A 56-year-old female developed, at the age of 51 years, chronic renal failure and was started on continuous ambulatory peritoneal dialysis (CAPD). She had recurrent pyelonephritis and underwent bilateral nephrectomy. One month after nephrectomy, the patient started suffering from fragility of her skin, with easy breaking on minimal trauma, painful blisters, hypertrichosis, and milia on sun-exposed areas. Her skin symptoms lasted all through the summer and remitted in the winter to relapse again in May the following year. Her medications were omeprazole, cisapride, senna, alfacalcidol, calcium and folic acid.

Her autoantibody screen profile was negative. Serum porphyrin screen showed an extremely high total porphyrin concentration of 664 nmol/l (normal: <11.2). As the patient was anuric, a faecal porphyrin sample was analysed and revealed a total isocoproporphyrin concentration of 159 nmol/g (normal: <200). No dialysate porphyrin profile was taken. Skin biopsy of the blisters showed only mild inflammation.

At the age of 55, the patient had a cadaveric renal transplant and was immunosuppressed with prednisone, cyclosporin and sirolimus. Her plasma creatinine fell to 110 μmol/l. A 24-h urine sample was collected for porphyrin analysis, and revealed a total porphyrin of 2061 nmol/24 h (normal: <410). Urinary 5-aminolaevulinic acid (ALA) levels were 4.8 μmol/mmol creatinine (normal: <3.8) and porphobilinogen (PBG) was 24.2 μmol/mmol creatinine (normal: <1.5). Faecal total porphyrins were in the normal range.

Cyclosporin was stopped and the patient was maintained on sirolimus and prednisone. A random urine sample showed that the concentration of ALA was 5.4 μmol/mmol creatinine (normal: <3.8) and PBG was 10.8 μmol/mmol creatinine (normal: <1.5). The patient was followed-up the next summer, with no recurrence of her blisters.

Questions

- What is the differential diagnosis of skin blisters in dialysis patients?
- What are the diagnoses before and after transplantation?
- What is the cause of elevation in ALA and PBG after transplantation?
Answers to the quiz on the previous page

This dialysis patient presented with skin blisters. Bullous dermatoses are well documented in patients with end-stage renal disease (ESRD). They have been divided classically into three groups: (i) the true porphyrias including porphyria cutanea tarda (PCT), variegate porphyria and hereditary coproporphyria; (ii) ‘pseudoporphyria’, which includes photosensitizing drugs (e.g. furosemide and naproxen), icodextrin peritoneal dialysis [1,2] and pseudoporphyria of renal failure (PRF), which is secondary to accumulation of non-dialysable porphyrins and their derivatives in the serum of dialysed patients; and (iii) other dermatoses that coincidentally happen in a renal failure patient (e.g. pemphigus vulgaris and epidermolysis bullosa) that can be diagnosed on the basis of skin biopsy [3].

The pre-transplant porphyrin profile (extremely high total porphyrin concentration of 664 nmol/l) of this patient was compatible with PCT/PRF. However, as the patient was anuric and had negative faecal coproporphyrins, we could not differentiate between these two entities. Common to both conditions is the accumulation of photosensitizing chemicals in the skin leading to skin blisters. In retrospect, as the patient improved after transplantation with no recurrence of her symptoms, it became clear that she was suffering from PRF.

The porphyria profile (elevated ALA and PBG) after transplantation was compatible with acute intermittent porphyria (AIP). Cyclosporin is a porphyrinogen and known to precipitate AIP attacks. In our case, on cyclosporin, the total porphyrins increased and reached 2061 nmol/24 h in the urine with high ALA and PBG whereas, after cyclosporin was stopped, plasma porphyrins returned to near normal values.

Discussion

The porphyrias are genetic or acquired deficiencies in the activity of enzymes in the haem biosynthetic pathway [4]. As a result of this enzymatic deficiency, metabolic intermediates are produced and excreted in excess, accumulate in tissues and result in neurovisceral (e.g. abdominal pain), psychiatric disorders and neurological symptoms such as AIP and/or photosensitive symptoms PRF/PCT. The diagnosis of each disorder is made by identifying the metabolite(s) produced or excreted in excess in red cells, plasma, urine and/or faeces. In many of the porphyrias, the diagnosis can be confirmed by directly measuring the enzyme activity in question in the appropriate tissue(s) and by the molecular analysis of the haem biosynthesis genes.

Porphyrias have been classified clinically as ‘acute’ and ‘non-acute’, depending upon the principal symptoms and signs they produce. These disorders are well defined at the molecular level. However, due to the overlap between the clinical signs and the molecular defect, they are best classified in terms of both the specific enzyme deficiencies and the tissues involved.

In this report, we presented a case of an anephric patient whose clinical manifestation (skin eruptions) and initial porphyria studies were consistent with PCT/PRF of renal failure. However, after renal transplantation, a repeat porphyrin profile confirmed the presence of AIP. Full evaluation of dialysis patients with suspected porphyria can be challenging. As acute porphyria attacks can be life-threatening, and precipitated by porphyrinogenic medications (e.g. cyclosporin A), correct and early diagnosis is important.

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References


Ali A. Haydar
Nabil Hujairi
Paramit Chowdhury
James Pattison
Allan Deacon
Robert Sarkany
David J. A. Goldsmith
1Renal and Transplantation Unit, Guy’s Hospital,
2SAS Porphyria Laboratory, King’s College Hospital,
3Photobiology Department, St John’s Dermatology Hospital, London, UK
Email: david.goldsmith@gstt.sthames.nhs.uk