Late Onset Warfarin Induced Skin Necrosis

Ritu Chakrabarti MD, Mohammed Abdulaaima MD, Simon Badin MD
Departments of Internal Medicine and Hematology/Oncology, Jersey City Medical Center RWJBH

INTRODUCTION

Warfarin induced skin necrosis (WISN) is a complication of warfarin therapy that results in hemorrhagic bullae and ultimately full-thickness skin injury. The exact etiology and pathophysiology remains unknown, however it is associated with initiation or high loading doses of warfarin in treatment of venous thromboembolism. Herein we present the case of a patient on 18 years of chronic warfarin therapy for metallic aortic valve who developed late-onset WISN.

HISTORY OF PRESENTING ILLNESS

- 77-year-old female presents with chief complaint of right breast skin irritation and burning sensation for one day.
- History of metallic aortic valve on warfarin for 18 years.
- Skin lesion had "bubbled," oozed of clear liquid, turned black, then peeled off. Similar areas on right arm.
- 10 days prior to symptom onset, daily dose of warfarin was changed from 5 to 6mg.

PERTINENT PHYSICAL EXAM

- All vitals were normal.
- Right breast revealed a well-demarcated, slough-off piece of necrotic skin with black eschar, 6x6 cm in size, surrounding the nipple and sparing the nipple tissue and some of the areola (Image 1A).
- Similar skin changes were seen on the anteromedial forearm and arm; these areas were not consistent with any dermatomal pattern.

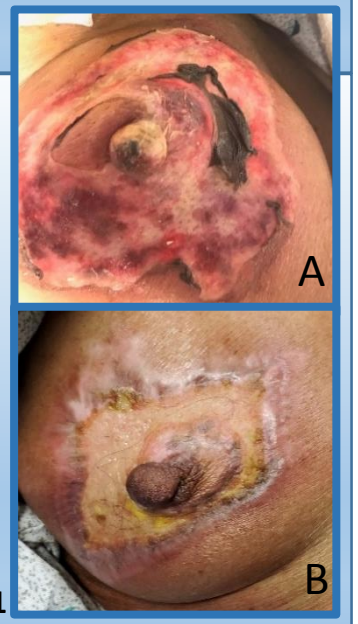


Image 1

LABS AND DIAGNOSTICS

- Complete blood count and serum chemistry were normal. INR was 4.9
- Severely reduced levels of Protein C (7%) and Protein S (<10%) activity.
- Positive Lupus Anticoagulant.
- Ultrasound of the right breast was unremarkable.
- Skin Punch biopsy: skin necrosis and dermal inflammation and hemorrhage (Image 2).

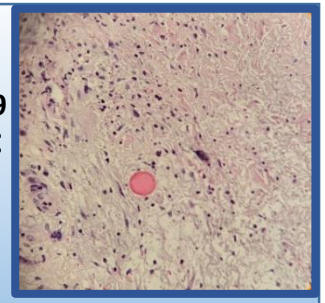


Image 2

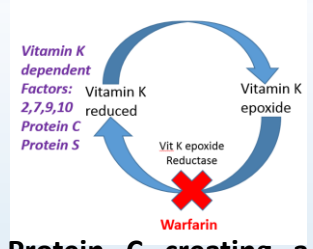
HOSPITAL COURSE

- Warfarin was discontinued on presentation.
- Patient received IV vitamin K, Lovenox 1mg/kg twice a day, Clindamycin, and the lesions were treated with topical silver sulfadiazine.
- Over the next ten days, the patient's affected areas on the breast and arm began to improve with appearance of granulation tissue and gradual resolution of pain.
- The patient was discharged on warfarin 7.5mg daily based on therapeutic INR with enoxaparin bridge therapy.
- 6 weeks later, the patient was followed up and found to have complete resolution of all symptoms with appropriate granulation tissue in all the skin lesions (Image 1B).

References:

1. Essex DW, Wynn SS, Jin DK. Late-onset warfarin-induced skin necrosis: case report and review of the literature. Am J Hematol. 1998;57(3):233-237. doi:10.1002/(sici)1096-8652(199803)57:3<233::aid-ajh10>3.0.co;2-b
2. Choudhary SV, Madnani A, Singh AL. Late onset Warfarin induced skin necrosis in human immunodeficiency virus infected patient with pulmonary tuberculosis. Indian J Sex Transm Dis AIDS. 2013;34(1):47-49. doi:10.4103/0253-7184.112940
3. Franson TR, Rose HD, Spivey MR, Maroney J, Libnoch JA. Late-onset, warfarin-caused necrosis occurring in a patient with infectious mononucleosis. Arch Dermatol. 1984;120(7):927-931.
4. Scarff CE, Baker C, Hill P, Foley P. Late-onset warfarin necrosis. Australas J Dermatol. 2002 Aug;43(3):202-6. doi: 10.1046/j.1440-0960.2002.00596.x. PMID: 12121399.

DISCUSSION:



WISN most commonly occurs in the first few days of warfarin use, with large loading doses, on discontinuation of heparin, or in patients with thrombophilia history.

Warfarin inhibits the activation of Protein C creating a hypercoagulable state leading to vascular occlusion and tissue infarction. With a predilection for fatty areas like the extremities and breast, WISN often follows a typical course starting from central erythema followed by edema, purpura, bluish-black or red rim surrounding the tissue, leading to eschar and sloughing of skin. Skin biopsy early on pathologically shows fibrin clots within blood vessels, but later can show areas of edema or necrosis as in our patient.

While WISN typically occurs in the first 3-6 days after warfarin therapy, there have been rare cases reported to occur months to years afterwards (1-4). Fluctuations in serum levels or non-compliance with warfarin have been considered as risk factors, along with history of thrombophilia. Interestingly, recent infection has also been implicated in late WISN (2-4). Our patient required 7.5mg of warfarin on discharge to maintain a therapeutic INR; her admission INR of 4.9 made us suspect she may have taken extra doses of warfarin 6mg causing rapid depletion of Protein C. Further her positive lupus anticoagulant testing suggest underlying thrombophilia; while the patient's symptoms resolved and her cardiologist recommended her to continue on warfarin, this underlying thrombophilia will need to be worked up further at a later time. To our knowledge, this is one of the latest onset of WISN cases that has been described. Though rare, it is important for clinicians to consider WISN in the differential diagnosis for patients presenting with skin necrosis as it has high morbidity if untreated.