Non Uremic Calciphylaxis:- A Rare But Potentially Serious Side Effect of Warfarin Use

K. Sherani, D. Patel, A. Vakil, H. Upadhyay, J. Raynor, S. Chauhan
Jamaica Hospital Medical Center, Jamaica, NY 11418

Introduction

Calciphylaxis is a rare but serious disease where calcium is deposited in the vasculature walls leading to thrombosis and skin necrosis. Calciphylaxis is most commonly seen in dialysis patients.

Non-uremic calciphylaxis has been rarely reported in patients on warfarin therapy. To the best of our knowledge less than 20 such cases have been published.

Here, we report a case of a patient on warfarin that presented with painful lower extremity lesions. After extensive work up she was found to have calciphylaxis secondary to warfarin therapy.

Clinical Case

A 68 year-old-female with hypertension and atrial fibrillation who had started on warfarin three months prior presented with bilateral, cramping leg pain. The pain restricted her ability to ambulate.

On examination, she was hemodynamically stable, with 2+ pulses palpable in femoral, pretibial and dorsalis pedis arteries. The lateral side of her right leg showed multiple irregular purpuric skin lesions with central greying areas of necrosis, the largest of which was 3x5cm (Figure 1). The patient denied having any similar symptoms prior to initiating therapy with warfarin.

Preliminary laboratory data revealed normal blood urea nitrogen (12mg/dl), creatinine (1.0mg/dl), serum calcium (8.6mg/dl), phosphorus (3.6mg/dl) and parathyroid hormone levels (19.0pg/ml).

Angiogram of the right lower extremity revealed extensive and heavy calcifications of arterial walls extending from the common iliac artery to popliteal artery, suggesting calciphylaxis (Image 2).

Extensive work up for connective tissue disorders including protein C and protein S levels were within normal limits.

Warfarin was discontinued. During the hospital course, she was treated with sodium thiosulfate, pain medications and local wound care. She had subsequent gradual improvement in her skin lesions.

Discussion

Though rarely reported, the majority of cases of calciphylaxis secondary to warfarin therapy have presented with co-occurring primary hyperparathyroidism, malignancy, alcoholic liver disease, glucocorticoid use or connective tissue diseases. Each of these conditions are known to be independent risk factors for the development of calciphylaxis.

Warfarin-induced calciphylaxis is usually mediated by a decrease in the vitamin K-dependent regeneration of a substance called matrix GLA protein, which plays a role in preventing vascular calcification.

Because calciphylaxis is a life threatening form of skin necrosis, early diagnosis and the knowledge about causative and associative factors is extremely important.

Literature suggests that cessation of warfarin followed by the use of sodium thiosulphate leads to successful treatment. The role of vitamin K2 as a potential therapeutic option has also been suggested.

Figure 1. Skin Lesions

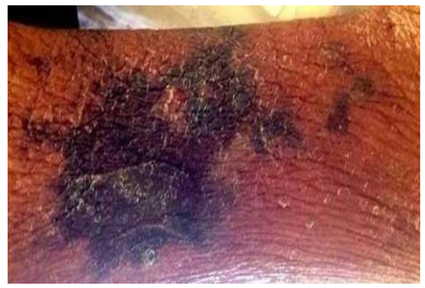


Figure 2. Right Lower Extremity Angiogram

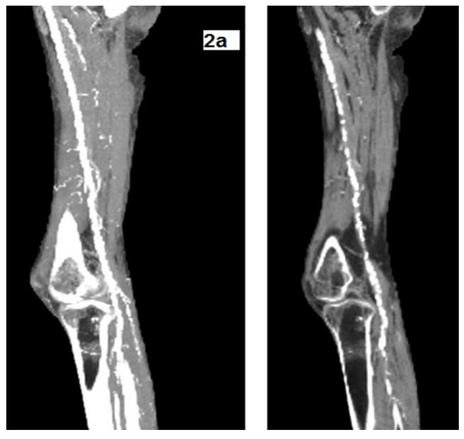
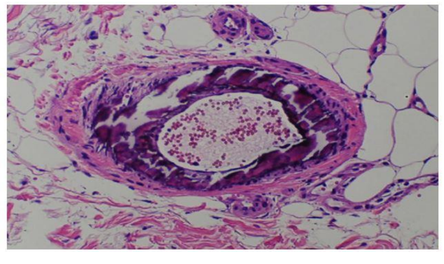


Figure 3. Histopathology



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