Acute interstitial nephritis associated with gentamicin and lincomycin therapy

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Summary
A case of acute oliguric renal failure following gentamicin and lincomycin therapy is described. Renal biopsy showed an acute interstitial nephritis. This was associated with high serum gentamicin levels and the later development of ototoxicity. Withdrawal of antibiotics and conservative measures was followed by rapid recovery of renal function. Attention is drawn to the association between gentamicin and lincomycin therapy and the development of an acute interstitial nephritis.

Introduction
Acute interstitial nephritis has been documented during chemotherapy with the penicillins (Gilbert et al., 1970), ampicillin (Woodroffe et al., 1975), methicillin (Baldwin et al., 1968), carbenicillin (Appel and Neu, 1977), rifampicin, sulphamides (Black-Schaffer, 1945) and, in a recent report, after numerous agents including co-trimoxazole and gentamicin (Saltissi, Pusey and Rainford, 1979).

In this report, the authors describe the characteristic histological features of interstitial nephritis in a patient receiving gentamicin and lincomycin. They believe that there has been no previous report of this association with lincomycin and only one with gentamicin.

Case report
A 71-year-old woman was admitted with a 4-day history of increasing tiredness, generalized aches and pains and a transient macular rash on her chest, back and hips. She had received no drugs before admission. Her temperature was 38°C, pulse 100/min and BP 100/70 mmHg. Abdominal examination revealed minimal tenderness on deep palpation in the left iliac fossa; rectal and vaginal examinations localized the tenderness to the left iliac fossa. There were no abnormal findings in the chest. A midstream specimen of urine was sterile, with no proteinuria or haematuria and urine microscopy showed no red cells or casts. Plain X-ray films of chest and abdomen were normal.

Hb, 14.5 g/dl; WCC, 8.9 x 10³/l; differential WCC neutrophils, 83%; lymphocytes, 8%; monocytes, 6%; eosinophils, 2%; basophils, 1%. ESR, 7 mm in 1st hr (Westergren). Liver function tests, normal; plasma urea, 10 ml/l; electrolytes normal; plasma proteins and serum protein electrophoresis, normal; ANF and Rose-Waaler test, negative; serum immunoglobulins, serum complement C3—C4 concentrations, normal; ASO titre, anti-DNA antibody titre, not elevated; HBsAg negative. In view of the possibility of intra-abdominal abscess and bacteraemia she was started on day one of her hospital admission, on gentamicin 80 mg i.v. every 8 hr and lincomycin 300 mg i.m. every 6 hr. The trough level on day 3 of gentamicin was 7 µg/ml. On day 4 she developed oliguric renal failure; urine output was 25 ml/hr; urine osmolality, 300 in osmol/kg. Plasma urea, 19 mmol/l; Na, 123 mmol/l; K, 4.9 mmol/l; Cl, 96 mmol/l; CO₂, 18 mmol/l. High dose i.v. urography demonstrated normal-sized kidneys with no evidence of obstructive uropathy. Measures implemented on day 4 were the i.v. administration of 250 mg of frusemide, dietary protein and oral fluid restriction, and discontinuation of gentamicin and lincomycin.

Repeated bacteriological culture of blood and urine were sterile. A viral serological screen was negative. Examination of the stool showed no significant pathogens. She did not develop peripheral blood eosinophilia, nor microscopic haematuria. Urinary protein loss averaged 0.37 g/24 hr. On day 11, 7 days after discontinuation of gentamicin and lincomycin, percutaneous renal biopsy was performed and showed the characteristic features of acute interstitial nephritis.

The most striking appearance was an intense infiltrate of neutrophils, plasma cells and lymphocytes in the medulla. There was interstitial oedema and many tubules showed degenerative changes (Fig. 1). Electron microscopy revealed focal lesions in the
proximal tubules in which numerous cytosegresomes containing laminar aggregates were seen, as well as dilated endoplasmic reticulum and swollen and disrupted mitochondria (Fig. 2).

On day 14, plasma urea was 40 mmol/l (240 mg/100 ml) and plasma creatinine 1:07 mmol/l. Her urine output subsequently increased to 50 ml/hr; with a urine osmolality of 600 mosmol/kg. Plasma urea fell to 20 mmol/l (120 mg/100 ml) on days 34 and 81, plasma urea was 10 mmol/l and plasma creatinine 0:36 mmol/l. During convalescence she was noted to have marked bilateral nerve deafness and vestibular dysfunction.

Discussion

This patient's acute interstitial nephritis was not associated with haematuria, blood or tissue eosinophilia or heavy proteinuria, features which, though commonly present, have been absent in some cases (Saltissi et al., 1979).

Although frusemide has been implicated in this type of kidney reaction (Lyons et al., 1973; Fuller,
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Barcenas and White, 1976; Fialk et al., 1974), it has only been noted in patients with prolonged exposure to the drug and never from a single dose as in this patient.

The acute renal failure in this patient was shown by biopsy to be due to acute interstitial nephritis. This developed following administration of gentamicin and lincomycin and resolved promptly after withdrawal of these drugs. Interstitial nephritis in association with gentamicin has been reported previously (Saltissi et al., 1979) and the high serum levels and ototoxicity observed in this case lend support to such a pathogenesis. In addition, the tubular changes noted on electron microscopy, although relatively non-specific, resemble those described in rats given gentamicin (Vera-Roman, Krishankantha and Cuppage, 1975; Kurtz and Feldman, 1962). A search for viral or bacteriological agents which might have accounted for renal lesion proved negative.

It is suggested that gentamicin and lincomycin, acting singly or together, produced acute renal failure due to acute interstitial nephritis which proved reversible on withdrawal of the drugs.

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