The spectrum of nephrocutaneous diseases and associations

Inflammatory and medication-related nephrocutaneous associations

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Learning objectives
After completing this learning activity, participants should be able to recognize the important relationship between the skin and the kidney with respect to pharmacology and understand and manage the complex relationship between the skin and kidneys with respect to systemic medications.

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There are a significant number of dermatoses associated with renal abnormalities and disease, and dermatologists need to be keenly aware of their presence in order to avoid overlooking important skin conditions with potentially devastating renal complications. This review discusses important nephrocutaneous disease associations and recommendations for the appropriate urgency of referral to nephrology colleagues for diagnosis, surveillance, and early management of potential renal sequelae. Part II of this 2-part continuing medical education article addresses inflammatory and medication-related nephrocutaneous associations. (J Am Acad Dermatol 2016;74:247-70.)

Key words: antihypertensive medication; autoimmune; dermatology; genetic; genodermatoses; immunosuppression; inflammatory; medication side effects; nephrocutaneous; nephrology; renal transplantation.

INFLAMMATORY CAUSES OF NEPHROCUTANEOUS DISEASE

In this first section of part II, we discuss the cutaneous and renal findings associated with numerous inflammatory dermatoses. Table I is a summary of the cutaneous and renal findings associated with the nephrocutaneous inflammatory syndromes with recommendations regarding appropriate referral to a nephrologist for work-up and management of potential renal complications. Clinical presentation of the patient should also be taken into consideration.

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Table I. Inflammatory nephrocutaneous diseases including associated cutaneous and renal manifestations and referral considerations

Disease	Cutaneous findings	Renal findings	Referral
Nephrogenic systemic fibrosis	Firm dermal plaques, cobblestone appearance, joint contractures, and skin induration	Renal failure (causative) with subsequent administration of gadolinium contrast	Potentially urgent
Henoch-Schönlein purpura	Palpable purpura and petechiae	Immunoglobulin A nephropathy, vasculitis, nephrotic syndrome, and end-stage renal disease	As clinically indicated
Granulomatosis with polyangiitis and microscopic polyangiitis	Palpable purpura, ulceration, tender nodules, and focal necrosis	Focal and segmental, necrotizing and crescentic, or pauciimmune glomerulonephritis and vasculitis	Potentially urgent
Polyarteritis nodosa	Purpura, livedoid lesions, subcutaneous nodules, and necrotic ulcers	Renal arterial hypertension, renal microaneurysms, and renal infarction	Potentially urgent
Systemic lupus erythematosus	"Butterfly" rash, photosensitivity, discoid plaques, alopecia, and oral or nasal ulcers	Immune complex–mediated glomerulonephritis and end-stage renal disease	As clinically indicated
Cryoglobulinemia	Purpura, acrocyanosis, ulcerations, necrosis, and livedo reticularis	Thrombotic vasculopathy and glomerulonephritis	Potentially urgent
Sarcoidosis	Dermal papules/plaques, nodules, ulcers, erythema nodosum, hypomelanotic patches, erythroderma, and ichthyosiform lesions	Granulomatous nephritis, nephrolithiasis, and renal failure	As clinically indicated
Systemic sclerosis	Raynaud phenomenon, sclerodactyly, scleroderma, "salt and pepper" pigmentation, and ventral pterygium	Hypertension, scleroderma, and renal crisis with acute renal failure	Potentially urgent

Nephrogenic systemic fibrosis

Clinical manifestations. Nephrogenic systemic fibrosis (NSF) is a recently identified fibrosing disorder that occurs in patients with severe kidney failure, either chronic or acute, the vast majority of whom have been exposed to gadolinium-based contrast agents.[1] The pathophysiology of this condition involves tissue deposition of gadolinium, which results in a marked expansion and fibrosis of the dermis in association with $CD34^+$ and procollagen 1^+ fibrocytes.[2] All patients appear to have skin involvement, which may include bilateral and symmetrical patterned plaques in the skin, cobblestone appearance of the skin, joint contractures, and marked induration/peau d'orange of the skin.[3] Affected individuals may also develop erythematous to purple-brown superficial patches with an irregular advancing edge or discrete dermal papules (Fig 1). Yellow scleral plaques may also be present in this patient population. The disease often involves deeper structures, such as muscle, fascia, the lungs, and the heart.

Diagnosis. The diagnosis of NSF is based on histopathologic examination of a biopsy specimen obtained from an involved site. There are no laboratory tests or imaging studies specific for this disease. Affected patients often have elevations in serum C-reactive protein, serum ferritin, and erythrocyte sedimentation rate.[4] The histologic findings of NSF include increased spindled and epithelioid cells, $CD34^+$ spindled or epithelioid cells with dendritic processes on either side of elastic fibers (so-called "tram-tracking"), and the presence of fine and ropey collagen surrounded by clefts.[3]

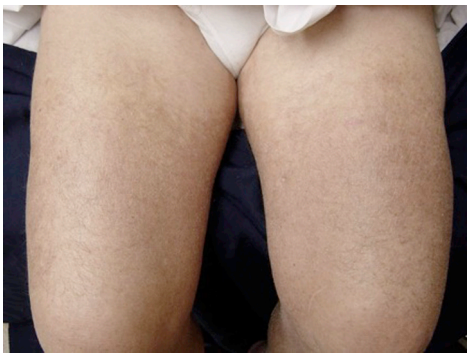

Fig 1. Nephrogenic systemic fibrosis. Note the induration, thickening, and hardening of the lower extremities with hyperpigmentation.

Therapy. NSF has a chronic and unremitting course in most patients, with a high mortality rate.[4]