

Kidney Disease and the Skin:

The What, Why and How

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Objectives

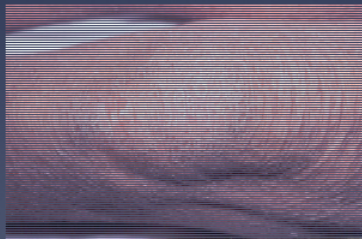
- * After today's session, you will be able to:
 - * - Identify the most common skin conditions seen in patients with chronic kidney disease.
 - * - Describe the basic pathophysiology behind why these conditions occur.
 - * - Implement evidence-based treatments for the most common skin conditions seen in renal patients.

What

- * Xerosis
- * Pruritis
- * Lindsay's Nails
- * Calcinosis Cutis
- * Calciphylaxis
- * Nephrogenic Systemic Fibrosis
- * Acquired Perforating Dermatoses
- * Non-melanoma Skin Cancer
- * Access Site Infection

What: Xerosis

- * Extensor surfaces of forearms, legs and thighs
- * Most common skin condition in chronic kidney disease (CKD) patients



What: Xerosis

- * 50 – 85% dialysis patients
- * 40 – 80% in pre-dialysis patients
- * Common even at the early stages of CKD, and becomes increasingly more likely as kidney function declines

Why: Xerosis

- * Dryness caused by dermal changes associated with uremia
- * Atrophy of sweat glands with impaired sweat secretion, disturbed stratum corneum hydration, sebaceous and eccrine gland atrophy, and abnormal terminal branching of free cutaneous nerve fiber endings
- * Diuretics

How to treat: Xerosis

- * Behavioral changes:
 - * Cooler water
 - * Less frequent bathing
 - * Dove for Sensitive Skin bar soap
 - * Moisturizing (petroleum based)



What: Pruritis

- * Extremely frustrating for patients and providers
- * More commonly seen along with xerosis
- * Can lead other conditions caused by pruritis such as: prurigo nodularis, lichen simplex chronicus, and perforating dermatoses



Why: Pruritis

- * 2 Main Hypotheses:

- * 1. Opioid hypotheses

- * Over expression of opioid receptors
 - * Can be prevented by κ opioid receptor stimulation
 - * Supported by successful treatment of some patients with opioid antagonists

Why: Pruritis

- * 2 Main Hypotheses:

- * 2. Immune Hypothesis

- * Manifestation of systemic state of inflammation
 - * High levels of c-reactive protein and interleukin-6



Why: Pruritis

- * Other:
 - * Calcium-phosphorus product which determines calcium phosphate precipitation in the skin also has an important role in pruritus.
 - * Drug side effects (angiotensin converting enzyme [ACE] inhibitors)
 - * Some kinds of dialysis membrane could be other causes of pruritus.

How to treat: Pruritis

- * Based on opioid theory, the use of the opioid antagonist naltraxone has been shown to give short term relief
- * Phototherapy with UVB has been shown to benefit patients on dialysis by suppressing histamine release and Vitamin A levels in the dermis
- * Higher dialysis quality, administration of erythropoietin, and optimal nutritional state all play a role in alleviating pruritus in renal patients
- * Definitive cure: Kidney transplant

What: Lindsay's Nails

- * Also known as "half n' half" nails
- * Discoloration of nail with proximal white portion and distal reddish-pink to brown portion
- * Does not grow out with nail or blanch with pressure



Why: Lindsay's Nails

- * Exact mechanism not understood, but an increase in the number of capillaries and capillary wall thickness in the nail bed has been observed
- * Can be found at any level of azotemia



How to Treat: Lindsay's Nails

- * Does not improve with dialysis
- * Does sometimes improve (and even disappear) with kidney transplantation



What: Calcinosis Cutis

- * Deposition of calcium salts into the skin and subcutaneous tissue, and is commonly seen in CKD
- * Occurs in about 1% of patients with ESRD on maintenance dialysis, annually
- * Yellow white adamant tumors characterized by papules, plaques, and nodules of different sizes within the skin
- * The most commonly involved sites are peri-articular areas and finger tips



What: Calcinosis Cutis

- * Lesions between joints are typically painless unless they affect joint movement
- * Fingertip lesions are usually painful
- * A white chalky substance can sometimes be expressed through the skin from the lesions



Why: Calcinosis Cutis

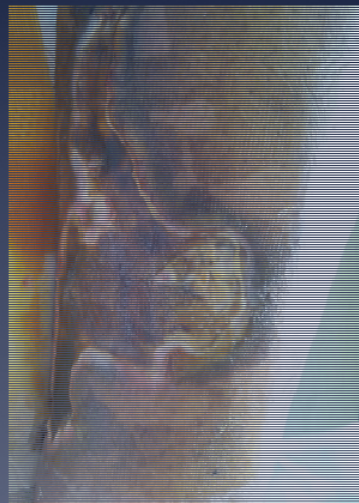
- * Secondary hyperparathyroidism, which results from hyperphosphatemia (decreased excretion of phosphorus) and hypocalcaemia (decreased intestinal absorption due to impaired synthesis of active forms of vitamin D)
- * Mobilization of calcium and phosphorus from bone into serum, causing elevated levels of both calcium and phosphorus
- * Accumulate in skin to form lesions

How to treat: Calcinosis Cutis

- * Normalization of calcium and phosphorus levels leads to regression of lesions
- * Phosphate binders and reducing dietary phosphate
- * Foods to limit: Dairy products, certain vegetables such as (broccoli and Brussels sprouts), oysters, salmon, beer, nuts, and wheat germ
- * Surgical parathyroidectomy

What: Calciphylaxis

- * Calcific uremic arteriopathy
- * Rare and often life-threatening occurrence in patients with end stage renal disease (ESRD)



What: Calciphylaxis

- * More common in dialysis patients, both hemodialysis and peritoneal dialysis
- * Reported incidence rate is about 1% in patients with CKD and up to 4% in those on dialysis
- * Kidney transplant recipients
- * Risk factors: female sex, Caucasian race, obesity, diabetes mellitus, malnutrition (low serum albumin levels), and warfarin therapy
- * Vitamin D analogs, calcium containing phosphate binders, iron-replacement therapy, and glucocorticosteroids

What: Calciphylaxis

- * Patients initially develop superficial violaceous skin lesions that are painful, hyperesthetic, or pruritic and surrounded by pallor or ecchymosis
- * Over a period of days or weeks, transforms into frank necrosis with eschar formation
- * Gangrenous infection may thereafter develop at the site



What: Calciphylaxis

- * Most common sites: Areas of thick adipose tissue such as breast, abdomen, thighs
- * Less common: Tongue, eye, penis; heart, lungs, pancreas
- * Proximal areas of necrosis (thighs, buttocks, and trunk) have an unfavorable prognosis: Mortality rate 60% to 80%
- * Distal and acral distribution (calves, forearms, fingers, toes, and penis): Mortality rate 20% - 30%

Why: Calciphylaxis

- * Multifactorial
- * Elevated serum phosphorus and decreased serum calcium levels
- * Vascular calcification and fibrosis
 - * Extravascular lesion: Ischemic necrosis with or without hemorrhage, which leads to cutaneous lesion
 - * Pain, sepsis, death

How to treat: Calciphylaxis

- * Supportive
- * Primary treatment: Controlling calcium and phosphate levels, which involves using noncalcium-based phosphate binders, increasing the frequency of dialysis (with low calcium dialysate), proper use of vitamin D analogs, and limiting the phosphate intake (43 mg/d)
- * Meticulous wound care, frequent debridement of necrotic tissue, systemic antibiotics to prevent and control infection, and adequate pain management
- * Elevated parathyroid hormone levels: Emergent parathyroidectomy indicated, which has shown survival advantage due to complete healing of ulcers within weeks after procedure

What: Nephrogenic Systemic Fibrosis (NSF)

- * Found uniquely in renal failure
- * Exposure to gadolinium contrast-enhanced MRI or MRA 2-3 months prior to symptom onset
- * Visible fibrosis of the skin consisting of hardened, thickened, tethered, hyperpigmented and/or shiny changes
- * Burning and itching
- * Occurrence across joints leads to flexion contractures and immobility
- * Most frequently in the feet, ankles, shins, thighs, fingers, hands, and lower arms

What: NSF

- * Rare: Risk of NSF in a patient with any gadolinium agent exposure reported to range 1.13-3.4%



Why: NSF

- * Related to increased collagen deposition, with fibrosis occurring in multiple organ systems, including the lungs, heart, and liver



How to Treat: NSF

- * Prevention**
- * No completely effective treatment
- * Topical or systemic corticosteroids, cyclophosphamide, thalidomide, plasmapheresis, immunoglobulin infusion, imatinib mesylate, and rapamycin may offer some improvement
- * Gadolinium agents only when absolutely necessary in ESRD patients

How to Treat: NSF

- * Determine patient kidney function prior to ordering test
- * Avoid in patients with acute or chronic kidney failure with a glomerular filtration rate of less than 30 mL/min
- * Gadolinium agents only when absolutely necessary in ESRD patients
- * Correct kidney acute kidney failure, and transplantation in chronic kidney failure

What: Acquired Perforating Dermatoses (APD)

- * Group of disorders with transepidermal elimination of collagen, elastic tissue, or necrotic connective tissue acquired in adulthood
- * Subset of APD, acquired perforating dermatosis of hemodialysis is characterized by hyperkeratotic papular lesions

What: Acquired Perforating Dermatoses (APD)

- * Occurs predominantly on trunk and extensor limb surfaces
- * Significantly more prevalent in diabetics



What: APD

- * Incidence in North America ranges between 4.5-10% of patients receiving chronic hemodialysis
- * Also in ESRD, in transplant recipients, and CKD patients not yet on dialysis



Why: APD

- * Exact pathophysiological mechanism for APD in ESRD is unknown, it is thought to be the result of dermal connective tissue dysplasia and decay
- * Local trauma and necrosis of the skin may be secondary to trauma induced by frequent scratching by patients with pruritus from CKD

How to Treat: APD

- * Lesions may resolve spontaneously
- * Topical retinoids, topical and intradermal steroids, and UVB light have been tried with variable results
- * Cryotherapy and keratolytics have been tried with variable success

What: Non-melanoma Skin Cancer (NMSC)

- * Squamous Cell Carcinoma (SCC) and Basal Cell Carcinoma (BCC)
- * Occurs at an incidence of 10% to 45% at 10 years post-transplantation (immunosuppression)
- * SCC is typically more aggressive, recurrent, and metastatic than BCC, and more aggressive in organ transplant recipient population

What: NMSC

- * Risk factors for NMSC's in renal transplant patients include dosage and duration of immunosuppression, older age (>55 years), male sex, white skin, history of skin cancer prior to transplantation, and lower peak panel reactive antibody (PRA) level



Why: NMSC

- * Immunosuppression: Anti-metabolites, high-dose corticosteroids, calcineurin inhibitors, and mammalian target of rapamycin (mTOR)
- * Sun-damage and other risk factors



How to Treat: NMSC

- * Excision for removal
- * Removal of NMSC located anywhere from the neck up requires Mohs surgery
- * Recurrent NMSC on other parts of body also require Mohs surgery
- * Full-body skin examination can help to identify these lesions early
- * Education for patients so they can perform skin checks at home and know how to identify suspicious lesions

How to Treat: NMSC

- * Alter immunosuppressive therapy in kidney transplant patients
- * Education for the patient regarding lesions needing to be addressed
- * Baseline skin cancer risk evaluation post-transplant
- * Regular skin checks

What: Access Site Infection

- * Not seen outpatient very often
- * Second only to coronary artery disease as cause for mortality in ESRD population
- * Responsible for 48-73% of all bacteremias in hemodialysis patients

What: Access Site Infection

- * One study of hemodialysis patients with multiple access types found that hemodialysis catheters have the highest risk of infection > grafts > native vessel fistulas



Why: Access Site Infection

- * Patients with ESRD have compromised immune function
- * More susceptible to infection
- * Any change to the appearance of an access, such as a new lesion on the surface, induration, or inflammation, warrants a more extensive evaluation
- * Include blood cultures and complete blood count

How to Treat: Access Site Infection

- * PREVENTION
- * Policy and procedure adherence
- * Strict hand washing between patients and the use of clean gloves during needle cannulation.
- * Patients should be instructed to wash their access arms with soap and water prior to cannulation
- * Won't always have fever or elevated white blood cell count with infection

Pearls

- * Uremic Frost



Pearls

- * Keeping patients comfortable
- * Immunosuppression:
 - * Look out for any type of infection: viral, bacterial, fungal, and parasitic
 - * Viral: Herpes simplex 1, herpes zoster
 - * Bacterial: Abscess, infection at site of trophic ulcers
 - * Fungal: Tinea Cruris, tinea corporis, and candida
 - * Parasitic: Scabies

Conclusion

- * With improved dialysis techniques and organ transplant survival rates, life expectancy of CKD patients and organ transplant recipients has increased
- * Measures can be taken to prevent or ameliorate these adverse skin conditions
- * Emollients, sunscreen and sun avoidance measures, oral hygiene, proper nutrition and nutritional supplementation to improve vascular health, and prompt recognition of infections

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