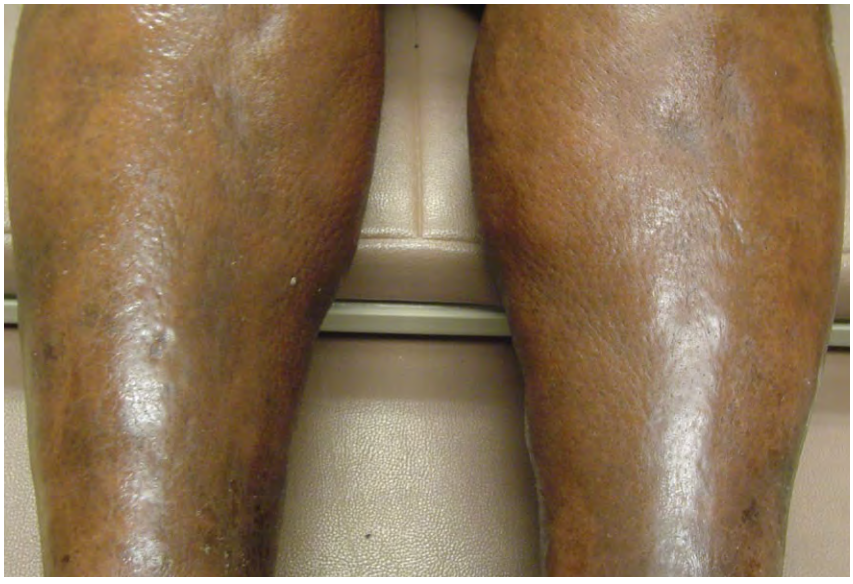
What Is Your Diagnosis?



A 54-year-old woman undergoing hemodialysis for a 4-year history of idiopathic end-stage renal disease presented with firm plaques distributed extensively over her anterior shins, inner thighs, and forearms. The development of the lesions coincided with her most recent gadolinium-enhanced magnetic resonance angiogram, which was performed 3 months prior. A review of her medical history showed no evidence of diabetes mellitus or hypertension.

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The Diagnosis: Nephrogenic Systemic Fibrosis

Physical examination of our patient revealed multiple ill-defined, hyperpigmented, indurated plaques that extended symmetrically from the inner thighs to the shins (Figure 1). Similar lesions were seen on the forearms. The lesions were tender to palpation. The remainder of the examination was unremarkable.

Histologic examination of a punch biopsy specimen from the right medial shin demonstrated a mild superficial perivascular lymphocytic infiltrate with a moderate proliferation of spindlelike cells (Figure 2). There was an increase in the density of collagen bundles in the reticular dermis and a decrease in the number of capillaries and atrophy of the eccrine glands. Mucin was observed throughout the collagen bundles. There were focal areas of $CD34^+$ spindle-shaped cells in the periphery of the lesion (Figure 3). The patient was referred to the nephrology department with a recommendation to limit future gadolinium-enhanced magnetic resonance angiography.

Nephrogenic systemic fibrosis (NSF), previously known as nephrogenic fibrosing dermopathy, is a rare acquired systemic fibrosing disorder that affects patients with renal insufficiency.[1] It often presents as an extensive symmetric thickening and hardening of the extremities with erythematous to brown hyperpigmentation, subcutaneous nodules, and papules. The plaques often have a peau d'orange appearance with irregular borders; they can be painful or pruritic.[2] Plaques typically are distributed from the ankles to the mid thighs, and the wrists to the mid upper arms. The trunk rarely is involved. Yellow scleral plaques, muscle weakness, and flexion contractures also are associated with NSF.[3] Involved joints can develop contractures, leading to debilitation within a few days or weeks.[4] In addition to these cutaneous findings, fibrosis and calcification of the heart, lungs, skeletal muscles, diaphragm, psoas muscle (major and minor), renal tubules, and rete testis have been reported.[3]

The proposed etiology of NSF involves macrophage phagocytosis of gadolinium deposited in

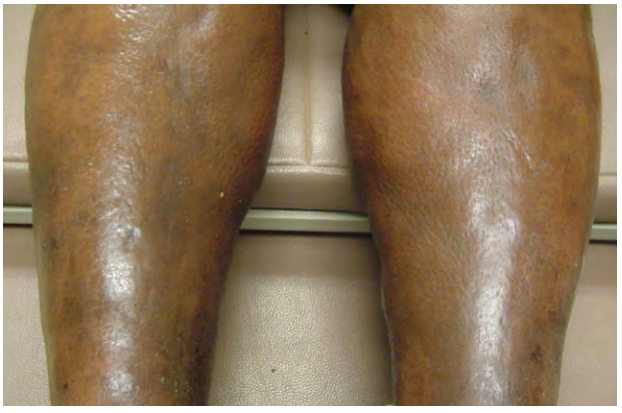

Figure 1. Multiple 1- to 2-cm well-circumscribed, violaceous, scaly nodules and plaques.

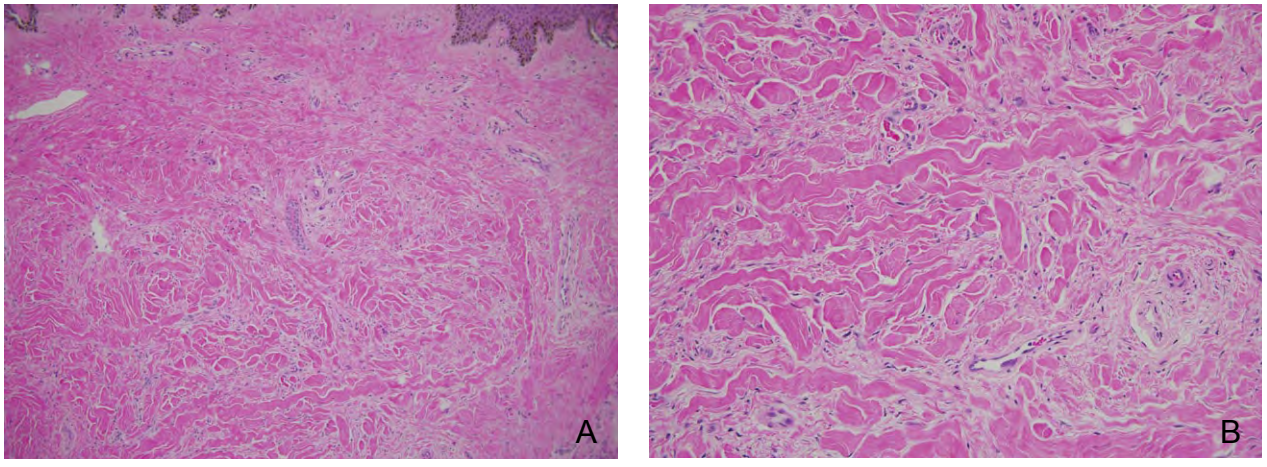

Figure 2. Histopathology demonstrated a mild superficial perivascular lymphocytic infiltrate with a moderate proliferation of spindlelike fibroblasts. There was an increased density of collagen bundles in the reticular dermis with a decreased number of capillaries and atrophy of the eccrine glands. Mucin was observed throughout the collagen bundles (A and B) (H&E; original magnifications ×10 and ×20, respectively).

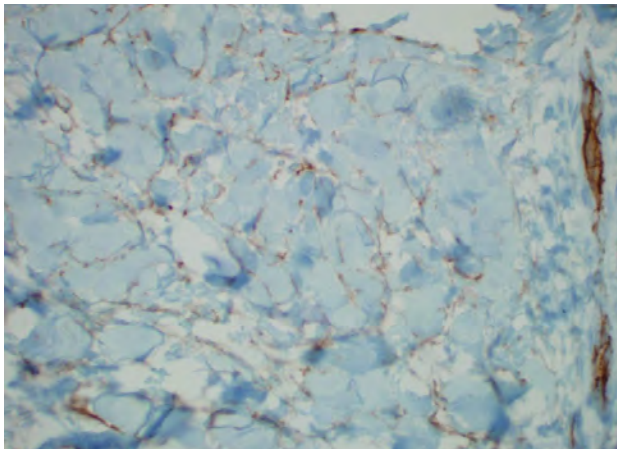

Figure 3. Histopathology demonstrated focal areas of $CD34^+$ spindle-shaped cells in the periphery of the lesion (original magnification ×20).

tissue. The amount of gadolinium in the affected tissue of patients with NSF has been shown to be 35- to 150-fold higher than the level of retained gadolinium in the tissue of healthy individuals with normal renal function. Free gadolinium, particularly in its ionic form ($Gd3^+$), may cause a toxic reaction, leading to NSF.[5]

The diagnosis of NSF can be confirmed through histology. Cowper et al[6] described NSF as a proliferation of spindle-shaped cells and elastic fibers with thickened collagen bundles with surrounding clefts and mucin deposition. The majority of the spindle-shaped cells are $CD34^+$ dendritic fibroblasts that form a dense interconnecting network.[7] $CD68^+$ multinucleated cells occasionally are present. Procollagen type I is strongly expressed in both NSF and scleromyxedema.[7]

Effective treatment of NSF is limited. Clinical improvement has coincided with a reversal of renal disease in some cases.[8] Although immunosuppressive therapy appears to be of little benefit, case reports involving the use of prednisone, topical calcipotriene, plasmapheresis, UV light therapy, and intravenous immunoglobulin have shown some success.[8,9]

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