DOI: http://dx.doi.org/10.3315/jdcr.2014.1182

Journal of Dermatological Case Reports

Cutaneous abnormalities in patients with end stage renal failure on chronic hemodialysis. A study of 458 patients.

Abderrahmen Masmoudi[1], *Mounira Hajjaji Darouiche*[1], *Haifa Ben Salah*[1], *Mohamed Ben Hmida*[2], *Hamida Turki*[1]

1. Department of Dermatology, Hedi Chaker Hospital, Sfax, Tunisia;
2. Department of Nephrology, Hedi Chaker Hospital, Sfax, Tunisia.

Corresponding author:

Dr. Mounira Hajjaji Darouiche

Department of Dermatology, Hedi Chaker Hospital

3029 Sfax, Tunisia

E-mail: *m.darouiche@hotmail.fr*

Key words:

adverse events, dry skin, hemodialysis, kidney, pruritis, xerosis

Abstract

Background: Cutaneous manifestations occurring in patients with end stage renal failure on hemodialysis are polymorphic and diverse.

Objective: The aim of our study was to assess the prevalence and characteristics of different cutaneous manifestations in patients on hemodialysis.

Patients and methods: We led a transverse investigation of all patients on hemodialysis in 12 haemodialysis centres of Sfax (Tunisia). We examined 458 patients (254 men and 204 women). The hemodialysis history ranged from 6 months to 24 years. A total of 394/458 (86%) patients had cutaneous abnormalities. These included pruritus (56.6% of patients), paleness (60.7%), xerosis (52.8%), hyperpigmentation or hypopigmentation (38.4%), venous dilation near the fistula (22.2%), eczema in the fistula area (14.8%), half-and-half nails (13.5%), onychodystrophy (6.1%), subungual hemorrhage (4.5%), leukonychia (4.5%), stomatitis (5.6%), xerostomia (3.2%), gingivitis (2.4%), uremic breath (2.1%), and skin calcificatins (0.4%). Nephrogenic fibrosing dermopathy was not detected in any of our patients.

Conclusion: Pruritus, paleness, dry skin as well as hyperpigmentation and hypopigmentation are the most frequent skin abnormalities observed in hemodialysis patients. The early recognition of some cutaneous conditions associated with end stage renal failure and hemodialysis may allow early therapeutic intervention and decrease morbidity. (*J Dermatol Case Rep*. 2014; 8(4): 86-94)

Introduction

End-stage renal disease (ESRD) is a common disease in our days. It is defined as progressive and irreversible kidney dysfunction that lasts longer than 3 months.[1] It has been found that 50-100% patients with ESRD have at least one associated cutaneous change.[2]

Cutaneous manifestations in renal failure are polymorphic and diverse. They may occur before or after initiation of dialysis and can be divided into two categories: specific events in cutaneous and other non-specific. Non-specific disorders include pigmentary disorders, pruritus, xerosis, acquired ichthyosis, and half-and-half nail. Specific disorders include acquired perforating dermatosis, calciphylaxis, bullous dermatoses, and fibrosing dermopathy of uremia.[1,3]

The aim of our study was to assess the prevalence and characteristics of different cutaneous manifestations in haemodialysis patients, discuss the pathogenesis of these skin lesions and the different therapies available.

We led transverse investigation concerning all hemodialysed patients in the 12 centres of dialysis of Sfax over a period of 1 month. Patients undergoing hemodialysis following a renal transplant failure, those who had undergone peritoneal dialysis, or those receiving less then three haemodialysis sessions per week were not included. Two patients refused to participate in the study. The study was performed by one investigator.

Patients and methods

The patients' age, sex, medications and present cutaneous illnesses were noted. We realized for each patient a peer review including: a careful history and the details about the onset

of skin lesions, the circumstances of their discoveries, triggering factors, their clinical characteristics and evolution. Then we completed a full clinical examination including a mucocutaneous examination. We reviewed the file record of each dialysis patient to be informed about initial kidney disease and the results of regular laboratory investigations: complete blood count, blood urea, phosphocalcic level and liver serology (HBV, HCV).

The data collected were analyzed using statistical software SPSS version 11. We used the chi-squared test (X^2) and the Fisher exact test (for small numbers) to compare the frequencies, the Student test (t) and the test of ANOVA for comparison of means to seek correlation between two variables. The difference was considered significant if p was less than or equal to 0.05 ($p \leq 0.05$).

Results

Patients' characteristics

The 458 patients were divided into 254 men and 204 women with a sex ratio of 1.2. Their average age was 61 years with extremes of 15 and 85 years. The cause of renal failure was known in 284 cases. The main cause was diabetic nephropathy found in 13.6% of cases (Table 1).

The vintage of haemodialysis ranged from 6 months to 24 years with an average of 6.7 years. Other chronic disease associated was found in 118 patients (25.7%) such as diabetes in 59 cases (12.8%), high blood pressure in 43 patients (9.3%), coronary insufficiency in 16 patients (3.4%), heart failure in 11 patients (2.4%), systemic lupus erythematosus

Table 1. Patient characteristics. Initial causes of nephropathy.

Probable cause of nephropathy	No of patients	Percentage
Diabetic nephropathy	64	13,60%
Chronic interstitial nephropathy	60	12,70%
Chronic glomerular nephropathy	33	7,00%
Polycystic kidney disease	29	6,20%
Nephrolithiasis	14	3,00%
Focal segmental hyalinosis	14	3,00%
Hypertension	13	2,70%
Congenital nephropathy	11	2,30%
Alport Syndrome	7	1.4%
Lupus nephritis	6	1.2%
Glomerulonephritis membranoproliferative	5	1,00%
Renal amyloidosis	4	0.8%
Bilateral nephrectomy for renal tumor	3	0.6%
Toxemia	3	0.6%
Ischemic nephropathy	2	0.4%
Extra membraneous glomerulonephritis	2	0.4%
Vascular nephropathy	2	0.4%
Prostatic adenoma	2	0.4%
Nephroangiosclerosis	2	0.4%
Reflux nephropathy	1	0.2%
Chronic kidney disease IgA	1	0.2%
Rheumatoid purpura	1	0.2%
Sarcoidosis	1	0.2%
Bilharzia	1	0.2%
Primary oxalosis	1	0.2%
Indeterminate	176	38,40%
Total	**458**	**100,00%**

in 6 patients (1.3%), peptic ulcer in 3 patients (0.6%), hypothyroidism in 2 patients (0.4%), a Kaposi's sarcoma in one patient (0.2%), prurigo in one patient (0.2%), Crohn's disease in a patient (0.2%), a schistosomiasis in one patient (0.2%) and polycystic ovary syndrome in one patient (0.2%).

Eighty six percent of patients had cutaneous manifestations related to their chronic renal failure or dialysis.

Uremic pruritus

Uremic pruritus was reported by 259 patients (56. 6%). Their average age was 62.3 years with male sex predominance (sex ratio 1.59). The correlation was not significant between the occurrence of pruritus and the age of patients ($t = 2.2$) whereas it was significant between the frequency of pruritus and male sex ($p = 0.047$).

Pruritus appeared before the beginning of dialysis in 33 patients (12.7%), during the first year of dialysis in 14 patients (5.4%), during the second year in 104 patients (40.2%) and after the second year in 114 patients (44%).

We did not find significant correlation between the occurrence of pruritus and the number of years of dialysis ($t = 0.7$). However, a significant correlation with chronic glomerular nephropathy has been established ($p = 0.028$).

In 53 cases (20.5%), pruritus was localized. It was localised in order of decreasing frequency in the back (22 cases), lower limbs (15 cases), upper limb (10 cases), facial (4 cases) and scalp (2 cases).

Rich phosphorus diet was found in 27 patients (10.4%). The correlation was significant between the presence of uremic pruritus and hyperphosphataemia ($p = 0.043$). It was not significantly associated with hypercalcemia ($p = 0.097$) and also between the presence of uremic pruritus and an elevation of phospho-calcium product ($p = 0.035$).

Twenty-one patients (35.6%) reported the exacerbation of uremic pruritus during dialysis, while 49 patients (18.9%) reported an improvement in pruritus during dialysis. One of our patients had an exacerbation of the pruritus outside the dialysis sessions. He took refuge to escape his sexual impotence.

Pruritus was continuous in 110 patients (42.5%), nocturnal increasing in 111 patients (42.8%) and diurnal increasing in 38 patients (14.7%).

Cutaneous signs accompanying found in patients with uremic pruritus were linear streaks in 142 patients (54.8%), skin xerosis in 165 patients (63.7%), lichenification in 11 patients (4.2%), keratosis pilaris in 17 patients (6.6%) and eczema in 3 haemodialysis patients (1.1%). The pruritus was well tolerated in 202 patients (78%).

Treatment was prescribed in 155 cases such as antihistamines in 111 cases (71.6%), emollient preparation in 27 cases (17.4%), parathyroidectomy for secondary hyperparathyroidism in 9 cases (5.8%) and phototherapy UVB in 8 cases (5.1%).

An improvement in uremic pruritus after treatment by antihistamines was observed in 27 cases, by phototherapy in 3 cases, by demulcent preparation in 3 cases and after parathyroidectomy in 3 cases.

Xerosis

Xerosis skin was observed in 242 patients (52.8%). It was diffuse in 27.2% of cases. It was located in the lower limbs in 17.4% of cases, upper limb in 7.6% and 5.3% in the face. It was mild in 155 patients (33.8%), moderate in 59 patients (12.8%) and severe in 28 patients (6.1%). Ichthyosiform appearance was found in 11 patients (2.4%). We did not find significant correlation between the presence of xerosis and patient age ($t = 0.34$), initial nephropathy ($p = 0.58$), duration of dialysis ($t = 0, 3$) and the presence of uremic pruritus ($p = 0.3$).

Cutaneous pallor

The pale skin was observed in 278 patients (60.7%) of cases. A significant correlation between the presence of mucocutaneous pallor and anemia was found ($p = 0.048$).

Pigmentary abnormalities

Pigmentation disorders were observed in 176 patients (38.4%) such as hyperpigmentation in 166 patients (36.2%) and hypopigmentation in 10 patients (2.2%) with acquired hair and skin fairness.

Keratotic disorders

Twenty four patients (5.2%) had keratotic disorders.

Follicular hyperkeratosis was present in 23 patients (95.8%). It was diffuse in 6 cases, localized to lower limbs in 17 cases, localized to the legs in 14 cases and affects the entire lower limb in 3 cases. There is no significant correlation between the presence of follicular hyperkeratosis and patient age ($t = 1.8$) or duration of haemodialysis ($t = 0.58$).

One patient had a pseudo-Kyrle's disease. He was a man of 43 years, with a history of peptic ulcer and coronary heart disease, chronic renal failure on haemodialysis since July 2000 due to chronic interstitial nephritis. For a year and a half, so five and a half years after the start of dialysis, he presented erythematous and papulo-nodular lesions, sometimes centred by a keratotic plug. This eruption was pruritic. The lesions were diffuse throughout the body, predominantly affecting the extensor surfaces of the members. The face was spared. A linear arrangement of lesions was observed in places in the limbs.

The patient received treatment with topical steroids and antihistamines, but without improvement. A skin biopsy confirmed the diagnosis of pseudo-Kyrle disease.

The patient was treated with topical steroids, topical retinoid and UVB phototherapy. We did not observe any skin lesions improved after 8 sessions.

Bullous dermatoses

Eleven patients (2.4%) had cutaneous manifestations of bullous dermatoses localized to areas exposed to phototype such as skin fragility in 7 cases, post-bullous skin erosions sometimes covered with scabs, bleeding in 4 cases,

clear bubbles in 2 cases and atrophic scarring in 8 cases. These lesions were found in photo-exposed areas: back of hands in 11 cases, forearm in 2 cases, legs and face in a case. They were pronounced in summer. None of our patients had hypertrichosis and milia. One patient was treated with furosemide and another with anti-inflammatory drugs and amiodarone for coronary artery disease. For the 9 remaining patients, there was no drug intake can lead to formation of bullous lesions.

A regression of bullous lesions was observed in patients after renal transplantation without recurrence after transplant rejection. The skin biopsy and the measurement of porphyrins in the plasma, urinary and faecal could not be charged. Pseudoporphyria diagnosis was subdued for the eleven patients at the lack of hypertrichosis and milia.

Calcifications

Two patients (0.4%) had cutaneous calcification. The first patient present nodular lesions with 2 cm in diameter, of indurated consistency, covered with a skin of normal appearance, sitting at the right ring. These lesions appeared for 7 months or 6 years after initiation of haemodialysis. These lesions were not accompanied by ulcers, livedo crosslinked or skin necrosis. Phospho-calcium balance was normal (serum calcium 2.7 mmol/l and phosphate: 3.2 mmol/l).

The second patient have Crohn's disease, dialyzed since December 1998. She had necrotic lesions in distal right leg since 2 years, necessitating amputation of the right leg. The diagnosis was a calciphylaxis. Phospho-calcium balance showed a calcium level of 2.9 mmol/l, phosphate 2.5 mmol/l and a product phospho-calcic to 72.5 $mmol^2/s^2$ (101.5 m^2 mg/dl^2). Parathyroid hormone (PTH) was elevated to 106 ng/L, suggestive of adynamic osteopathy.

Disorders appendages

Involvement of nails was found in 134 patients (29.3%) such as half and half nail in 62 cases (46.3%), nail dystrophy in 28 cases (20.9%), under ungueal haemorrhage in 21 cases (15.7%), leukonychia in 21 cases (15.7%), thinned nails in 10 cases (7.5%), disappearance of the lunula in 10 cases (7.5%) and double white lines in 4 cases (3%). We did not found any significant relationship between the presence of an nail disease and patient age ($t = 0.36$), duration of haemodialysis ($r = 0.63$), level of hemoglobin ($t = 0.064$) or level of calcium ($t = 0.097$).

Affected hair was observed in 51 patients (38%) such as hair loss in 35 cases, blond hair in 14 cases and brittle hair in 2 cases.

Table 2. Distribution of patients according to different cutaneous manifestations.

Mucocutaneous manifestations	Staff	Frequency
Paleness	278/458	60.7%
Uremic pruritus	259/458	56.6%
Dry skin (xerosis)	242/458	52.8%
Hypopigmention or hyperpigmentation	176/458	38.4%
Venous dilation near the fistula	102/458	22.2%
Eczema near the fistula	68/458	14.8%
Stomatitis	26/458	5.6%
Xerostomia	15/458	3.2%
Gingivitis	11/458	2.4%
Uremic breath	10/458	2.1%
Half-and-half nails	62/458	13.5%
Subungual hemorrhage	21/458	4.5%
Leukonychia	21/458	4.5%
Onychodystrophy	28/458	6.1%
Actinic keratosis	24/458	5.2%
Pseudoporphyria	11/458	2.4%
Skin calcifications	2/458	0.4%

Oral mucosal lesions

Oral effects were observed in 60 patients (13.1%) such as stomatitis in 26 cases (43.3%), xerostomia in 15 cases (25%), gingivitis in 11 cases (18.3%) and uremic breath in 10 cases (16.7%).

Disorders associated with the arteriovenous fistula

These complications were observed in 155 patients (33.8%). Dilation of the venous segment near the fistula was found in 102 patients (22.2%), pain fingerprints in 4 patients (0.8%), trophic disorders in 2 patients (0.4%) and swelling next to the fistula in one patient (0.2%). Eczema around the arteriovenous fistula was noted in 68 patients (14.8%). The allergen was the tape in 39 cases and antiseptic (Betadine®, Dakin®) in 14 cases. In the 15 remaining cases, the allergen has not been tagged.

Other skin lesions

Senile lesions were found in 75 cases (16.3%): senile purpura such as senile purpura in 55 cases, solar lentigo in 19 cases, actinic keratoses in 11 cases and malignant skin cancer such as basal cell carcinoma in 9 cases and Favre-Racouchot disease in 7 cases. These lesions are correlated with the vintage of dialysis ($p = 0.048$).

Fungal infections were found in 20 patients (4.3%) such as onychomycosis in 18 cases, fungal foot in 13 cases, tenia pedis in 6 cases and pityriasis versicolor in 3 cases.

Other injuries have been reported as an androgen-genetic alopecia in 35 cases (7.6%), lesions of vascular fragility type of petechiae or bruising in 20 cases (4.3%), dermatitis tan legs in 14 cases (3%), folliculitis back in 9 cases (1.9%). These folliculitis have been associated with pruritus and the absence of comedones in all cases and pityriasis versicolor (Malassezia folliculitis: 3 cases), molluscum pendulum in 7 cases, red eyes in 6 cases, cystic lesions of the face or scalp in 6 cases, amputation of the extremities due to diabetic gangrene in 5 cases, dandruff of the scalp in 5 cases, a seborrheic keratosis in 5 cases, 4 cases of oral herpes, warts in 3 cases, plantar perforating ulcer in 3 cases, psoriasis in 3 cases, rosacea in 2 cases, seborrheic dermatitis of the face in 2 cases, intercostal zoster in 2 cases, acne in 2 cases, alopecia areata in 1 cases and vitiligo in 1 case.

Discussion

Our study demonstrates the polymorphism and the frequency of cutaneous manifestations in haemodialysis patients. The incidence of cutaneous manifestations was ranging from 50 to 100% in different studies.[1-11]

Uremic pruritus is the most common symptom in our series. Its prevalence varies from 15% to 90%.[12,13] In our study, the incidence of uremic pruritus is 56.6%. Pruritus occurs frequently during the 6 months after initiation of hemodialysis.[14] It is independent of the disease leading to end stage renal disease (ESRD).

Uremic pruritus does not seem to differ according to the age, the sex or vintage of dialysis. But a significantly correlation with chronic glomerular nephropathy has been established.

Pruritus may be localized or generalized commonly with equal proportions.[15-17] In our study, pruritus was most often localized than generalized. There is more pruritus in the areas most accessible to scratching such as back, legs, face and arms.[18] Nearly half of patients undergoing haemodialysis have continued pruritus. For others, it occurs occasionally with episodes of exacerbation.[17] The potential link between pruritus and dialysis is controversial in the literature. Gilchrest reported that pruritus would occur only during the dialysis sessions (during or immediately after) in approximately 25% of patients and it would be exacerbated during the sessions in 40% of patients.[18] In contrast, in three other studies, worsening of pruritus during dialysis is described less.[19]

The exacerbation of pruritus during dialysis sessions, like that seen at sunset or at night, seems primarily associated with inactivity in these periods.[18,20] In our study, pruritus was mostly nocturnal exacerbation and less during the dialysis session. Atrophy of sebaceous glands associated with a decreased lipid film surface found in patients with ESRD leads to dehydration of the stratum corneum. These alterations promote pruritus.[19,21,22]

In our study, we found no statistically significant correlation between pruritus and xerosis. Although several studies have shown increased frequency of uremic pruritus in haemodialysis patients with xerosis compared to those without xerosis.[23,24,25] In addition, patients with uremic pruritus have a reduced hydration of the stratum corneum in comparison with those not suffering from pruritus. These findings suggest a direct relationship between xerosis and uremic pruritus.[25]

The role of hyperparathyroidism in uremic pruritus has been discussed by reason of the dramatic improvement in pruritus after parathyroidectomy. Indeed, parathyroid hormone could increase serum levels of histamine and mast cell proliferation.[26] In our series, a regression of uremic pruritus after parathyroidectomy was observed only in 3 cases. Several studies have reported a significant increase in skin concentrations of calcium, magnesium, aluminum and phosphorus in hemodialysis patients with pruritus, compared with haemodialysis patients without pruritus and control subjects.[15,17,27,28,29,30] An increase in the concentration of these molecules is the cause of microprecipitation in the skin that would cause pruritus. Few studies show a significant correlation between serum levels of these ions and the presence of pruritus.[31-35]

Cohen showed that the severity of pruritus is not related to hyperphosphataemia.[36] In our series, we found a significant correlation between the presence of uremic pruritus and hyperphosphatemia.

A more recent study showed increased levels of epidermal calcium in chronic haemodialysis patients with uremic pruritus.[37] Another study found a higher incidence of uremic pruritus in dialysis patients with significant elevation of calcium, phosphate and calcium × phosphorus product in the serum.[28]

The frequency of uremic pruritus appears to have declined in recent years and this along with an increase in dialysis efficiency.[38] Indeed, since 2007 there was introduced into the hemodialysis centers in Tunisia of synthetic dialysis membranes which have replaced cellulose membranes. This suggests that dialysis quality may improve pruritus. Hiroshige[39] has concluded that a good efficiency of dialysis associated with a balanced diet (protein levels normally catabolized is more than 0.8 g/kg/day) reduces the prevalence and intensity of pruritus in hemodialysis patients. This strongly suggests that pruritus depends on a dialysable substance.

Skin xerosis is a frequent complication in haemodialysis patients. It can be seen in chronic renal failure before haemodialysis, but a significant rise in its frequency is found after the start of dialysis. It disappears after renal transplantation. The frequency of uremic xerosis is variable according to the authors between 28% and 80.5%.[40-41] Most studies did not find any direct relationship between xerosis and uraemic pruritus.[24,21,42] Add that, emollients have only a partial improvement in pruritus.

Despite our sunny country, the incidence of hyperpigmentation was not different from other studies reported in the literature.[43] Infection with hepatitis C appears to increase skin pigmentation in hemodialysis, especially in photo-exposed areas.[44]

The acquired hair and skin fairness in chronic haemodialysis patients is an exceptional event. Only a few cases have been reported.[45] The first case was reported by El Matri in 1989.[45] Although the exact mechanism involved in this entity remains obscure, it was to be correlated with a disturbance of phenylalanine metabolism.[46] In our study, we found 10 cases.

The pseudo-Kyrle's disease was first described by Garcia-Bravo *et al*. Between 1981 and 1983, 6 cases of perforating dermatitis associated with chronic renal failure and diabetes have been reported. Acquired perforating dermatitis often occurs in chronic renal failure patients with diabetic nephropathy.[47] Acquired perforating dermatitis is more common in cases of type 1 diabetes than type 2. They are often associated with severe diabetes with degenerative complications and they affect 4.5 to 11% of haemodialysis patients.[47]

The incidence of pseudo-Kyrle's disease is 4.5 to 10% of haemodialysis patients.[48,49] The elementary lesion is a hyperkeratotic papule or nodule with 2 to 10 mm in diameter. In most patients, pruritus precedes or occurs at the same time as nodular papulopustular lesions.[50,51] Kobner phenomenon is frequently observed.[52] The lesions are at the extensor surface of limbs, trunk and rarely on the face.[50,52] Chang found in a series of 9 cases of acquired perforating dermatitis that the lesions were nodular and papulopustular when the duration of chronic kidney disease outdate 2 years and papular when chronic renal failure has been evolving for less than 2 years.[52]

Haemodialysis patients may develop 2 types of bullous dermatoses in photo-exposed areas: the true porphyria or porphyria cutanea tarda (PCT) and the pseudoporphyria. In our study, bullous lesions photo-exposed areas were found in 11 patients, or 2.4% of cases. It is probably a pseudoporphyria, the measurement of urinary porphyrins, faecal and in plasma could not be performed. Skin symptoms often begin insidiously with increased skin fragility. Then, gradually appear vesiculobullous bubbles from 0.25 to 1 cm in diameter at the extensor surfaces of the forearms and back of hands.[53] Other areas may also be affected such as ingers, the extensor surface of legs, chest and face.[53] Atrophic scars, grains of milium or hyperpigmentation can be developed secondarily.[1] Hypertrichosis, scleroderma plaques and dystrophic calcification may be seen especially in cases of PCT.[1,53,54]

Calciphylaxis is a rare disease, affecting mainly chronic renal failure. Their diagnosis is clinical and histological. The phospho-calcium exploration can show elevated serum levels of calcium, phosphate and PTH. Female predominance was reported, it may be related to the greater importance of adipose tissue in women.[55-57] In fact, this tissue is poorly vascularized, so it is more sensitive to ischemia.

Nail diseases are frequent in patients on haemodialysis with an incidence of 52-82%.[58] The pathogenesis of these nail disorders remains unclear: some of them may be directly related to renal disease, others appear to be related to its complications or to different therapies received. This nail disorders were found in 1/3 of patients in our series. They are essentially represented by half nails, absence of lunula and subungual haemorrhage.[57,58] Our results find no significant relationship between the ungual disorders and patient age or duration of haemodialysis. This has also been described in others studies.[58,59,60] Some authors have shown a positive correlation between nail changes and duration of haemodialysis.[61] Anaemia is an important etiological factor.[62] Hypoalbuminemia is a known complication of chronic renal failure and suggested to be an etiological factor of nail changes.[1] Several studies found no significant relationship between hypoalbuminemia and nail disorders.[58-60] Half and half nail was found in 4-50% of haemodialysis patients.[10,58,59,60] It can be found in other diseases such as Kawasaki disease, liver cirrhosis, zinc deficiency, Crohn's disease and pellagra.[58] Onycholysis is common in chronic renal failure and can be attributed to different local and systemic causes.[58] Some drugs can also induce photo-onycholysis such as cephalordin or cloxacillin.[58,62] In 75% of cases, it is an infection with *Trichophyton rubrum*.[59] Under ungeual haemorrhage is seen in 11-12% of haemodialysis patients.[9,58,60] It is an extravasation of blood from parallel longitudinal vessels of the bed of the nail. It is often seen as the result of microtrauma. The exact pathogenesis remains unclear, but the capillary fragility and Platelet dysfunction, common in chronic renal failure, may contribute to the development of these haemorrhages.[58] Leukonychia is seen in cases of acute or chronic renal failure, in cirrhosis of liver, in case of typhoid fever, in patients receiving chemotherapy, and it is the most common nail disorders in renal transplant patients.[58,60,64] The disappearance of the lunula was found in 2% of our patients. In other studies, it represents the most common nail disorders in hemodialysis patients with a prevalence of 30%.[58] It is reported that the absence of lunula is attributed to anemia in chronic renal failure.[65] It is possible that other metabolic changes associated such as anemia who are implicated in this nail affection.[58] However, the absence of lunula can be seen in normal subjects, without any renal insufficiency.

Bacterial infection is a common complication of the arteriovenous fistula (AVF). In some cases, systemic manifestations may exist and they are suggestive of bacteremia or sepsis.[66] Infection with *Staphylococcus aureus* is the most common and represents 32-53% of all infections of the AVF.

In our study, dilation of the venous segment near the AVF was found in 1/4 of cases. The diversion of arterial blood through the fistula determines an array of chronic distal ischemia.[67] Allergic complications of the AVF are common. Their frequency is 34% according to Kessler.[68]

Nephrogenic fibrosing dermopathy (NFD) is a rare fibrosing disease, recently emerged and not observed in our study. There are currently about 200 cases reported in the International Register of nephrogenic systemic fibrosis.[69]

Conclusion

The cutaneous manifestations occurring in our chronic renal failure are diverse. Pruritus, hyperpigmentation and xerosis remain the most skin disorders encountered in hemodialysis patients. The acquired hair and skin fairness is particular in our study. The prevalence of calciphylaxis was relatively low compared to literature. The pathogenesis of most of these cutaneous manifestations remains unclear. The treatment is in most cases symptomatic. The renal transplantation is the best treatment.

References

1. Abdelbaqi-Salahab M, Shalhub S, Morgan MB. A current review of the cutaneous manifestations of renal disease. *J Cutan Pathol*. 2003; 30: 527-538. PMID: 14507400.
2. Madiha S, Shahbaz A, Muhammad N, Atif Hasnain K. Dermatologic manifestations in patients of renal disease on hemodialysis. *Journal of Pakistan Association of Dermatologists*. 2010; 20: 163-168.
3. Masmoudi A, Ben Hmida M, Mseddi M, Meziou TJ, Walha N, Hachicha J, Turki H, Zahaf A. Cutaneous manifestations of chronic hemodialysis. Prospective study of 363 cases. *Presse Med*. 2006; 35(3 Pt 1): 399-406. PMID: 16550129.
4. Bah AO, Balde MC, Kaba ML, Camara A, Cisse A, Kaba A, Bah MO, Diakite M. Aspects cliniques des manifestations dermatologiques de l'insuffisance rénale chronique. *Ann Dermatol Venereol*. 2008; 135: 318-320. PMID: 18420084.
5. Leena JA, Noman MU, Islam MMSU, Ahmed AS, Ahmed DS, Rahma MM. Cutaneous Manifestations of Chronic Kidney Disease – An Observational Study in 100 Cases. *Faridpur Med Coll J*. 2012; 7: 33-36.
6. Tajbakhsh R, Dehghan M, Azarhoosh R, Haghighi AN, Sadani S, Zadeh SS, Kabootari M, Qorbani M. Mucocutaneous manifestations and nail changes in patients with end-stage renal disease on hemodialysis. *Saudi J Kidney Dis Transpl*. 2013; 24: 36-40. PMID: 23354189.
7. Khan R, Quaiser S, Haque SF, Sachdeva S. Cutaneous Manifestations in Patients of Chronic Kidney Disease. *Int J Cur Bio Med Sci*. 2011; 1: 113-115.
8. Headly CM, Wall B. ESRD-associated cutaneous manifestations in a hemodialysis population. *Nephrol Nurs J*. 2002; 29: 525-527. PMID: 12596603.
9. Picó MR, Lugo-Somolinos A, Sánchez JL, Burgos-Calderón R. Cutaneous alterations in patients with chronic renal failure. *Int J Dermatol*. 1992; 31: 860-863. PMID: 1478764.
10. Udayakumar P, Balasubramanian S, Ramalingam KS, Lakshmi C, Srinivas CR, Mathew AC. Cutaneous manifestations in patients with chronic renal failure on hemodialysis. *Indian J Dermatol Venereol Leprol*. 2006; 72: 119-125. PMID: 16707817.
11. Lupi O, Rezende L, Zangrando M, Sessim M, Silveira CB, Sepulcri MA, Duarte DJ, Cardim P, Fernandes MM, Santos Oda R. Cutaneous manifestations in end-stage renal disease. *An Bras Dermatol*. 2011; 86: 319-326. PMID: 21603815.
12. Yosipovitch G, Reis J, Tur E, Sprecher E, Yarnitsky D, Boner G. Sweat secretion, stratum corneum hydratation, small nerve function and pruritus in patients with advanced chronic renal failure. *Br J Dermatol*. 1995; 133: 561-564. PMID: 7577584.
13. Gilchrest BA, Stern RS, Steinman TI, Brown RS, Arndt KA, Anderson WW. Clinical features of pruritus among patients undergoing maintenance hemodialysis. *Arch Dermatol*. 1982; 118: 154-156. PMID: 7065661.
14. Roujeau JC. Pruritus of chronic renal insufficiency. *Ann Dermatol Venereol*. 1986; 113: 265-268. PMID: 3530095.
15. Ponticelli C, Bencini PL. Uremic pruritus: a review. *Nephron*. 1992; 60: 1-5. PMID: 1738396.
16. Ståhle-Bäckdahl M. Uremic pruritus. Clinical and experimental studies. *Acta Derm Venereol Suppl (Stockh)*. 1989; 145: 1-38. PMID: 2773616.
17. Szepietowski JC, Schwartz RA. Uremic pruritus. *Int J Dermatol*. 1998; 37: 247-253. PMID: 9585892.
18. Gilchrest BA, Stern RS, Steinman TI, Brown RS, Arndt KA, Anderson WW. Clinical features of pruritus among patients undergoing maintenance hemodialysis. *Arch Dermatol*. 1982; 118: 154-156. PMID: 7065661.
19. Kato A, Hamada M, Maruyama T, Maruyama Y, Hishida A. Pruritus and hydratation state of stratum corneum in hemodialysis patients. *Am J Nephrol*. 2000; 20: 437-442. PMID: 11146309.
20. Ståhle-Bäckdahl M, Hägermark O, Lins LE. The sensivity of uremic and normal human skin to histamine. *Acta Derm Venereol*. 1988; 68: 230-235. PMID: 2455416.
21. Deleixhe-Mauhin F, Piérard-Franchimont C, Krezinski JM, Rorive G, Piérard GE. Biometrological evaluation of the stratum corneum texture in patients under maintenance haemodialysis. *Nephron*. 1993; 64: 110-113. PMID: 8502314.
22. Ostlere LS, Taylor C, Baillod R, Wright S. Relationship between pruritus, transepidermal water loss, and biochemical markers of renal itch in hemodialysis patients. *Nephrol Dial Transplant*. 1994; 9: 1302-1304. PMID: 7816295.
23. Balaskas EV, Chu M, Uldall RP, Gupta A, Oreopoulos DG. Pruritus in continuous ambulatory peritoneal dialysis and hemodialysis patients. *Perit Dial Int*. 1993; 13 Suppl 2: S527-532. PMID: 8399656.
24. Szepietowski JC, Sikora M, Kusztal M, Salomon J, Magott M, Szepietowski T. Uremic pruritus: a clinical study of maintenance hemodialysis patients. *J Dermatol*. 2002; 29: 621-627. PMID: 12432992.
25. Szepietowski JC, Reich A, Schwartz RA. Uraemic xerosis. *Nephrol Dial Transplant*. 2004; 19: 2709-2712. PMID: 15328388.

26. Neiman RS, Bischel MD, Lukes RJ. Uremia and mast-cell proliferation. *Lancet*. 1972; 1: 959. PMID: 4112122.

27. Cho YL, Liu HN, Huang TP, Tarng DC. Uremic pruritus: roles of parathyroid hormone and substance P. *J Am Acad Dermatol*. 1997; 36: 538-543. PMID: 9092738.

28. Noordzij M, Boeschoten EW, Bos WJ, Dekker FW, Bossuyt PM, Krediet RT, Korevaar JC. Disturbed mineral metabolism is associated with miscle and skin complaints in a prospective cohort of dialysis patients. *Nephrol Dial Transplant*. 2007; 22: 2944-2949. PMID: 17597087.

29. Ronsen T. Uremic pruritus: a review. *Cutis*. 1979; 23: 790-792. PMID: 380932.

30. Blachley JD, Blankenship DM, Menter A, Parker TF 3rd, Knochel JP. Uremic pruritus: skin divalent ion content and response to ultraviolet phototherapy. *Am J Kidney Dis*. 1985; 5: 237-241. PMID: 4003393.

31. Akhyani M, Ganji MR, Samadi N, Khamesan B, Daneshpazhooh M. Pruritus in hemodialysis patients. *BMC Dermatol*. 2005; 24: 5-7. PMID: 15975150.

32. Carmichael AJ, McHugh MM, Martin AM, Farrow M. Serological markers of renal itch in patients receiving long term haemodialysis. *Br Med J (Clin Res Ed)*. 1988; 296: 1575. PMID: 3135016.

33. Cohen EP. Uremic pruritus. *Nephrologie*. 1993; 14: 215-219. PMID: 8159250.

34. Dar NR, Akhter A. Clinical characteristics of uremic pruritus in patients undergoing haemodialysis. *J Coll Physicians Surg Pak*. 2006; 16: 94-96. PMID: 16499798.

35. Mesić E, Tabaković M, Habul V, Atić M, Lekić S, Resić H, Halilbasić A, Trnacević S, Halilbasić A. Clinical characteristics of puritus in hemodialysis patients. *Acta Med Croatica*. 2004; 58: 377-380. PMID: 15756803.

36. Cohen EP, Russel TJ, Garancis JC. Mast cells and calcium in severe uremic itching. *Am J Med Sci*. 1992; 303: 360-365. PMID: 1605164.

37. Momose A, Kudo S, Sato M, Saito H, Nagai K, Katabira Y, Funyu T. Calcuim ions are abnormally distributed in the skin of hemodialysis patients with uremic pruritus. *Nephrol Dial Transplant*. 2004; 19: 2061-2066. PMID: 15187190.

38. Masi CM, Cohen EP. Dialysis efficacy and itching in renal failure. *Nephron*. 1992; 62: 257-261. PMID: 1436334.

39. Hiroshige K, Kabashima N, Takasugi M, Kuroiwa A. Optimal dialysis improves uremic pruritus. *Am J Kidney Dis*. 1995; 25: 413-419. PMID: 7872318.

40. Falodun O, Ogunbiyi A, Salako B, George AK. Skin changes in patients with chronic renal failure. *Saudi J Kidney Dis Transpl*. 2011; 22: 268-272. PMID: 21422624.

41. Moon SJ, Kim DK, Chang JH, Kim CH, Kim HW, Park SY, Han SH, Lee JE, Yoo TH, Han DS, Kang SW. The impact of dialysis modality on skin hyperpigmentation in haemodialysis patients. *Nephrol Dial Transplant*. 2009; 24: 2803-2809. PMID: 19342419.

42. Park TH, Park CH, Ha SK, Lee SH, Song KS, Lee HY, Han DS. Dry skin (xerosis) in patients undergoing maintenance haemodialysis: the role of decreased sweating of the eccrine sweat gland. *Nephrol Dial Transplant*. 1995; 10: 2269-2273. PMID: 8808224.

43. Deleixhe-Mauhin F, Krezinski JM, Rorive G, Piérard GE. Quantification of skin color in patients undergoing maintenance haemodialysis. *J Am Acad Dermatol*. 1992; 27(6 Pt 1): 950-953. PMID: 1479099.

44. Choi HK, Thomé FS, Orlandini T, Barros E. Increased skin pigmentation in patients with chronic renal failure undergoing hemodialysis infected with the hepatitis C virus. *Rev Assoc Med Bras*. 2003; 49: 24-28. PMID: 12724808.

45. El Matri A, Aissa F, Ben Abdallah T. Bondissement du système pileux associé à une pseudoporphyrie cutanée tardive chez un hemodyalisé chronique. *Néphrologie*. 1990; 11: 53.

46. Hmida MB, Turki H, Hachicha J, Reygagne P, Rabier D, Zahaf A, Jarraya A. Hypopigmentation in hemodialysis. Acquired hair and skin fairness in a uremic patient undergoing maintenance hemodialysis: case report and review of the literature. *Dermatology*. 1996; 192: 148-152. PMID: 8829500.

47. Ohe S, Danno K, Sasaki H, Isei T, Okamoto H, Horio T. Treatment of acquired perforating dermatosis with narrowband ultraviolet B. *J Am Acad Dermatol*. 2004; 50: 892-894. PMID: 15153890.

48. Chua SL, Kulkarni K, Saihan E. Hyperpigmented keratotic nodules: acquired perforating collagenosis. *Arch Dermatol*. 2007; 143: 1201-1206. PMID: 17875890.

49. Morton CA, Henderson IS, Jones MC, Lowe JG. Acquired perforating dermatosis in a britch dialysis population. *Br J Dermatol*. 1996; 135: 671-667. PMID: 8977664.

50. Hong SB, Park JH, Ihm CG, Kim NI. Acquired perforating dermatosis in patients with chronic renal failure and diabetes mellitus. *J Korean Med Sci*. 2004; 19: 283-288. PMID: 15082904.

51. Martín-Serradilla JI, Bajo del Pozo C, Oñate Cuchet JM, Escudero Bueno G, Cuadrado de Valles C, Sousa Pérez F. Papular keratotic lesions in a diabetic female patient with a chronic renal failure. *Rev Clin Esp*. 2002; 202: 567-568. PMID: 12361560.

52. Chang P, Fernández V. Acquired perforating disease: report of nine cases. *Int J Dermatol*. 1993; 32: 874-876. PMID: 8125688.

53. Green JJ, Manders SM. Pseudoporphyria. *J Am Acad Dermatol*. 2001; 44: 100-108. PMID: 11148469.

54. Pérez L, Fernández-Redondo V, Toribio J. Porphyria cutanea tarda in a dialyzed female patient. *Actas Dermosifiliogr*. 2006; 97: 115-117. PMID: 16595112.

55. Kang AS, McCarthy JT, Rowland C, Farley DR, van Heerden JA. Is calciphylaxis best treated surgically or medically? *Surgery*. 2000; 128: 967-971. PMID: 11114631.

56. Llach F. The evolving clinical features of calciphylaxis. *Kidney Int Suppl*. 2003; 85: S122-124. PMID: 12753282.

57. Fine A, Zacharias J. Calciphylaxis is usally non-ulcerating: risk factors, outcome and therapy. *Kidney Int*. 2002; 61: 2210-2217. PMID: 12028462.

58. Salem A, Al Mokadem S, Attwa E, Abd El Raoof S, Ebrahim HM, Faheem KT. Nail changes in chronic renal failure patients under hemodialysis. *J Eur Acad Dermatol Venereol*. 2008; 22: 1326-1331. PMID: 18540986.

59. Dyachenko P, Monselise A, Shustak A, Ziv M, Rozenman D. Nail disorders in patients with chronic renal failure and undergoing hemodialysis treatment: a case-control study. *J Eur Acad Dermatol Venereol*. 2007; 21: 340-344. PMID: 17309455.

60. Saray Y, Seçkin D, Güleç AT, Akgün S, Haberal M. Nail disorders in hemodialysis patients and renal transplant recipients: a case-control study. *J Am Acad Dermatol*. 2004; 50: 197-202. PMID: 14726872.

61. Tercedor J, López Hernández B, Manuel Ródenas J. Nail diseases in hemodialysis patients: case-control study. *Br J Dermatol*. 2001; 144: 445-446. PMID: 11251608.

62. Rutherford T, Sinclair R. Photo-onycholysis due to indapamide. *Australas J Dermatol*. 2007; 48: 35-36. PMID: 17222300.

63. Kuvandik G, Cetin M, Genctoy G, Horoz M, Duru M, Akcali C, Satar S, Kiykim AA, Kaya H. The prevalence, epidemiology and risk factors for onychomycosis in hemodialysis patients. *BMC Infect Dis*. 2007; 7: 102. PMID: 17760994.

64. Zaiac MN, Daniel R. Nails in systemic diseases. *Dermatologic therapy*. 2002; 15: 99-106.

65. Robinson-Bostom L, DiGiovanna JJ. Cutaneous manifestations of end-stage renal disease. *J Am Acad Dermatol*. 2000; 43: 975-986. PMID: 11100013.

66. Padberg FT Jr, Calligaro KD, Sidawy AN. Complications of arteriovenous hemodialysis access: recognition and management. *J Vasc Surg*. 2008; 48(5 Suppl): 55S-80S. PMID: 19000594.

67. Tordoir JH, Dammers R, van der Sande FM. Upper extremity ischemia and hemodialysis vascular access. *Eur J Vasc Endovasc Surg*. 2004; 27: 1-5. PMID: 14652830.

68. Kessler M. Accidents allergiques à l'oxyde d'éthyléne en hémodialyse. *Rev Fr Allergol*. 1987; 27: 147-148.

69. Agarwal R, Brunelli SM, Williams K, Mitchell MD, Feldman HI, Umscheid CA. Gadolinium-based contrast agents and nephrogenic systemic fibrosis: a systematic review and meta-analysis. *Nephrol Dial Transplant*. 2009; 24: 856-863. PMID: 18952698.