Pseudoporphyria induced by dialysis treated with oral N-acetylcysteine

Pseudoporfiria induzida pela diálise tratada com N-acetilcisteína oral

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Abstract: Pseudoporphyria is a rare bullous dermatosis that clinically and histopathologically is similar to porphyria cutanea tarda. It mainly affects patients with chronic renal failure on peritoneal dialysis or hemodialysis. Medications can also be involved in the etiology. Diagnosis and management of this condition is a challenge for dermatologists. The authors report a case of pseudoporphyria related to dialysis with favorable outcome after the use of oral N-acetylcysteine.
Keywords: Acetylcysteine; Dialysis; Porphyrias; Renal dialysis

Resumo: Pseudoporfiria é dermatose bolhosa rara, semelhante clínica e histopatologicamente à porfiria cutânea tardia. Acomete, principalmente, pacientes renais crônicos em diálise peritoneal ou hemodiálise. Medicamentos também podem ser envolvidos na etiologia. O diagnóstico e o manejo desta entidade é um desafio para os dermatologistas. Os autores demonstram um caso de pseudoporfiria, relacionada à diálise, com evolução favorável após o uso de N-acetilcisteína oral.
Palavras-chave: Acetilcisteína; Diálise; Diálise renal; Porfirias

Pseudoporphyria (PP) is a bullous dermatosis caused by phototoxicity that affects chronic renal failure patients on peritoneal dialysis or hemodialysis. Its clinical and histopathological changes are similar to chronic hepatic porphyria cutanea tarda. Other factors such as drugs, tanning beds, PUVA, were also connected with the etiology of PP (Chart 1). Except for the suspension of the causative agents and photoprotection, up to now, there is no treatment based on available evidence. There are reports of clinical control after the use of oral N-acetylcysteine.[1-5]

It is presented here the case of a female patient, aged 32, who had been suffering from Goodpasture's syndrome for five years, evolving into chronic renal failure (anuria) and renal replacement therapy (peritoneal dialysis) and placed on a transplant waiting list. The patients had been presenting recorrent bullae with hyaline content on the backs on the hands and feet for one year. Lesions were painless, non-pruritic and evolved with rupture and cicatricial hyperpigmentation (Pictures 1A and 1B). The patient had no lesions in other body areas, hyperthricosis, hyperpigmentation or *milia*. She denied use of alcohol and intense sun exposure. The patient was using the following medicines: captopril, atorvastatin, prednisone, erythropoetin, domperidone, folic acid, sevelamer, calcium carbonate and calcium acetate. Histopathology showed: subepidermall vasicle with festooned dermal papillae and mild superficial perivascular lymphocytic infiltrate with deposit of hyaline

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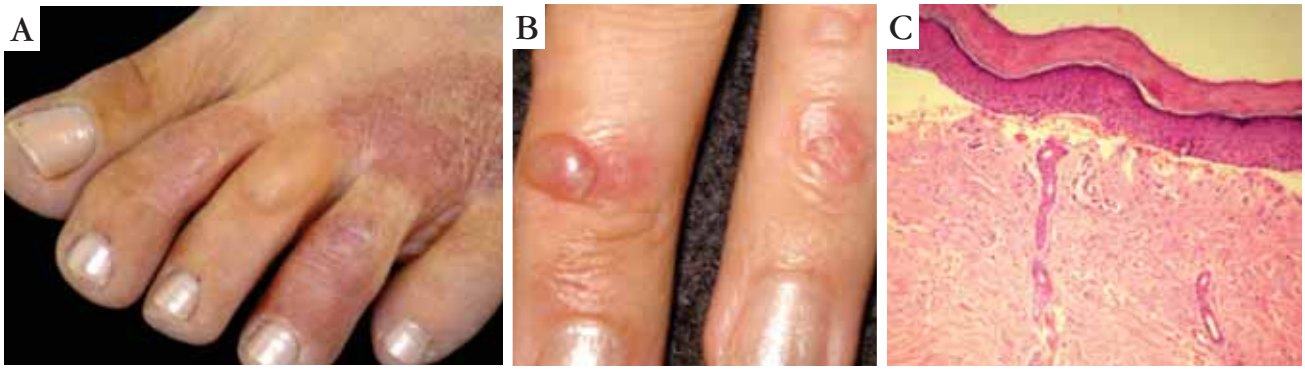

Figure 1: Bulla with serous content on the back of the third left toe (A) and serous vesicles on the back of the left fingers (B). Histopathology showing subepidermal cleft with preservation of papillae, without prominent inflammatory infiltrate – HE 200x (C)

material on the wall vessels (Picture 1C). Direct immunoflorescence examination was normal. CBC (Complete Blood Count) shows normocytic normochromic anemia (Hb: 11,5g/dl, VCM: 91,5 μmm^3), ferritin of 1421ng/ml, creatinine of 9,4mg/dl, urea of 101mg/dl; liver biochemistry and blood glucose were normal. Serum porphyrin were 1,4μg/g Hb (VR<20).

Diagnosis of PP secondary to dialysis was established and we began the treatment with N-acetylcysteine 600mg/d. The patient presented good evolution of the dermatological condition and after 20 days of use of the medication lesions disappeared. One month after the introduction of the medication the patient presented bacterial peritonitis and remained on hemodialysis for three months. During such intercurrence the bullae on the hands and feet reappeared even under medication.

PP presents clinical and histopathological resemblance with porphyria cutanea tarda. However, it can be distinguished by the normal serum and urinary levels and faecal porphyrin,[6-9] .Both can be present in chronic renal patients . This condition affects up to 13% of the patients with chronical renal failure on hemodialysis.[1,6,9] Some medications described in the literarture like nonsteroidal anti-inflammatory, antibiotics and erythropetin may trigger PP. Excessive sun exposure and Uva radiations in tanning beds can also induce lesions. (Chart 1).[1]

The exact pathophysiological mechanism of PP is not known. The formation of phototoxic metabolites in individuals geneticaly predisposed can be responsible for triggering bullous lesions. Oxigen free radicals were also incriminated in the genesis in patients on hemodialysis.[2-4] As for PP secondary to drugs, the suspension of these drugs leads to remission of the skin condition.[1] The treatment is based on avoiding sun exposure, topical steroids and also on avoiding potential medication involved. Case reports of prolonged use of N-acetylcysteine in such patients on hemodialysis have shown success.[2-6] The suspension of the drug leads to recurrence of the bullous lesions. Patients on hemodialysis and peritoneal dialysis are at high risk of oxidative stress due to deficiency of glutathione in blood and erythrocytes. N- acetylcysteine is a precursor of glutathione which presents anti-oxidant properties and can reduce the levels of serum creatinine. N- acetylcysteine is also used in prophylactic therapy of contrast nephropathy as it prevents the increase of oxidative stress after contrast infusion.[1,6,10]

We present a case of PP secondary to dialysis with good response to the use of oral N- acetylcysteine. The patient maintained the use of erythropetin and presented improvement of the lesions, suggesting that the condition was not medicamental. On the

Chart 1: Medications and conditions associated with the development of pseudoporphyria

Dialysis / hemodialysis

Ultraviolet A radiation: sun exposure, phototherapy and tanning beds.
Phototherapy with UVB *Narrowband*

Medications
Diuretics: Furosemide, chlorthalidone, butamida, triamterene/hydrochlorothiazide
Nonsteroidal Antiinflammatory Drugs: Naproxen, diflunisal, ketoprofen, nabumetone, oxaprozin, mefenamic acid, rofecoxib, aspirin (AAS)
Antibiotics: nalidixic acid, tetracycline, oxytetracycline, ampicillin-sulbactam, cefepime, fluoroquinolones
Antifungal: Voriconazole
Retinoids: Isotretinoin, etretinate/acitretin
Others: Erythropoietin, amiodarone, 5-fluorouracil, cyclosporine, dapsone, carisoprodol, pyridoxine, flutamide, oral contraceptive, coca-cola (coke)

other hand, after the onset of the infection the lesions were recurrent even during the treatment suggesting that the condition might be due to a new oxidative stress and to the change from peritoneal dialysis to hemodialysis. The cases already described presented no medical complications that could increase oxidative stress. It is worth mentioning the need for more studies on the use of such medication to understand the pathogenesis of PP so as to improve the quality of life of such patients once only a few of them have the privilege of undergoing a kidney transplant. ❑

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