Pseudoporphyria or Porphyria Cutanea Tarda? Diagnostic and Treatment Difficulties

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Sir,

Porphyria cutanea tarda (PCT) is a vesiculobullous skin disorder of heme biosynthesis in which there is an enzyme defect of uroporphyrinogen decarboxylase (Uro-D), leading to accumulation of porphyrins mainly in urine but also in stool and plasma.

Pseudoporphyria is clinically similar to PCT, but usually lacks the biochemical abnormalities, and is difficult to distinguish clinically and histologically. This case report shows how challenging differential diagnosis between PCT and pseudoporphyria can be, especially in the setting of renal failure and haemodialysis, and it emphasizes the treatment difficulties with renal failure patients and pseudoporphyria. A qualitative and quantitative examination of urine, plasma and stool porphyrins and Uro-D enzyme test in red blood cells is required.

CASE REPORT

An 81-year-old man was referred to our dermatology department with known renal failure due to proliferative glomerulonephritis and was treated with high-flux haemodialysis three times a week. In addition, he had diabetes mellitus type-2, Waldenström's macroglobulinaemia not requiring treatment, and had been cardiac bypass operated.

His medications were: warfarin (Marevan®), glimepiride (Amaryl®), carvedilol (Kredex®), sevelamer (Renagel®), pantoprazole (Somac®), insulin injections (Insulatard®) and darbepoetin alfa (Aranesp®).

He had several erosions on the dorsal sides of both arms and hands (Figs 1 and 2) in addition to an intact blister on his right hand with clear fluid. Histology of the blister showed subepidermal bulla with vessel changes and fibrosis in the dermis.

Immunofluorescence showed homogeneous deposits of IgG in vessel walls in the dermis and weaker deposits of C3, and IgM and IgA

Blood and faecal tests were analysed for porphyrins. Unfortunately, the first set of tests had not been delivered light-protected. The tests were nevertheless analysed, but with the limitation that the values could be too low. The patient had not been able to produce enough morning urine due to his renal failure; therefore the urine test could not be performed.

Tests were positive for plasma porphyrins, but with plasma fluorescence at 616 nm and emission peak at 330 mV (excitation 405/emission 616 nm). PCT usually has plasma fluorescence of 618–622 nm and higher peak value. Uro-D activity was 1.9 IU/l erythrocytes (normal: 1.2–2.2 IU/l erythrocytes) and there were no mutations found in the Uro-D gene. Faecal porphyrins were normal.

A second set of light-protected tests were taken and urine was collected over 2 days while light protected. The results showed no porphyrins in the urine or faeces, but porphyrins in the plasma. This time plasma showed fluorescence at 617 nm, before haemodialysis and there was no significant reduction in plasma peak in the sample taken directly after haemodialysis (peak 398 mV).

Our patient refrained from drinking alcohol and was HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) negative. He had normal haematological parameters, liver enzymes, ferritin and total iron-binding capacity. Only his renal tests were out of the normal range; creatinine: 585 (60–105), urea: 14.4 (3.5–8.1) glomerular filtration rate: 9 ml/min/1.73m^2 (60–114).

Considering pseudoporphyria the most likely diagnosis, we started treatment with N-acetylcysteine (Muco-

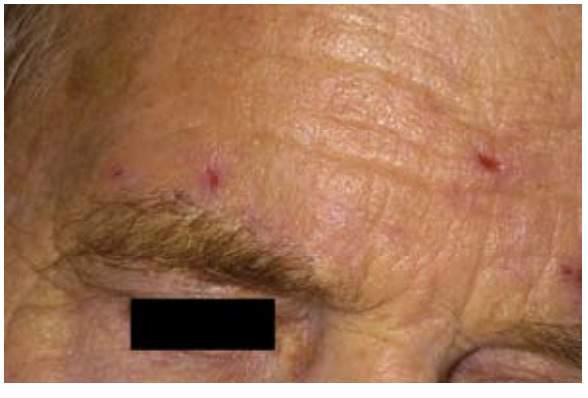

Fig. 1. Erosions on the forehead.

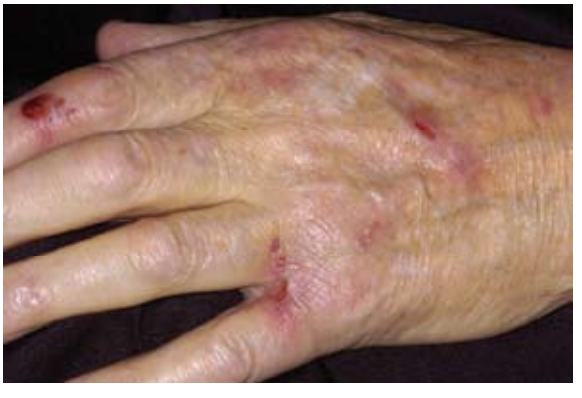

Fig. 2. Erosions, milia and scarring on the dorsum of the hand.

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myst®) 400 mg×2 day based on previous aspects (1–3). After 3.5 months of treatment there was no improvement in his skin lesions, and treatment was stopped. We decided to test hydroxychloroquine (Plaquenil®) because of uncertain diagnosis and difficulties in differentiation between pseudoporphyria and PCT. He was started on 200 mg tablets once a week. This therapy did not have any impact on his skin problems and therapy was stopped after 3 months.

DISCUSSION

The patient proved to be a diagnostic problem, and even more difficult to treat when the presumed diagnosis was pseudoporphyria. Usually a morning urine sample of 20 ml is analyzed for porphyrins, but due to severe renal failure and anuria this was difficult. Due to the first tests not being light-protected, and urine collected over 3 days in the other sample (light-protected) there was some uncertainty about whether the tests were representative. The main problem was the elevated plasma porphyrins with fluorescence slightly outside the normal range for PCT (618–622 nm), and with an emission peak with a lower amplitude than what is usual in PCT.

Considering the cause of his skin problems pseudoporphyria, it was most likely due to his renal failure and inadequate haemodialysis of porphyrins (4–7). Although the exact mechanism of pseudoporphyria in association with renal failure is not known, there are several theories, such as inadequate clearance of porphyrins due to renal failure and due to that porphyrins have too high molecular weight to be cleared by the haemodialysis membrane (2). Azotaemia has also been suggested to reduce the activity of uroporphyrinogen decarboxylase resulting in increased plasma porphyrins (7). He did not take any medications that are known to elicit pseudoporphyria (8, 9). Erythropoietin is listed as a medication that may elicit pseudoporphyria in one article, but was suggested as treatment for pseudoporphyria in another (10, 11). There is disagreement on whether pseudoporphyria has a completely normal porphyrin profile or may have elevated plasma porphyrins, especially in the setting of renal failure (1–5, 7, 10, 12–15). Hydroxychloroquine is thought to form complexes with porphyrins that are cleared by the kidneys (4). Therefore, one would not expect it to help relieve symptoms with renal failure patients on haemodialysis, because the complexes would be of too high molecular weight to be cleared by the dialysis membrane (7). Failure of improvement during hydroxychloroquine treatment also supports our diagnosis of pseudoporphyria. Unfortunately he did not respond to treatment with N-acetylcysteine, and we were therefore left only with symptomatic treatment for his skin lesions.

In general, vesiculobullous skin disorders may be a diagnostic problem in patients with renal failure undergoing haemodialysis. It is important to make a full porphyrin investigation of plasma, stool and, if possible, urine, although this may be difficult with anuric patients. Further investigations are needed to find a proper treatment for patients with pseudoporphyria, especially in the setting of renal failure and haemodialysis.

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