Denouement and Comment

Warfarin-Induced Skin Necrosis

Differential diagnosis for the necrotic plaques included calciphylaxis, cryoglobulinemia, an embolic phenomenon, vasculitis, and warfarin necrosis. Based on the temporal development of necrotic cutaneous plaques in the context of protein S deficiency and noncompliance with warfarin therapy in combination with consistent histologic features, the patient's diagnosis was warfarin-induced skin necrosis (WISN).

Warfarin-induced skin necrosis is a rare and unpredictable complication of anticoagulant therapy, which occurs in 0.01% to 0.1% of all warfarin-treated patients.[1] Currently, there have been more than 500 reported cases with several risk factors associated with WISN. Both extremes of high and low dosages of warfarin have been implicated in increasing susceptibility to WISN.[2] Abnormal coagulation conditions are also significant risk factors, which include protein C and protein S deficiencies, activated protein C resistance, and factor V Leiden defects.[2]

The typical patient is an obese middle-aged woman being treated for deep vein thrombosis or a pulmonary embolism.[3] The common clinical history is characterized by the rapid development of necrotic skin lesions, typically 3 to 10 days after the commencement of warfarin therapy.[4] Late onset can occur when there is lack of drug compliance, as in this patient, or a decrease in the synthetic function of the liver or drug interactions.[5] Although necrotic lesions can occur anywhere on the body, they tend to appear in areas of rich microcirculation and subcutaneous fat, such as the breast, buttocks, abdomen, and thighs.[6] Approximately 35% of patients have multiple lesions,[2,4] which often initially present as poorly demarcated erythema. Patients often complain of paresthesia or pain surrounding the lesions. Lesions then progress to a blue-black patch with a central hemorrhagic bullae, followed by the development of necrosis and eschar formation.[2]

Histologic changes include diffuse fibrin thrombi occluding superficial and deep dermal vessels and endothelial cell damage, which results in ischemic skin necrosis.[6] The precise mechanism of the development of WISN is unknown. Several reports have suggested that a paradoxical hypercoagulable state is formed by warfarin-induced inhibition of vitamin K–dependent factors. This establishes an imbalance between procoagulation and anticoagulation, which occurs before the anticoagulant takes effect.[6]

Recovery from WISN necessitates prompt recognition of this serious therapeutic complication. Immediate warfarin withdrawal will arrest the progression to extensive skin necrosis. Administration of heparin is recommended as the substitute to continue anticoagulant therapy.[3,6] Supportive treatment with fresh frozen plasma or vitamin K is aimed to restore the levels of proteins C and S to avoid recurrence.[6]

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