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Short reports

Rifampicin induced light chain proteinuria and renal failure

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Light chain proteinuria is a recognised cause of renal disease and renal failure.[1] In 1973 Graber *et al* described light chain proteinuria occurring in patients given rifampicin[2] and there have since been two case reports of renal failure due to rifampicin induced light chain proteinuria.[3,4] We report a third case, which with that of Warrington and others[3] suggests that dehydration predisposes to this rare complication of rifampicin treatment.

Case report

A 57 year old man presented with a three week history of haemoptysis and weight loss of 10 kg over nine months. His serum creatinine concentration was 45 μmol/l, blood urea 9·5 mmol/l, plasma sodium 126 mmol(mEq)/l. Plasma and urine osmolalities were 267 and 685 mmol(mosm)/kg respectively. There was no proteinuria. A chest radiograph showed bilateral abnormal shadowing and direct smears of sputum stained positively for alcohol and acid fast bacili.

Antituberculous treatment was started with rifampicin 600 mg, isoniazid 300 mg, and ethambutol 900 mg daily. For the first five days after presentation ampicillin (2 g/day) was also given. He developed increasing confusion, which was attributed to the syndrome of inappropriate antidiuretic hormone secretion. Fluid restriction (800 ml/24 h) was started, and demeclocycline (600 mg/day) given. After nine days he developed an urticarial rash and all drugs were stopped; at that time renal function was normal and the plasma sodium concentration 129 mmol/l. Antituberculous treatment was restarted after three days and restriction of fluids to 800 ml a day continued.

During the following month he showed a response to antituberculous treatment. At this time his blood urea and urine output were normal, although proteinuria was noted. Six weeks after antituberculous chemotherapy had been restarted, however, he was found to be in renal failure, with a serum creatinine concentration of 730 μmol/l (8·26 mg/100 ml) and blood urea of 26 mmol/l (156·6 mg/100 ml). He was transferred for further investigation. There were red blood cells and tubular casts in the urine and proteinuria of 2·6 g in a 24 hour volume of 1100 ml. Immunoelectrophoresis of the urine showed free polyclonal K and λ light chains and trace albumin. A direct antiglobulin test was weakly positive but there were no rifampicin dependent antibodies.

A renal biopsy was carried out and showed an inflammatory infiltrate composed of plasma cells, lymphocytes, and eosinophils. The glomeruli were normal. The interstitial tissue was oedematous and there was widespread evidence of tubular atrophy. The tubules contained casts; immunohistochemical staining techniques showed these to be composed of light chains. There was no evidence of amyloid.

Treatment with rifampicin was stopped and oral prednisolone was given at an initial dose of 60 mg/day. There was a rapid recovery of renal function and one month later the serum creatinine concentration was 135 μmol/l (1·5 mg/100 ml) and there was no proteinuria.

Discussion

Rifampicin induced interstitial nephritis appears to be of two types. The form described in our patient is probably less common, has a gradual onset, and is associated with light chain nephropathy. The other type is more characteristic of a drug induced interstitial nephritis, being of abrupt onset and associated with systemic symptoms, occurring typically when the drug is restarted after an interruption of treatment.[5,6] A strongly positive direct result from the antiglobulin test with rifampicin dependent antibodies may be found in these patients.[7]

Ampicillin, a recognised cause of interstitial nephritis, may have been responsible for the rash seen shortly after presentation. The absence of associated fever, eosinophilia, disturbance of renal function, or haematuria at this time, however, makes this an unlikely cause of the renal impairment seen in our patient. Tubular disorders have been reported following demeclocycline but interstitial nephritis is not known to occur. Recovery of renal function in our patient was seen only when rifampicin was stopped, two months after he had last received ampicillin and demeclocyline. This close temporal relationship between stopping rifampicin and recovery of renal function, together with the presence of significant light chain proteinuria and the biopsy appearances of tubular casts containing light chains, is highly suggestive of a direct association between rifampicin associated proteinuria and renal damage.

Heterogeneous light chain proteinuria has been demonstrated in patients receiving rifampicin but has not been found in those being treated with other antituberculous chemotherapy.[2] The exact mechanism for this is not known but it is postulated that rifampicin interferes with heavy chain synthesis making that portion of the immunoglobulin molecule unavailable for combination with light chains, with a resultant spillover of the latter in the urine.

Light chains have been shown to inhibit metabolic

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activity of rabbit renal slices in vitro[8] and in man disorder of both proximal and distal tubular function is known to accompany light chain proteinuria.[1] Rifampicin induced light chain proteinuria has been implicated in the pathogenesis of nephritis in two previous reports.[3,4] In these, as in our patient, systemic symptoms were absent, antibodies to rifampicin were not detected, and where appreciable impairment of renal function was seen it had developed over several weeks. Renal biopsy had been performed in one patient,[3] but streptomycin had been administered concurrently and thus this could not be excluded as a cause of the renal impairment.

This case demonstrates a clinically important mechanism by which rifampicin may cause renal damage. Dehydration in such patients would be expected to increase the tubular concentration of light chains and may have been an important factor contributing to the impairment of renal function. Hyponatraemia is commonly seen in extensive pulmonary tuberculosis, but is very rarely of clinical importance and fluid restriction in such patients treated with rifampicin may increase the risk of light chain mediated renal failure. We suggest that fluid restriction for treatment of the syndrome of inappropriate antidiuretic hormone secretion should be avoided wherever possible in patients receiving rifampicin.

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