Skinternal Medicine: Cutaneous Manifestations of Systemic Disease

Vinod E. Nambudiri MD MBA | October 30, 2016

Conflicts of Interest/Disclosures

- No disclosures relevant to this talk.
- Other Disclosures
  - McGraw Hill: Textbook Authoring Royalties
  - Member of SC ACP Planning Committee

PLEASE NOTE:

DUE THE PRESENCE OF PATIENT IMAGES IN THIS TALK,

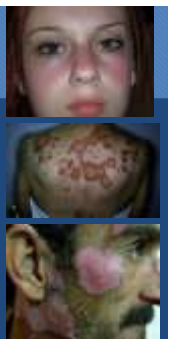
AN ABBREVIATED CONTENT VERSION IS BEING UPLOADED ONLINE.

Clinical Images

Fabry Disease

- Lysosomal storage disease
- Accumulation of abnormal products of cell degradation
  - Alpha-galactosidase A deficiency
- XLR
- **Kidney**: Proteinuria, renal failure due to accumulation of ceramide trihexoside
- Systemic associations
  - Neuro: Acral pain and paresthesias
  - Skin: Hypohidrosis
  - Eye: Corneal and lenticular opacities
  - **CV:** Hypertrophic cardiomyopathy, coronary artery disease, CVAs

Systemic Lupus Erythematosus



- Skin Manifestations
  - Acute Cutaneous Lupus: malar rash
  - Subacute Cutaneous Lupus: polycyclic, photodistributed
  - Chronic Cutaneous Lupus: discoid lesions, scarring lesions
- Other Cutaneous findings
  - Oral ulcerations
  - Alopecia
- Systemic findings: ACR / EULAR criteria
- Neonatal Lupus
- Kidney: Lupus Nephritis

Scleroderma

- Collection of diseases with all feature areas of skin tightening and decreased skin motion
- May be localized or systemic
  - May be limited (CREST) or diffuse
- Clue: pruritus
- Systemic organ involvement
  - GI Tract: Esophagus, oropharynx
  - Joints: mobility decrease
  - Heart
  - Lungs
- Kidney Involvement

Henoch Schoenlein Purpura: Classic

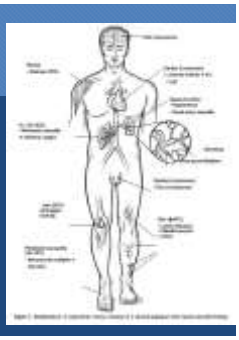
AT LEAST TWO OF THE FOLLOWING:	
Palpable purpura;	
Age ≤ 20 years at disease onset;	
Abdominal pain or gastrointestinal bleeding;	
Vessel wall granulocytes on biopsy	
Diagnostic Criteria	**Description**
Purpura (mandatory)	Purpura or petechiae with lower limb predominance
PLUS ONE OF THE FOLLOWING:	
Abdominal pain	Diffuse and colicky
Histopathology	Leucocytoclastic vasculitis or proliferative glomerulonephritis with predominant IgA deposit.
Arthritis or arthralgia	Acute onset joint pain or swelling
Renal involvement	Proteinuria or haematuria

Polyarteritis Nodosa

- Inflammation and necrosis of medium-sized and small muscular artery walls.
- The inflammatory infiltrates consist of neutrophils and mononuclear cells that invade the vessel wall.
- Peak age: 40 - 60 years.
- Up to 50% of cases occur in the setting of recently acquired hepatitis B virus infection, a more prevalent association in younger patients presenting with polyarteritis nodosa.
- Presentation:
  - Fever, arthralgia, myalgia, abdominal pain, and weight loss.
  - Most patients have peripheral nerve manifestations, most commonly mononeuropathy or mononeuritis multiplex.

PAN: Renal Involvement

- Up to one third of patients
- Renal arteriolar involvement
- Renovascular hypertension without glomerulonephritis



Granulomatosis w/ Polyangiitis (WG)

- Granulomatosis with polyangiitis is a systemic necrotizing vasculitis that predominantly affects the upper and lower respiratory tract and kidneys.
- More than 70% of patients have upper airway manifestations such as sinusitis or nasal, inner ear, or laryngotracheal inflammation.
- The disease is highly destructive if untreated, potentially resulting in cartilage erosion with nasal septal perforation and saddle nose deformity.
- Ocular involvement includes scleritis, uveitis, keratitis, and inflammatory retro-orbital pseudotumor with extraocular muscle dysfunction and proptosis. Purpura and ulcers are common skin manifestations. Mononeuritis multiplex may also occur.
- Characteristic radiographic findings include multifocal infiltrates or nodules, some of which may cavitate; diffuse opacities are seen in patients with pulmonary hemorrhage

Sarcoidosis

- Approximately 25% to 30% of patients with sarcoidosis have cutaneous involvement.
- Sarcoidosis has been called "the great imitator," and a multitude of sarcoidosis-related skin lesions have been described.
- Classic cutaneous sarcoidosis appears as violaceous papules or infiltrative plaques; this is in contrast to other inflammatory lesions that occur in this distribution, such as the violaceous erythema of dermatomyositis or the malar rash of lupus, which are flat areas of inflammation without a palpable component.
- Sarcoidal granulomatous lesions show a predilection for sites of trauma, including surgical scars or tattoos.

Renal Disease in Sarcoidosis

- Renal manifestations include
  - Abnormal calcium metabolism – Hypercalciuria, hypercalcemia
  - Nephrolithiasis and nephrocalcinosis
  - Elevated ACE levels
  - Acute interstitial nephritis with or without granuloma formation

Pruritus

- Patients with chronic kidney disease often develop intense, refractory, unremitting pruritus, and patients with end-stage kidney disease (ESKD) frequently have intensely dry, xerotic skin.
- Management includes the use of over-the-counter thick, bland emollients, such as plain white petrolatum.
  - Warm -- not hot – showers
  - Best time to moisturize: right after bathing
  - Reapplication frequently
- Severe pruritus may require topical corticosteroids, or, in some persons, phototherapy.
- As a result of chronic pruritus and scratching, patients with ESKD may develop a variety of clinical lesions, including prurigo nodules (hyperpigmented, hyperkeratotic papules and nodules resulting from chronic, repetitive scratching); lichen simplex chronicus (thickened, chronic eczematous hyperpigmented and scaly patches); and in some cases the perforating papules of Kyrle disease (hyperpigmented, umbilicated papules with a central keratinaceous core).

Calciphylaxis

- Calciphylaxis is caused by metastatic calcification within the lumen of arterial vessels.
- It usually occurs in states of extremely dysfunctional calcium and phosphorus balance seen in patients with ESKD. This dysfunctional metabolic process leads to impaired circulation, ischemia, and necrosis of the skin.
- Calciphylaxis is rare; it affects fewer than 5% of patients with ESKD. Its presence confers a high risk for mortality, with 60% to 80% of patients dying within 6 months of diagnosis, frequently from sepsis, which is often secondary to bacterial colonization with invasion of the necrotic skin lesions.
- Lesions of calciphylaxis are typically intensely painful, angulated, lacy or netlike retiform purpuric patches with areas of central dusky or black necrotic tissue that may form bullae, ulcerate, and leave a hard, firm eschar.
- Although calciphylaxis can affect any blood vessel, patients usually present with lesions on the lower extremities. More proximal lesions may be a sign of more severe vascular injury, as the proximal location suggests that larger vessels are involved, and these patients have a worse prognosis.
- Management sodium thiosulfate. Meticulous wound care. Limited debridement. Cinacalcet. Parathyroidectomy.

Nephrogenic Systemic Fibrosis

- AKA nephrogenic fibrosing dermopathy
- Patients present with distal extremity skin thickening, fibrosis, and limited mobility.
- Pain → distal edema that rapidly becomes fixed and indurated, giving the limbs a woody feel.
- Erythematous plaques and nodules are commonly seen in the early stages of disease. Although the diagnosis may be suspected in the appropriate clinical context, histopathologic evaluation of a skin biopsy specimen remains the gold standard diagnostic test. Skin biopsy is generally a low-risk procedure; however, patients with NSF often have peripheral vascular disease, and as these lesions are firm and indurated, closure of the biopsy site and healing of the wound may be challenging.
- NSF is gradually progressive. Although there are case reports suggesting some benefit with various therapeutic modalities, including phototherapy, photopheresis, and antifibrotic agents, kidney transplantation seems to be the most effective treatment.
- Epidemiologic studies suggest that gadolinium-based MRI contrast agents play a key role in inciting this disease, although the limited numbers of patients with NSF (approximately 300 to date) compared with the numbers of contrast-enhanced MRI studies performed in patients with ESKD suggest that there may be other important causative factors of NSF.

Skin Cancer following Renal Transplant

- Patients who undergo solid organ transplantation are at increased risk for the development of cutaneous malignancies, particularly nonmelanoma skin cancer.
- In the general population, basal cell carcinoma is more common than squamous cell carcinoma; in kidney transplant recipients, this ratio is reversed, with transplant recipients up to 30 times more likely to develop squamous cell carcinoma than healthy hosts.
  - This may result from the types of immunosuppressive drugs used to prevent organ rejection (with OKT-3 and tacrolimus conferring an increased risk and rapamycin potentially affording a mild protective effect) and partially to the presence of human papillomavirus, an oncogenic virus identified in high frequencies in samples of squamous cell carcinoma taken from kidney transplant recipients.
- Patients who receive organ transplants should be evaluated by a dermatologist annually to check for skin cancer.

Summary

- Cutaneous manifestations of renal disease: many!
- Be especially on the lookout in patients with known ESRD as well as post-renal transplant

Thank You!

vinod.nambudiri@hcahealthcare.com