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CLINICAL REPORT

Successful Outcome of Haemodialysis-induced Pseudoporphyria after Short-term Oral N-Acetylcysteine and Switch to High-flux Technique Dialysis

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Pseudoporphyria is a blistering disease with skin fragility and shallow scarring that clinically and histopathologically closely resembles porphyria cutanea tarda. The two conditions can be distinguished by porphyrin levels that typically are elevated in porphyria cutanea tarda, but not or only slightly in pseudoporphyria. Pseudoporphyria can be induced by various medications (e.g. non-steroidal anti-inflammatory drugs, antibiotics, diuretics, retinoids), intense UV(A) exposure, or haemodialysis. Treatment of haemodialysis-associated pseudoporphyria is not yet standardized. We report here a 65-year-old male patient with chronic renal failure due to Waldenström's macroglobulinaemia who was treated with conventional 3 times/week haemodialysis. He developed blistering skin changes on both hands, which were diagnosed as pseudoporphyria based on clinical, histopathological, and laboratory findings, and could be successfully managed with initial oral N-acetylcysteine and a switch from low-flux to high-flux membrane haemodialysis. The beneficial effect of the high-flux membrane technique in haemodialysis-associated pseudoporphyria has not been previously reported. ***Key words: pseudoporphyria; haemodialysis; high-flux membrane; N-acetylcysteine.***

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Pseudoporphyria is a photo-distributed bullous skin disease in patients undergoing haemodialysis for chronic renal failure that clinically and histopathologically resembles porphyria cutanea tarda, but with normal or near-normal porphyrin levels in serum, urine and stool (1–3). It is now known that about 13% of patients with chronic renal failure under haemodialysis develop pseudoporphyria (2, 4). The condition has also been reported in association with medications, such as non-steroidal anti-inflammatory agents, antibiotics, diuretics, oral contraceptive pills or retinoids, chronic ultraviolet A radiation (UVA) in tanning beds, or excessive sun exposure (5, 6). The pathophysiological mechanism of pseudoporphyria is poorly understood, but formation of phototoxic metabolites in genetically predisposed individuals has been suggested as the most likely mechanism (6, 7). Free radicals of oxygen have been discussed as possible cause in the subset of patients undergoing haemodialysis (7). In most patients with drug-induced pseudoporphyria symptoms clear after discontinuing the offending agent (8), but symptoms of haemodialysis-induced pseudoporphyria may persist during this procedure, thus posing a therapeutic challenge.

CASE REPORT

A 65-year-old man with a 9-year history of Waldenström's macroglobulinaemia had to be treated with conventional haemodialysis 3 times/week since 10 months because of progressive chronic renal failure. He was referred to our department after a 1-month history of recurrent blisters, followed by erosions and scars on the back of his hands (Fig. 1). No other parts of the body were involved and he had no hypertrichosis, hyperpigmentation, milia, or sclerodermoid changes. The patient denied regular drinking of alcohol or intensive sun/UVA exposure. His daily medication included low-molecular-weight heparin, acetylsalicylic acid, methyldigoxin, thiamine hydrochloride, metoprolol, calcitriol, folic acid, and erythropoietin. Diuretics had been stopped with start of haemodialysis. Histopathological examination of lesional skin revealed subepidermal blister formation with intracorneal haemorrhages but no inflammatory dermal infiltrate (Fig. 2). Direct immunofluorescence examination of perilesional skin showed granular C3 staining along the basement membrane. Indirect immunofluorescence and the antinuclear antibody titre were negative. Complete blood cell count revealed pancytopaenia (erythrocytes 2,200,000/mm^3, haematocrit 24.9%, haemoglobin 8.8 g/dl, leukocytes 2800/mm^3, platelets 69,000/mm^3), creatinine was 2.7 mg/dl, BUN 154 mg/% while liver function tests, blood glucose, and iron status were within normal ranges. Serological tests for hepatitis B and C were negative. The total plasma porphyrin level was 5.5 μg/dl (normal up to 2 μg/dl)

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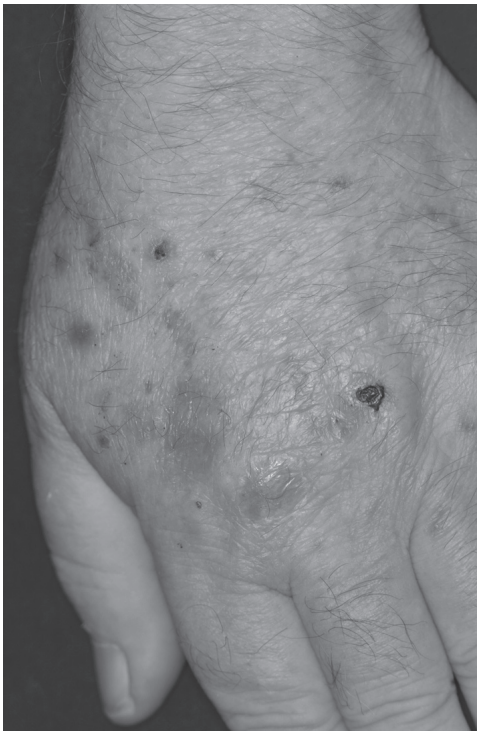

Fig. 1. Erosions and haemorrhagic crusts following recurrent blisters on the dorsal aspect of the left hand in a 65-year-old man with haemodialysis-associated pseudoporphyria.

but separation and identification of porphyrins by thin-layer chromatography revealed normal uroporphyrins (20%; normal, 0–20%) and protoporphyrins (80%; normal, 0–80%). The diagnosis of haemodialysis-induced pseudoporphyria was made and the patient started on oral N-acetylcysteine (200 mg q.i.d.) accompanied by topical steroids for one week. Furthermore, conventional haemodialysis 3 times/week low flux (< 250 ml/min) was replaced by haemodialysis 3 times/week high flux (300 ml/min) using a polysulphone membrane. Skin lesions resolved completely 3 weeks after initiation of N-acetylcysteine (Fig. 3). Despite stopping N-acetylcysteine after 5 weeks, no recurrence of blistering has been observed during a follow-up period of 24 months under continued application of high-flux haemodialysis.

DISCUSSION

Both pseudoporphyria and porphyria cutanea tarda may occur in patients with chronic renal failure under haemodialysis (1–3, 9). Cutaneous changes of the two conditions are clinically and histopathologically similar, but differentiation is possible by their different porphyrin profiles (3, 6, 10). Proposed trigger factors for haemodialysis-induced pseudoporphyria include various drugs (diuretics, nifedipine, aluminium hydroxide, erythropoietin), haemosiderosis, hepatitis C infection, polyvinyl chloride dialysis tubing, and silicone particles (6). Erythropoietin is unlikely to be the major culprit as pseudoporphyria often occurs before its introduction (6). It has also been postulated that chronic renal failure patients under dialysis are more susceptible to free-radical injury, because of defective antioxidant mechanisms, which is reflected by decreased levels of glutathione (a potent antioxidant) in plasma and circulating erythrocytes (7, 11). Treatment of pseudoporphyria includes avoidance of possibly inducing drugs and UV exposure, and the application of topical steroids (6). Effective long-term therapy with oral N-acetylcysteine, a metabolic precursor of glutathione, has recently been reported in haemodialysis-associated pseudoporphyria (7, 11). Its discontinuation, however, quickly led to recurrence of blistering (7, 11).

We report here a 65-year-old man who developed blisters on both hands during conventional haemodialysis 3 times/week for chronic renal failure due to Waldenström's macroglobulinaemia. Clinicopathological correlation, chromatographic porphyrin analysis,

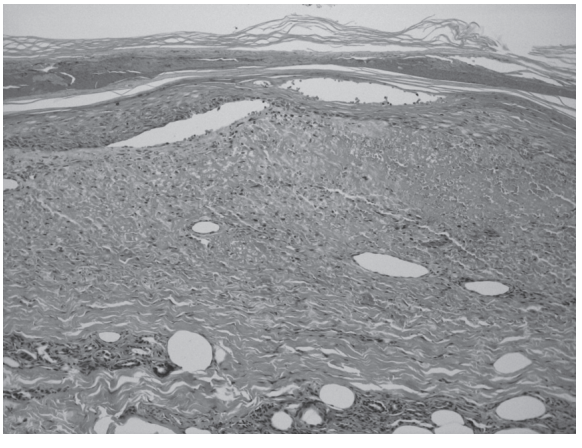

Fig. 2. Histopathological examination of lesional skin reveals subepidermal blister formation with intracorneal haemorrhages without an inflammatory infiltrate in the dermis (haematoxylin and eosin (HE) ×40).

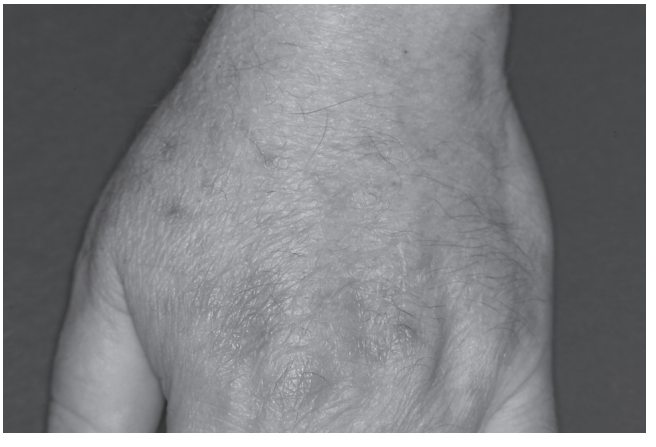

Fig. 3. Complete resolution of skin lesions 3 weeks after therapy with oral N-acetylcysteine and switch to high-flux membrane dialysis.

and the absence of other trigger factors led to the diagnosis of haemodialysis-induced pseudoporphyria. The patient was given oral N-acetylcysteine for 5 weeks, and conventional 3 times/week low-flux (< 250 ml/min) haemodialysis was switched to high blood flow (300 ml/min) polysulphone membrane haemodialysis. High-flux haemodialysis has been effective in porphyria cutanea tarda of chronic renal failure patients under dialysis (12), but so far not been used in pseudoporphyria. The combined approach with N-acetylcysteine and high-flux haemodialysis led to rapid clearing of our patient's skin manifestations. Blisters did not relapse during 2 years after discontinuation of N-acetylcysteine, when the patient was maintained on high-flux haemodialysis only. Thus, the high-flux mode seems to be capable of treating and even preventing haemodialysis-associated pseudoporphyria. This effect could be due to the recently described influence of high-flux haemodialysis on oxidant and carbonyl stress-related apoptosis and cytokine induction by activated complement (13, 14).

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