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Coumadin-induced skin necrosis in a 64 year-old female despite LMWH bridging therapy

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Summary

Background: Coumadin is the standard oral anticoagulant used in a variety of clinical conditions. Coumadin inhibits the vitamin-K dependent gamma-carboxylation of coagulation factors II, VII, IX, X and the anticoagulant proteins C and S. Rarely, skin necrosis occurs when the resultant initial procoagulant state in the first few days of starting coumadin leads to thrombosis and formation of blood clots tin the dermal capillaries. This in turn causes skin necrosis due to interruption in blood supply to the skin.

Case Report: We are presenting the case of a 64 year-old female admitted for acute respiratory distress secondary to newly-diagnosed pulmonary embolism. The patient was started on therapeutic doses of low molecular weight heparin (LMWH) and coumadin. After 5 days of treatment, the patient started complaining of pain and numbness in both upper extremities. Overnight, this rapidly progressed to manifest hemorrhagic bullae with necrotic areas. This was immediately recognized as coumadin-induced skin necrosis. Coumadin was stopped immediately. Vitamin K was administered and local wound care was provided. Therapeutic LMWH was continued. The skin lesions began to show improvement after 3 days.

Conclusions: In coumadin-induced skin necrosis, the patient initially presents with pain and erythema, followed by petechial lesions which progress to become purpuric. Hemorrhagic bullae with necrosis and eschar formation may soon develop. Once it is suspected, coumadin should be stopped and the patient should be given Vitamin K and FFP to reverse the effects of coumadin.

key words: **coumadin • skin necrosis • low molecular weight heparin • pulmonary embolism**

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Background

Coumadin is the standard oral anticoagulant used in a variety of clinical conditions. Coumadin inhibits the vitamin-K dependent gamma-carboxylation of coagulation factors II, VII, IX, X and the anticoagulant proteins C and S. Rarely, skin necrosis occurs when the resultant initial procoagulant state in the first few days of starting coumadin leads to thrombosis and formation of blood clots tin the dermal capillaries. This in turn causes skin necrosis due to interruption in blood supply to the skin. Skin necrosis usually develops with initial large doses of coumadin (>10 mg/day) without bridging with heparin in the initial few days. Early recognition of this complication is very important because a delay in the diagnosis may lead to serious complications such as limb amputation.

Case Report

Our patient is a 64 year old Caucasian female with PMH of morbid obesity, obstructive sleep apnea, chronic obstructive pulmonary disease, diabetes, hyperlipidemia and hypertension who was sent to our institution from the nursing home because of acute respiratory distress. At our emergency department, the patient was immediately intubated. ABGs showed respiratory acidosis with a pH of 7.30 and pCO2 of 64. A-a gradient was increased at 400. The patient was afebrile but tachycardic at a rate of 110 beats per minute. CXR showed small bilateral pleural effusions. CBC showed leukocytosis of 13.2, normocytic anemia with a hemoglobin of 10.5 mg/dL, and normal platelets. The patient's blood urea nitrogen and creatinine are within normal limits. Brain natriuretic peptide was only 124, troponin I was 0.01, but D-dimer level was elevated at 2036. Urinalysis wa normal. Initial assessment was respiratory failure secondary to COPD exacerbation and possible health-care associated pneumonia. The patient was started on steroids and antibiotics. CT angiography of the chest showed a small filling defect within a peripheral left upper lobe vessel. The patient was started on therapeutic doses of enoxaparin. Venous Doppler of both lower extremities were negative for any deep venous thrombosis. On the 3rd hospital day, the patient was started on 2.5 mg of coumadin, which was increased to 5 mg on the 6th hospital day since the patient's INR was still subtherapeutic. On the 7th hospital day, the patient started complaining of pain and numbness of both hands. Overnight, she developed erythematous and necrotic bullous lesions on the upper extremities (Figure 1). INR was 2.3.

Coumadin-induced skin necrosis was immediately suspected. Coumadin was stopped and hematology consult placed for further evaluation. The patient was given 10 mg of vitamin K, and enoxaparin was continued. Venous and arterial imaging of the upper extremities were done. It was negative for any venous thrombosis or arterial insufficiency. The necrotic lesions started improving 3 days after the discontinuation of coumadin. Furthermore, the patient was extubated on the 11th hospital day and was observed in the general medical floor for one day before she was transferred to a subacute rehabilitation facility.

Discussion

Coumadin is an oral anticoagulant used in a variety of clinical conditions. Its mechanism of action involves the inhibition of vitamin K-induced gamma carboxylation of coagulation factor II, VII, IX, X and anticoagulant proteins C and S. Skin necrosis is a rare and unpredictable but well recognized complication associated with coumadin use. This typically develops during the first few days of coumadin therapy, and usually with doses >10mg/day. It occurs in 0.01% to 0.1% of patients started on coumadin. This develops secondary to the paradoxical transient hypercoagulable state produced by the suppression of the activity of the anticoagulant protein C within the first few days of coumadin use. Coumadin inhibits protein C and factor VII stronger than the other coagulation factors during its initial stages of therapy. This can be attributed to the short half-lives of these two proteins – 1.5 to 6 hours for factor VII and 8 hours for protein C. The resultant hypercoagulable state leads to thrombosis and blood clots the in the dermal capillaries which causes skin necrosis due to interruption in the blood supply to skin. For this reason coumadin should be overlapped with parenteral anticoagulants for 4–5 days. Protein C deficiency is present in only one third of patients who develop coumadin-induced skin necrosis. Breasts, buttocks, abdomen, thighs, extremities are common sites of involvement because of the large amount of subcutaneous tissue in these areas.

Coumadin-induced skin necrosis typically develops in middle-aged, peri-or post-meopausal, obese females treated with coumadin for deep venous thrombosis or pulmonary embolism. The patient usually complains of intense pain and paresthesias in the affected areas. Lesions usually begin as an area of erytherma which progresses to form ecchymoses,

Figure 1. The patient's hand showing various stages of coumadin-induced skin necrosis.

petechiae and hemorrhagic bullae with necrosis of the skin and subcutaneous tissue.

The common differential diagnosis of coumadin-induced skin necrosis are pyoderma gangrenosum, necrotizing fasciitis, cellulitis, ecthyma, and Fournier's gangrene (when lesions occur in the penis).

The initial diagnosis of coumadin-induced skin necrosis is based on clinical grounds. A high index of suspicion is required for diagnosis and intervention. Coumadin should be immediately discontinued once it is suspected. Vitamin K and fresh frozen plasma should be administered to reverse the effects of coumadin. Unfractionated or low molecular weight heparin should be started to prevent further clotting and necrosis. Activated protein C use should be also be considered. Proper local wound care with topical antibiotics and frequent dressing is an important part of treatment. Some wounds can heal without surgical intervention, but many patients need surgery for debridement and skin grafting. Early wound care consult, surgery and plastic surgery consult should also be obtained as needed. Hyperbaric oxygen therapy should be considered as an important adjunctive therapy in patients at high risk for developing significant morbidity and mortality. Its use has been detailed in a few case reports.

CONCLUSIONS

In coumadin-induced skin necrosis, the patient initially presents with pain and erythema, followed by petechial lesions which progress to become purpuric. Hemorrhagic bullae with necrosis and eschar formation may soon develop. Once it is suspected, coumadin should be stopped and the patient should be given Vitamin K and FFP to reverse the effects of coumadin.

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