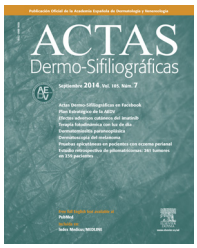
Actas Dermosifiliogr. 2015;106(8):609–622

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org



REVIEW

Skin manifestations of chronic kidney disease

J.C. Robles-Mendez, O. Vazquez-Martinez, J. Ocampo-Candiani*

Dermatology Department, University Hospital ''José Eleuterio González'', Autonomous University of Nuevo León, Monterrey, Mexico

Received 18 May 2015; accepted 21 May 2015
Available online 17 June 2015

KEYWORDS
Chronic kidney disease;
Nephrogenic systemic fibrosis;
Calciphylaxis;
Porphyria cutanea tarda

Abstract Skin manifestations associated with chronic kidney disease are very common. Most of these conditions present in the end stages and may affect the patient's quality of life. Knowledge of these entities can contribute to establishing an accurate diagnosis and prognosis. Severe renal pruritus is associated with increased mortality and a poor prognosis. Nail exploration can provide clues about albumin and urea levels. Nephrogenic systemic fibrosis is a preventable disease associated with gadolinium contrast. Comorbidities, such as diabetes mellitus and secondary hyperparathyroidism, can lead to acquired perforating dermatosis and calciphylaxis, respectively. Effective and innovative treatments are available for all of these conditions.

PALABRAS CLAVE
Enfermedad renal crónica;
Fibrosis sistémica nefrogénica;
Calcifilaxis;
Porfiria cutánea tarda

Manifestaciones Cutáneas de la Enfermedad Renal Crónica Skin manifestations of Chronic Kidney Disease

Resumen Las manifestaciones cutáneas asociadas a enfermedad renal crónica son muy comunes. La mayoría de estas enfermedades se presentan en la etapa terminal y pueden afectar la calidad de vida del paciente. El conocimiento de estas condiciones puede ser útil para establecer un diagnóstico y pronóstico preciso. El prurito renal severo está asociado a un incremento en la mortalidad y a un pobre pronóstico. La exploración ungueal puede proveer datos acerca del nivel plasmático de albumina y urea. La fibrosis sistémica nefrogénica es una enfermedad prevenible asociada a contrastes con gadolinio. Comorbilidades como la diabetes mellitus y el hiperparatiroidismo secundario, pueden causar dermatosis perforante adquirida y calcifilaxis, respectivamente. Existen tratamientos efectivos e innovadores para todos estos padecimientos.

* Corresponding author.
E-mail address: Jocampo2000@yahoo.com.mx (J. Ocampo-Candiani).

http://dx.doi.org/10.1016/j.ad.2015.05.007

Introduction

Patients with chronic kidney disease (CKD) commonly exhibit cutaneous manifestations associated with impaired renal function (Table 1). These skin lesions may affect their quality of life, and some conditions could even be life threatening. Knowledge of these lesions is important for an accurate diagnosis and prognosis. This review focuses mainly on classic specific disorders associated with CKD (Table 2), but other common nonspecific conditions are also discussed.

Although the pathogenesis is not clear in the majority of cases, effective and innovative treatments are available for these conditions (Table 3).

By definition, CKD comprises a structural renal injury (which may be evident in urine, blood, imaging studies or tissue biopsies) or a functional impairment (manifested as a decreased glomerular filtration rate of less than 60 ml/min/1.73 m^2) over a period of 3 months. Most skin manifestations of renal impairment occur in patients with end-stage CKD (stage 5) with a glomerular filtration rate less than 15 ml/min/1.73 m^2.[1,2]

Renal pruritus

Renal pruritus is observed in 50–90% of patients with end-stage CKD, primarily in individuals who have been on hemodialysis.[3] The severity rating scales typically used in renal pruritus include the visual analogue scale and the Yospovitch validated questionnaire.[4] Pruritus causes anxiety, depression and sleep disorders, and severe pruritus has been described as an independent risk factor for increased mortality and a poor prognosis.[5]

The cause of renal pruritus is multifactorial. Risk factors such as male sex and high levels of uraemic nitrogen, calcium, phosphorus, β2 microglobulin, magnesium, aluminium, vitamin A, histamine and mast cells, have been reported.[6,7]

Renal pruritus is considered to be a manifestation of a chronic inflammatory state, which involves cytokines such as TNF, IFN-γ, and IL2 and acute phase reactants such as C-reactive protein. Pruritus is transmitted by C fibres. Opioids stimulate C fibres through μ receptors and inhibit C fibres through κ receptors. C fibre stimulation via serotonin, histamine and prostaglandins might also play an important role. Abnormal innervation patterns, nerve damage and central sensitisation are additional proposed mechanisms. A genetic predisposition particularly associated with HLA B35 has been described.[6,7]

Clinical manifestations include localised or generalised pruritus, with the back being the most commonly affected site. Pruritus is often prolonged and severe and is exacerbated by heat, sweating and xerosis. Skin lesions, such as excoriations, lichen simplex, nodular prurigo and keratotic papules, may result from scratching (Fig. 1).[6,7]

In terms of treatment, the main objective is to relieve itching and improve the quality of life. Definitive treatment involves kidney transplantation. It is important to mention that antihistamines are not effective, and the majority of available treatments are only empirical and lack strong evidence.[6,7]

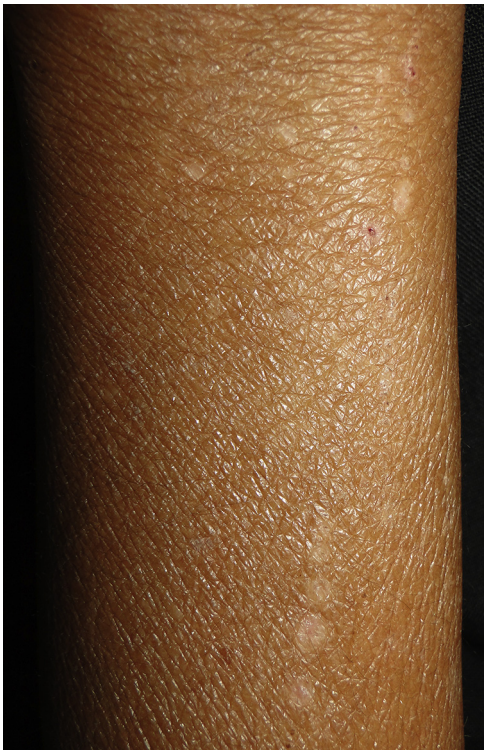


Figure 1 Xerotic skin with excoriations marks secondary to renal pruritus.

General treatment consists of improving the quality of haemodialysis, increasing efficiency Kt/V urea > 1.4 (Kt/V = dialysis adequacy. K, clearance. t, time. V, volume of distribution) using low calcium and magnesium dialysates, reducing calcium–phosphorus products and using more biocompatible membranes, such as those made of polymethylmethacrylate.[8]

Erythropoietin efficiently relieves itching by decreasing histamine levels. Its effect is not associated with haemoglobin levels and it is lost when administration is discontinued.[9] It is important to avoid xerosis, sweating and heat. Moisturisers constitute the first line of therapy, especially those containing gamma linoleic acid, glycerol and paraffin.[10] The addition of endocannabinoids to moisturisers has been proven effective.[11]

Topical treatment is preferred for localised pruritus. Studies have reported the efficacy of capsaicin and pramoxine. Capsaicin depletes P substance from C fibres, thus blocking pain and pruritus transmission; it is used as 0.025% cream four times daily.[12] Pramoxine lotion, a topical anaesthetic, used twice daily for 1 month has been proven effective.[13] The use of calcineurin inhibitors is controversial and is not recommended.[14,15]

Systemic treatment with gabapentin, a GABA agonist, is effective and safe. Due to its renal clearance, gabapentin is administered at low doses of 300 mg after each haemodialysis session.[16–18] The serotonin inhibitor 5 HT3 granisetron (1 mg twice daily for 1 month) is also effective.[19,20] The opioid agonist nalfurafine has proven to be effective.[21] Phototherapy with narrowband UVB has been used to decrease the production of cytokines by lymphocytes and to reduce phosphorus levels in the skin.[22] Among surgical treatments,