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Warfarin-induced skin necrosis within psoriatic plaques

Gerhard Eichhoff MD PhD FRACP

Affiliations: Dermatology Service Capital & Coast and Hutt Valley District Health Board, Wellington Regional Hospital, New Zealand

Corresponding Author: Gerhard Eichhoff MD, PhD, Wellington Regional Hospital, PB 7902, New Zealand, Tel: 64-43855999, Email: gerhard.eichhoff@ccdhb.org.nz

Abstract

A myriad of different phenomena exist in the dermatological literature which are based on the concept of *locus minores resistentiae*. The most commonly described phenomenon is the Koebner phenomenon, which is classically associated with the emergence of psoriatic lesions post trauma. Warfarin-induced skin necrosis (WISN) is a rare but severe side effect that leads to necrosis of the skin, predominantly on areas with increased subcutaneous fat. The presented case reports on WISN within psoriatic plaques.

Keywords: warfarin, necrosis, Koebnerization, Koebner, psoriasis, Wolf isotopic response

Introduction

Heinrich Koebner first described the isomorphic phenomenon in 1872. Koebnerization has been described to be associated with a myriad of dermatoses and elicitors, whereas true Koebnerization is reserved for cases of isomorphic lesion formation after an external injury and is classically linked to psoriasis [1, 2]. The isotopic response of Wolf is a condition characterized by the appearance of a new dermatosis on the same place as that of healed cutaneous lesions [7]. In current medical practice, warfarin, a vitamin K antagonist, is one of the most frequently used anticoagulants for primary and secondary prevention of thromboembolic disorders. With a prevalence of 0.01%–0.1%, warfarin-induced skin necrosis (WISN) is a rare complication with a high morbidity [3]. The presented case describes WSIN within psoriatic plaques.

Case Synopsis

A 41-year-old woman who was overweight and had long-standing psoriasis developed an embolic stroke owing to aortic valve vegetations and had to undergo emergency aortic heart valve replacement surgery. She developed psoriasis in her mid-twenties. After a failed response to methotrexate and cyclosporine, etanercept was introduced in 2015 and was successful. However, owing to wishing for a child, the patient decided to stop etanercept treatment three months prior to the stroke. Since then, psoriasis was treated with topical corticosteroids.

Warfarin was introduced immediately after surgery. On the third day after surgery, the patient developed painful purpuric lesions on the bilateral lower legs.

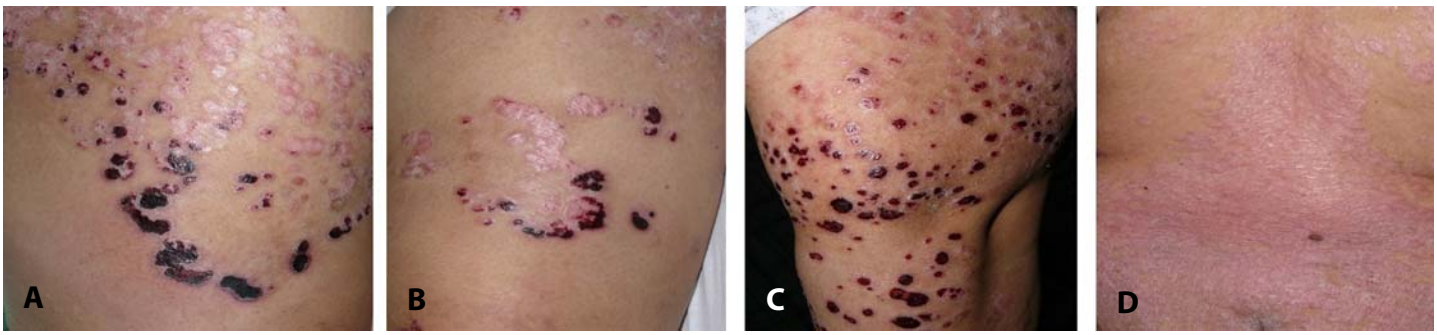

Figure 1. *Hemorrhage and skin necrosis within psoriatic plaques together with non-affected psoriatic plaques **A**, **B)** on both thighs, and **C)** on the right forearm. **D)** There is extensive psoriasis without skin necrosis on the back.*

Over the next few days, the lesions progressed to blood-filled blisters with cutaneous necrosis. At the time of dermatologic evaluation, severe psoriasis was revealed, with a PASI of 18 along with hemorrhage into the psoriatic plaques on both thighs and on the right forearm (**Figure 1**). Subsequently, the lesions progressed to superficial necrosis. The psoriatic plaques of the patient's back were not affected by hemorrhage.

Biopsies taken from the upper and lower extremities showed dermal and subcutaneous vessels containing fibrin deposits without inflammatory elements together with epidermal necrosis and remnant features of psoriasis (**Figure 2**). Laboratory analyses were negative for heparin-induced thrombocytopenia and the platelet count was normal. Blood cultures remained negative. The level of creatinine was increased to 138µmol/L (normal range 45-90µmol/L) and that of calcium was 1.98mmol/L (normal range 2.15-2.55mmol/L). Laboratory work-up indicated normal levels of protein C, protein S, antithrombin III, and anti-phospholipid antibodies.

The diagnosis of WISN within psoriasis, was made. Warfarin was discontinued and replaced by heparin; thereafter, long-term treatment with warfarin was cautiously reinitiated without further complications. Topical treatment with 0.1% betamethasone valerate for psoriasis was continued and secukinumab was introduced three weeks after the stroke. The necrotic lesions were regularly dressed and they subsequently healed with conservative care.

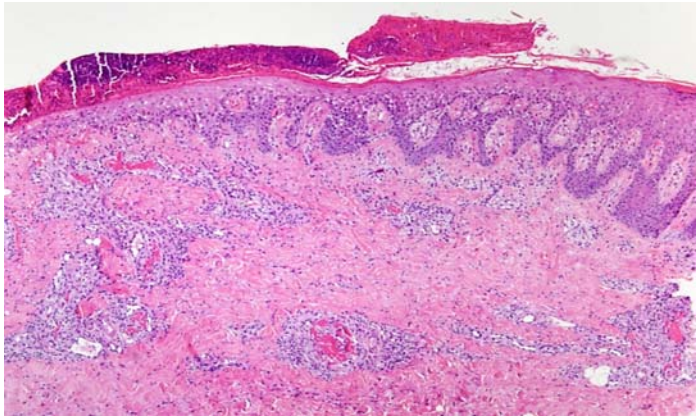

Figure 2. *Epidermal necrosis together with thrombotic vasculopathy including psoriatic skin with elongation of rete ridges. H&E, 40×.*

Case Discussion

Koebner phenomenon has been described to occur mainly in psoriasis and other inflammatory cutaneous diseases post trauma, but therapeutics, including medications, radiation, and phototherapy have been documented as Koebner stimuli, in addition to inflammatory skin diseases and infectious dermatoses [1, 4].

Psoriasis as elicitor of another dermatosis seems extremely rare. In 1964, Vivkers and Ghadially reported on keratoacanthomas arising from psoriatic patches [5]. Eruptive lentiginosis in resolving psoriatic plaques have been occasionally described in the literature and may be called Wolf isotopic response [6, 7]. The presented case of WISN within psoriatic plaques can be considered as Wolf isotopic co-response, which refers to the appearance of a disease at the same anatomic site as another still active second disease [8].

Happle and Kluger, however, recently questioned the term Wolf response and argued that the Wolf isotopic response is a mere variant of Koebner phenomenon and therefore should be abandoned. The concept of *locus minores resistentiae* underlies both phenomena in an effort to explain why certain locations predispose to disease [9, 10].

Warfarin-induced skin necrosis usually appears three to eight days after initiating warfarin treatment in susceptible individuals. The pathogenesis of WISN is not yet fully understood, but a temporary hypercoagulable state may result in thrombi formation in the skin microvasculature. Further, immunologic hypersensitivity to warfarin or a direct toxic effect of warfarin and its congeners on the small vessels are the possible mechanism of WISN [11].

The risk factors are most commonly female sex and obesity, followed by deficiency in protein C, protein S, or antithrombin III. Areas with abundant subcutaneous fatty tissue, such as the breasts and thighs, are predominantly affected and approximately one third of patients were reported to have involvement of multiple sites [3]. The entities in

the differential diagnosis of WISN are calciphylaxis, septic or cholesterol microembolization, heparin-induced skin necrosis as a result of thrombocytopenia, purpura fulminans, and necrotizing fasciitis [12].

In this present case, cutaneous emboli originating from the aortic valve seemed unlikely because the necrotic skin lesions appeared three days after the removal of the valve. The clinical manifestations, temporal connection with warfarin initiation, absence of chronic renal failure with nearly normal calcium levels, and absence of inflammatory markers led to the diagnosis of WISN. The histopathological findings of WISN are non-specific. Characteristic features, as found in the presented case, were described as the presence of thrombi within dermal and subcutaneous vessels, resulting in skin ischemia without inflammatory features [13].

The presented patient belongs to the WISN risk group of middle-aged obese women, who are most commonly affected by this adverse cutaneous reaction [3]. Other hematological contributions were not detectable. In addition to the affected lower legs, she developed WISN in the pre-existing psoriatic plaques on areas with increased subcutaneous fat, such as the extremities, with sparing of the back. The mechanism of the herein described findings remains unclear, but the author hypothesizes that an increased blood flow in the papillary dermis of the psoriatic lesions and/or local inflammation in the psoriatic skin may have triggered WISN.

Conclusion

Herein, a case of warfarin-induced skin necrosis within preexisting psoriatic plaques is shown and represents a newly described finding, which can be explained by the concept of *locus minores resistentiae*.

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Potential conflicts of interest

The authors declare no conflicts of interests.

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