg, oral antihypertensive drugs, and diabetes medications used by the patient were continued, and antibiotherapy and antidiuretic treatment were added. Petechia-purpura type rashes were seen on all extremities at the time of hospitalization.

Cranial computed tomography angiography was performed in the patient who developed blurred consciousness, left deflection in the mouth, and loss of strength in the right extremity, and thrombus was detected in the left medial cerebral artery (figure 1). The patient was consulted by neurology and interventional radiology, and thrombolytic therapy or thrombectomy was not considered due to the INR value of 3.18. The patient, who lost consciousness and had shallow breathing, was intubated and transferred to the intensive care unit (ICU) on the 6th day of her admission to the emergency critical care unit.

Figure I. Thrombus image in the left medial cerebral artery in the patient's cranial computed tomography angiography



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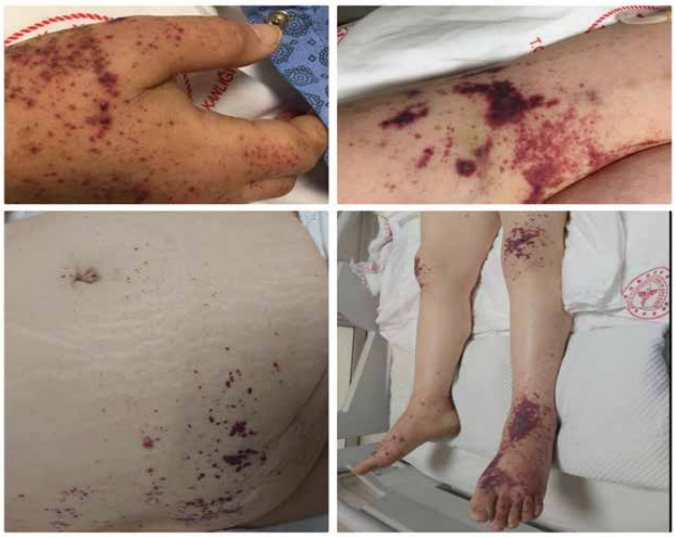
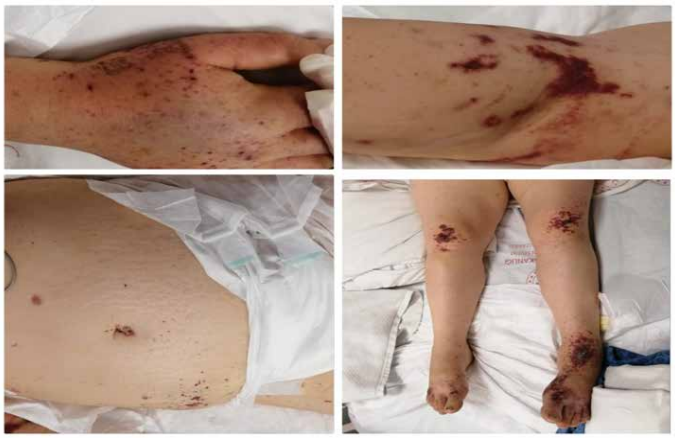
Vasopressor therapy was started in the patient whose hemodynamics deteriorated on admission to the ICU. On the physical examination of the patient who was admitted to the ICU, sharply demarcated areas of blue-black ecchymotic discoloration and petechial hemorrhages were observed mainly in all extremities, especially in the distal regions and lower umbilical region (figure 2).

Figure II. Sharply demarcated areas of blue-black ecchymotic discoloration and petechial hemorrhages



In reviewing her medical history, it was learned that she started on a daily 5 mg warfarin treatment after a mitral valve operation 5.5 years ago. The patient suspected of WISN was consulted at the dermatology clinic, and the patient was diagnosed with WISN clinically based on the medical history and typical lesions. Warfarin treatment was discontinued and enoxiparin treatment was started. Fresh frozen plasma and vitamin K replacement were applied to the patient with an INR of 5.2. After warfarin discontinuation, the lesions began to regress (figure 3). The patient died on the 5th day of ICU admission.

Figure III. The skin lesions regressed after the discontinuation of warfarin use.



DISCUSSION

WISN is a rare (0.01% to 0.1%) but serious complication of warfarin therapy. It can be fatal if early diagnosis is not made and necessary precautions are not taken . Although WISN is usually seen between 3-10 days of warfarin treatment, there are cases in the literature reporting that WISN develops months or even years after the start of warfarin treatment (2). In our case, WISN occured after 5.5 years of warfarin therapy. There are very few cases of late-onset WISN in the literature, and 2 cases with WISN were found years later, like ours (3,4).

WISN is common in middle-aged and obese patients, especially females. This disease begins with complaints of severe pain in the affected area and erythema, leading to ecchymosis, petechiae, discoloration, hemorrhagic bullae. Later, necrosis occurs in the skin and subcutaneous tissue. WISN most commonly occurs on the breasts, buttocks, abdomen, thighs, and extremities, which are areas with large subcutaneous adipose tissue (5). Our 53-year-old postmenopausal obese female patient had lesions similar to the WISN described above, more intensely in all extremities, especially in the distal regions and lower umbilical region.

The histopathological findings of WISN are capillaries in the skin and subcutaneous regions; diffuse microthrombus in the venules and deep veins; and dense erythrocytes outside the veins. In the case of major skin necrosis or secondary infection, biopsies are generally of no diagnostic value due to the rapid change in histopathological findings (2). The diagnosis of WISN can be made clinically by careful anamnesis and physical examination, excluding differential diagnoses. In our case, we established the diagnosis of WISN by clinical anamnesis and careful physical examination.

In the differential diagnosis of WISN, calcilaxis, heparin-induced skin necrosis, microembolization, leukocytoclastic vasculitis, DIC, cryoglobulinemia, purpura fulminans, inflammatory breast cancer, necrotizing fasciitis, and decubitus ulcers should also be considered (1).

The exact cause of WISN is unclear. Direct toxic effects of warfarin, protein C, protein S, antithrombin III deficiency, Factor V Leiden mutation, hyperhomocysteinemia, antiphospholipid antibodies, drug interactions are possible risk factors (5). Possible causes of late-onset WISN are improper discontinuation of oral anticoagulation and its subsequent re-start, drug interactions, and disruption of the procoagulant-anticoagulant balance as a result of liver synthesis dysfunction. There are WISN cases with congestive heart failure in the literature (6). In these cases, it was assumed that the synthesis function of the liver was affected secondary to right heart failure, resulting in a procoagulant-anticoagulant imbalance. In our case, the patient's reason for admission was pulmonary edema due to heart failure.

Early diagnosis and discontinuation of warfarin use, rapid recognition of complications, taking necessary precautions will stop the progression of necrosis and save life and limb. As a supportive treatment, patients can be given vitamin K and fresh frozen plasma. If necessary, local debridement of the area, grafting, topical antibiotic application can be performed. Our patient was diagnosed on the 6th day of her admission to the hospital and died five days after the diagnosis.

In conclusion, awareness of WISN should be increased in patients using warfarin presenting with skin lesions. A high clinical suspicion should always be maintained for this rare, but potentially fatal, reaction to warfarin.

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