SHORT REPORTS

Sulphinpyrazone-induced acute renal failure

Many drugs have been associated with acute renal failure, which may present as acute tubular necrosis, interstitial nephritis, glomerulonephritis, arteritis, or intrarenal tubular obstruction. We report on a patient who developed acute tubular necrosis while taking sulphinpyrazone.

Case report

A 57-year-old man with no history of renal disease presented with acute renal failure. He had a two-year history of gout, for which he had taken sulphinpyrazone, and sulphinpyrazone had been restarted one week before admission for a recurrence of the disease. Three days before admission he had developed bilateral loin pain and oliguria. His only other medications were digoxin, frusemide, and amiloride. Physical examination showed mild fluid overload but no other abnormality.

Initial blood urea concentration was 16.9 mmol/l (102 mg/100 ml) and creatinine 0.72 mmol/l (8.1 mg/100 ml). There was no eosinophilia. Urine microscopy showed microscopic haematuria but no casts. Intravenous pyelography showed slightly enlarged kidneys with faint but persistent nephrograms. Cystoscopy and retrograde pyelography disclosed no abnormality. A renal biopsy specimen showed a mild focal increase in mesangial cell nuclei and matrix. Proximal tubules were normal. Distal tubules contained densely staining proteinaceous casts. There were foci of tubular atrophy with basement-membrane thickening. A moderate increase in interstitial tissue, without inflammation, was seen. Medium-sized arteries showed moderate fibrous intimal thickening, but arterioles were normal (figure). Immuno-

Renal biopsy specimen. Masson's trichrome $\times 400$ (original magnification).

fluorescence tests showed only ++ C3 in small vessels and hilar arterioles. Serum complement values and protein electrophoresis and immunoelectrophoresis patterns were normal. Urine protein electrophoresis and immunoelectrophoresis showed no evidence of myeloma. Tests for rheumatoid factor, antinuclear antibody, hepatitis B antigen and antibody, syphilis serology, leptospira serology, antistreptolysin O, and urine culture were all negative. Twenty-four-hour urinary protein excretion was initially 2.7 g but 12 days after admission was 0.4 g.

Urine output was initially 40 ml/h and had increased to over 250 ml/h by the third hospital day without diuretics. The serum creatinine concentration rose to a maximum of 0.79 mmol/l (8.9 mg/100 ml) on the second hospital day and then declined steadily to 0.12 mmol/l (1.4 mg/100 ml) on the seventh day. All treatment apart from sulphinpyrazone was continued throughout the hospital stay (although digoxin was suspended during the episode of acute renal failure). Five weeks after admission he was well with a creatinine concentration of 0.11 mmol/l (1.2 mg/100 ml).

Comment

Sulphinpyrazone is a uricosuric and antiplatelet drug structurally related to phenylbutazone. It has recently been shown to decrease

the risk of sudden death after acute myocardial infarction.¹ Sulphinpyrazone-related acute renal failure has been reported only once but renal biopsy was not performed.²

In the present case of acute oliguric renal failure, acute tubular necrosis was found on biopsy with no evidence of acute interstitial nephritis. In addition there was no eosinophilia, rash, or fever to suggest an acute allergic phenomenon. The mechanism of this acute tubular necrosis is not clear but presumably represents acute tubular toxicity caused by the drug. The structural relation of sulphinpyrazone to phenylbutazone and the biopsy specimen changes in acute renal failure induced by phenylbutazone³ support a direct acute tubular toxicity by sulphinpyrazone. Other non-steroidal anti-inflammatory drugs, however, have been reported as causing acute allergic interstitial nephritis.⁴

Acute urate nephropathy is a possibility. This has been reported with another uricosuric drug, ticrynafen,⁵ although not with sulphinpyrazone or probenecid despite widespread use. In the present case serum urate values were high, but this was most probably a consequence of the renal failure rather than a cause. No urate crystals were seen on urine microscopy. Although the renal biopsy specimens were not fixed in alcohol, the changes were not suggestive of urate nephropathy.

In view of the increasing use of sulphinpyrazone we report this case as a warning of a potentially serious toxic effect.

¹ Anturane Reinfarction Trial Research Group. Sulfinpyrazone in the prevention of sudden death after myocardial infarction. *N Engl J Med* 1980;302:250-6.

² Braun J. Abnormalities of urinary sediment and renal failure following sulfinpyrazone therapy. *Arch Intern Med* 1976;136:1060-1.

³ Lipsett MB, Goldman R. Phenylbutazone toxicity: report of a case of acute renal failure. *Ann Intern Med* 1954;41:1075-9.

⁴ Brezin JH, Katz SM, Schwartz AB, Chinitz JL. Reversible renal failure and nephrotic syndrome associated with non-steroidal anti-inflammatory drugs. *N Engl J Med* 1979;301:1271-3.

⁵ Bennett WM, Van Zee BE, Hutchings R. Acute renal failure from ticrynafen. *N Engl J Med* 1979;301:1179-80.

(Accepted 19 November 1980)

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Peripheral corneal melting syndrome in association with psoriasis: a report of two cases

Peripheral corneal melting syndrome is a rare disease consisting of marginal corneal thinning, sometimes to the extent of perforation. It is most often seen in association with rheumatoid arthritis and is also described in Sjögren's syndrome, polyarteritis nodosa, and Wegener's granulomatosis,¹ but it may also occur in the absence of systemic disease. We describe two cases of peripheral corneal melting syndrome with psoriasis.

Case reports

CASE 1

A 62-year-old housewife was admitted to hospital as an emergency in March 1978 with a one-month history of generalised erythroderma, painful red eyes, blurred vision, and arthralgia affecting the neck, wrists, and shoulders. She had a 10-year history of stable, chronic plaque psoriasis affecting the knees and elbows, but the reason for its generalisation was not apparent. There was no other relevant previous medical, family, or drug history.

Examination showed generalised erythroderma with sheets of pustular psoriasis in many areas. She was icteric with gross ankle and sacral oedema and had synovial swelling of the wrists. During the first few days she was

intermittently febrile with episodes of toxic confusion. Her uncorrected visual acuity was 6/36 in each eye. There was considerable hyperaemia of the conjunctivae, which also affected the episclera.

Peripheral corneal melting syndrome was diagnosed by the finding of circumferential, peripheral, corneal ulcers (figure) that were infiltrated with inflammatory cells but appeared avascular.

Circumferential peripheral corneal ulcer highlighted by reflected light.

Investigations showed: haemoglobin 13.1 g/dl, leucocytes $17.8 \times 10^9/l$ (neutrophils $15.7 \times 10^9/l$ with many immature forms suggestive of a leukaemoid reaction; lymphocytes $2.1 \times 10^9/l$), plasma viscosity 2.19 mPa s (2.19 cp), plasma bilirubin 67 $\mu\text{mol/l}$ (3.9 mg/100 ml), alkaline phosphatase 65 KA units, aspartate aminotransferase 34 IU/l, plasma albumin 24 g/l, globulin 4.1 g/l, serum electrophoresis—raised α_1 - and α_2 -globulins, normal serum immunoglobulin concentrations, antinuclear factor titre 1/20, DNA binding <1%, HLA type A2, B15 W44. The rheumatoid arthritis latex test was negative and plain radiographs of joints showed no erosions.

She was treated with azathioprine 150 mg daily (body weight 65 kg) and prednisone 20 mg daily. No corticosteroid preparation was applied locally to the eyes. During the next two weeks the eye condition improved. The hyperaemia and infiltration disappeared, the cornea returned to normal thickness, and the ulcers re-epithelialised. The eventual uncorrected visual acuity of the right eye was 6/9 and of the left eye 6/36. After a further two weeks the blood neutrophil count had returned to normal with disappearance of immature forms. Results of liver function tests were also normal.

After six months' observation her psoriasis was controlled on azathioprine alone. There was no recurrence of peripheral corneal melting syndrome and regular blood counts were normal.

CASE 2

A 70-year-old man had suffered from chronic, extensor plaque psoriasis affecting the knees, elbows, sacrum, and scalp for 40 years. For 20 years he had had recurrent peripheral corneal melting syndrome, which was particularly severe in the left eye. Several operations had been necessary. The visual acuity of the left eye was reduced to perception of light only and the right eye could see hand movements. No systemic treatment had been used. He had recently suffered an attack of herpes zoster ophthalmicus on the right eye which seemed to encourage further erosions and marginal activity on the area of donated cornea. Investigations showed that HLA type was A1, A30, B8, B13.

Comment

Peripheral corneal melting syndrome is associated with connective tissue diseases such as rheumatoid arthritis, and psoriasis is associated with joint disease. We suggest that in our two patients the association between psoriasis and peripheral corneal melting syndrome was not coincidental. The first patient had arthralgia with evidence of synovitis, which may have been psoriatic arthritis, though erosions were not shown radiologically. We know of no cases of arthralgia due to generalised erythroderma, but it may be argued that the process (possibly an infection) which triggered this patient's erythroderma was responsible for the arthralgia.

The pathogenesis of peripheral corneal melting syndrome is unclear but corneal damage is probably mediated by collagenases.² However, cysteine, acetylcysteine, and penicillamine eye drops seem to be ineffective,³ while systemic azathioprine and prednisone may produce a valuable response in some patients.^{3, 4}

¹ Gudas PP Jr, Altman B, Nicholson DH, Green WR. Corneal perforations in Sjögren's syndrome. *Arch Ophthalmol* 1973;90:470-2.

- ² Berman M, Dohlman CH, Grading M, Davison P. Characterization of collagenolytic activity in the ulcerating cornea. *Exp Eye Res* 1971;11:255-7.
- ³ Jayson MIV, Easty DL. Ulceration of the cornea in rheumatoid arthritis. *Ann Rheum Dis* 1977;36:428-32.
- ⁴ Easty DL, Madden P, Jayson MIV, Carter C, Noble BA. Systemic immunosuppression in marginal keratolysis. *Trans Ophthalmol Soc UK* 1978;98:410-7.

(Accepted 26 November 1980)

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Vaginal manipulation and anaerobic breast abscesses

Anaerobic breast abscesses occur in non-puerperal women with inverted nipples, the organisms often being commensals of the vagina and oropharynx rather than the bowel.¹ We report three cases in which anaerobes of the vagina were isolated from breast abscesses after gynaecological manipulation.

Patients, methods, and results

Case 1—A 37-year-old Ghanaian woman with two children presented with a left breast abscess three days after hysterosalpingography. The nipple had been inverted for two years. Despite a course of antistaphylococcal antibiotics, drainage on two occasions, and a partial-thickness wedge resection of the affected area the breast continued to discharge foul-smelling pus. Examination of this showed the presence of *Bacteroides bivius* (on three occasions), *B melaninogenicus*, and peptococci. A high vaginal swab grew a mixture of aerobic and anaerobic organisms including *B bivius*, *B melaninogenicus*, and peptococci. Full-thickness wedge resection and metronidazole 400 mg thrice daily for seven days were effective in treating the infection.

Case 2—A 46-year-old Caucasian woman presented with a right sub-areolar breast abscess that had developed two weeks after dilatation and curettage for menorrhagia and had failed to respond to tetracycline prescribed by her family doctor. Both nipples had been inverted since birth. Foul-smelling pus drained spontaneously and yielded *B bivius*, peptostreptococci, peptococci, and fusobacteria on culture. No anaerobes were isolated from a high vaginal swab, which was taken during a course of metronidazole. The abscess resolved after drainage and metronidazole 400 mg thrice daily for seven days, and had not recurred after 18 months.

Case 3—A 22-year-old Caucasian woman presented with a left breast abscess three weeks after a postnatal vaginal examination. Neither nipple was inverted and she was not breast-feeding. Treatment with flucloxacillin proved ineffective and the abscess discharged spontaneously. Pus grew *B corrodens*, *B bivius*, *B melaninogenicus*, and peptococci. The infection recurred six months later and was treated with erythromycin by her family doctor. No high vaginal swab was taken.

Comment

Anaerobic breast abscess is usually seen in non-puerperal women of childbearing age with an inverted nipple. In two of our patients surgical trauma of the upper vagina and cervical region had occurred, and vaginal examination had been performed in the third during the puerperium.

It has been reported that 10% of bacteraemias occurring in hospital are caused by anaerobes² and that even sigmoidoscopy may produce transient *B fragilis* in the blood.³ Possibly disturbance of the upper vagina in our three cases may have caused a transient bacteraemia. Although the organisms grown may also be present in the oropharynx, our cases would seem to provide circumstantial evidence that they originated from the female genital tract. Inversion of the nipple