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Review article

Dermatological problems in CKD; ocular manifestations in CKD

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ABSTRACT

Chronic kidney disease is a leading cause of morbidity and mortality worldwide. Advances in last five decades have brought forth striding changes in understanding the etiopathogenesis of the various pertinent renal disorders as well as in their management strategies. However, with increasing prevalence of diabetes and its varied complications, hypertension, infections, drug induced nephropathies, obstructive uropathies etc, chronic kidney disease is still a major health concern in our country. Skin being the largest organ of the body and eye being the window to the surroundings, their related problems assume significance. Their evaluation pertains to thorough clinical examination skills and the ease to which they can be accessed, give an opportunity for prompt diagnosis and treatment. Skin related problems like pruritus, xerosis, etc are frequent and need early intervention to reduce patient's morbidity. Ocular manifestations need a keen eye to detect the illness and an interdisciplinary approach to aggressively treat the underlying conditions in chronic kidney disease.

1. Introduction

Skin being the largest organ in the body is in no way spared of the protean manifestations of chronic kidney disease. Skin and its appendages including hair, nails incorporate various signs and symptoms which are critical part of patient's complaints and their physical examination respectively as the spectrum of chronic kidney disease evolves. Skin related disorders entail excessive morbidities and must be recognized early and treated promptly. This review deals with various dermatological manifestations in a patient with chronic kidney disease.

2. General skin appearance

General physical survey reveals pallor with dry and coarse texture of skin. Anemia, a ubiquitous entity in this disease, imparts pale appearance to skin. Retention of urochrome and carotene imparts yellowish hue due to its deposition in epidermis and subcutaneous tissues. Failure to effectively metabolize melanocyte stimulating hormone and its raised levels leads to increased melanin concentration which causes increased pigmentation on sun exposed areas of skin.[1] Grayish discoloration of skin could be caused by hemosiderin deposition commonly seen due to multiple blood transfusions received in this patient population. Uremic frost is the presence of yellowish-white powdery deposits on the skin of face, neck, trunk region which is attributed to significantly raised levels of urea in blood (>250–300 mg/dl) for a long duration and no treatment for kidney disease is taken. This entity is nowadays not frequently seen clinically due to early treatment sought by patients when symptomatic.[2,3]

Oral mucosal changes are frequently seen in CKD patients. Teeth markings with swollen tongue (tongue sign of uremia)

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are frequently seen in advanced renal failure. Oral ulcers, chelitis, loss of papillae on tongue are also manifested in these patients.[1]

Premature senescent features of the skin may be appreciated due to loss of subcutaneous fat, deranged collagen network with resultant wrinkling of skin and loss of hair follicles. Shiny skin is seen in hypoalbuminemic patients with associated edema secondary to incessant proteinuria as a sequelae to nephrotic/subnephrotic states and malnutrition commonly seen in advanced kidney disease and during dialysis therapy. The skin may appear cracked and may show mosaic pattern.

Xerosis or dry skin is seen frequently due to decreased sebaceous and sweat secretions causing coarse and dry texture of skin. It may or may not be associated with pruritus. The distribution is mainly over the extensor surfaces of the lower extremities. Decreased sweat and sebaceous secretions lead to diminished hydration status of stratum corneum with associated abnormal arborization of free, cutaneous type C fibers. Adequate hydration of skin with application of emollients helps in maintaining the film of moisture trapped within it.[4]

Nails in chronic kidney disease may show white proximal two third regions with dark or normal colored distal region which is due to increased capillary density of the nail bed (Lindsay's nails or half and half nail sign). It is observed in 20% of CKD patients and finger nails are more commonly involved than toe nails. The other frequent nail changes seen are koilnychia – seen with iron deficiency anemia, splinter hemorrhages, onycholysis, onychomycosis, Mee's lines – single transverse white strips, Muehrcke's lines – double white transverse subungual bands in uremic patients. Venous hypertension secondary to arteriovenous fistula can lead to pincer deformity in the nails while triangular lunulae are seen in patients with nail patella syndrome.[5]

Hair abnormalities in chronic kidney disease include dry lusterless hairs with sparse distribution. Alopecia may be sparse or diffuse and seen especially in the period prior to or after dialysis therapy initiation.[2]

2.1. *Pruritus*

It is a common clinical symptom in patients with stage IV and in stage V CKD patients on dialysis. It is defined as three or more episodes of itch in 2 weeks period or regular itching over 6 months period which could be localized or generalized.[6] Pruritus as a sensation is a primary event and skin changes like excoriation, Koebner's phenomenon are resultant skin manifestations. Uremia associated pruritus is commonly associated with xerosis. Other pertinent factors which may contribute to pruritus include hyperparathyroidism and anemia. Hypercalcemia, coexistent hypothyroidism, cholestasis, drug induced hypersensitivity should be excluded in these patients. Factors which aggravate pruritus include dry skin, sweating, external heat, stress and are more severe at night. The risk factors are male gender, elevated blood urea, underdialysis, more common with hemodialysis than peritoneal dialysis, elevated beta-2 micro globulin levels, increased levels of calcium, phosphorous, aluminum, magnesium.[7–9] It has been shown that adequate dialysis and a good nutritional status reduced the prevalence of pruritus. Increased pruritus leads to poor quality of life and may even lead to poor outcome in chronic hemodialysis patients. Other effects include generalized excoriations with secondary superimposed infections, lichenification of skin and prurigo nodularis[8,9] (Fig. 1).

The pathogenesis is complex and involves uremic and nonuremic factors. Opioid hypothesis includes opioid receptor dysregulation which leads to up regulation of μ receptors and down regulation of k receptors in dermal cells and lymphocytes. Patients get relief on administration of k receptor agonist nalfurafine as well as naltrexone which confirm to opioid hypothesis. Immune hypothesis suggests pruritus as manifestation of inflammatory systemic disease with increase in T_H1 lymphocytes and interleukins (IL-2, IL-6), chemokines (CXCR3), CRP. Thalidomide and ultraviolet B therapy lead to immune modulation and show therapeutic benefit testify to immunological arm in the etiology of pruritus. Other factors which contribute to pruritus include

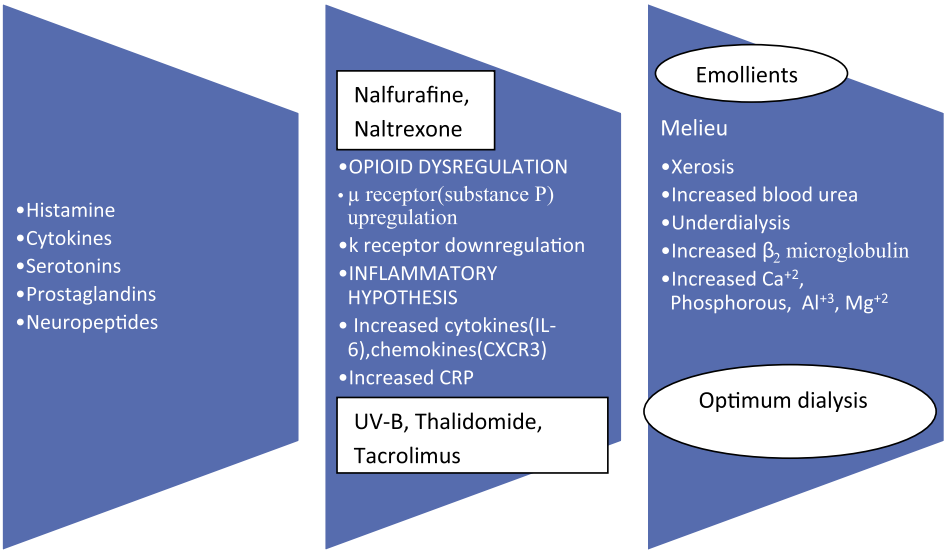

Fig. 1 – Pathogenesis and treatment options for uremic pruritus.