Case reports

References


Treatment of pulmonary tuberculosis in a patient on maintenance haemodialysis

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Summary

A case of pulmonary tuberculosis in a patient on maintenance haemodialysis is reported. A 37-year-old man who had received intermittent haemodialysis for 5 years, developed pulmonary tuberculosis which was treated initially with isoniazid, sodium aminosalicylate (PAS) and rifampicin. Isoniazid and PAS were discontinued and treatment continued with rifampicin alone. One year later, the patient is well, has no evidence of active tuberculosis and undertakes his own dialysis at home.

Introduction

Pulmonary tuberculosis is a serious and not uncommon complication of chronic renal failure treated by maintenance haemodialysis (Brunner et al., 1972). Adequate therapy for the condition is difficult to assess clinically as the major therapeutic agents, including streptomycin, sodium aminosalicylate (PAS), isoniazid and ethambutol, are normally excreted in the urine (Welch, 1954) and produce important toxic effects if blood levels become elevated. Thus, in oliguric or anuric patients, safe and effective
therapy is possible only when the blood levels of these drugs are routinely measured.

Rifampicin, however, is excreted in the bile and does not accumulate in the serum of anuric patients (Spring, 1968). The value of this drug in the treatment of pulmonary tuberculosis in a patient on maintenance haemodialysis is illustrated in the following case report.

Case report

Mr W. R., a 37-year-old electrician with chronic glomerulonephritis, was started on maintenance haemodialysis in April 1967. He was dialysed for 14 hr twice weekly on a flat bed dialyser with a surface area of 1 m² and remained well for 5 years; then he developed a non-productive cough with increasing dyspnoea. Despite repeated investigations, no diagnosis was made at this time but in June 1972 a chest radiograph revealed patchy, ill-defined areas of consolidation (Fig. 1) and acid-fast bacilli were demonstrated in the sputum. Μ. tuberculosis was subsequently cultured. Haemodialysis treatment was increased to 10 hr thrice weekly and therapy was started with isoniazid 200 mg and PAS 8 g as Pasinah-D and rifampicin 600 mg daily. Blood levels of PAS, measured 8 hr after the administration of the drug by a modification of the method of Bratton and Marshall (1939) varied between 8 mg/100 ml and 10 mg/100 ml; this exceeds the therapeutic range defined by Emerson and Kuper (1964). PAS dosage was accordingly reduced to 4.5 g daily and satisfactory serum levels of between 2 mg/100 ml and 4.5 mg/100 ml before dialysis were recorded. Serum rifampicin levels measured before dialysis by a bioassay method using Sarcina lutea as the test organism (Jeannes, Jessamine and Eidus, 1972) were between 3-75 μg/ml and 4 μg/ml and thus were within the therapeutic range (Spring, 1968).

The M. tuberculosis cultured from the sputum was shown in vitro to be sensitive to all the commonly prescribed agents but was particularly sensitive to rifampicin. Two months after commencing treatment, the patient developed severe diarrhoea, PAS and isoniazid were withdrawn, treatment was continued with rifampicin alone and the diarrhoea gradually improved. As the reintroduction of PAS coincided with a further exacerbation of the gastrointestinal symptoms, treatment with this drug was finally discontinued and the patient experienced no further bowel upset. At this time, however, a pericardial effusion was detected (Fig. 2) and the patient's condition deteriorated. This effusion was considered to be tuberculous, not uraemic in origin, as the blood urea levels before dialysis did not exceed 177 mg/100 ml. Despite the relatively short duration of therapy, the possibility of a drug-induced lupus syndrome produced by either isoniazid or PAS was considered.

![Fig. 1. Chest radiograph showing patchy, ill-defined areas of consolidation.](http://pmj.bmj.com/)

![Fig. 2. Chest radiograph showing pericardial effusion.](http://pmj.bmj.com/)
(Alarcon-Segovia, 1969). However, LE cells were not detected in the peripheral blood and the antinuclear factor was consistently negative. During the following 2 months the effusion began to diminish and 7 months after starting anti-tuberculous therapy the patient was able to start training for home dialysis. He remains well; his chest X-ray has returned almost to normal (Fig. 3) and acid-fast bacilli have not been isolated from the sputum during the past 12 months. The patient now undertakes his own haemodialysis at home thrice weekly and continues on rifampicin 450 mg daily.

**Fig. 3.** Chest radiograph after successful chemotherapy.

**Discussion**

The treatment of pulmonary tuberculosis in patients on maintenance haemodialysis is complicated by the potential toxicity of the commonly prescribed anti-tuberculous drugs. Streptomycin, which is largely excreted in the urine (Welch, 1954), has been reported to produce vestibular damage in a patient on haemodialysis at a time when serum levels of the drug were not elevated and when a total dose of only 11 g had been administered (Ogg, Toseland and Cameron, 1969). Thus streptomycin, even when blood levels are carefully monitored, cannot be regarded as a safe drug in patients with diminished renal function. Ethambutol, a powerful drug with well documented anti-tuberculous activity both *in vitro* and *in vivo* has been widely used in the treatment of pulmonary tuberculosis in recent years. Retrobulbar neuritis and visual impairment are, however, not infrequent side effects of therapy (Garrod and O’Grady, 1971); indeed it has been suggested (Wechsler, 1971) that not only should blood levels of the drug be monitored routinely but also that all patients should have complete eye examinations before and during treatment. As excretion is by the kidneys (Wechsler, 1971), ethambutol may not be administered with safety to patients with renal failure.

Isoniazid is only partially excreted in the urine and thus an accumulation of potentially toxic metabolites which cannot be monitored is an important possibility (Ogg et al., 1969): generalized seizures have been reported following isoniazid therapy for tuberculosis in a patient with uraemia (Aach and Kissane, 1972). It has been suggested recently that the acetylation phenotype of the individual is more important than renal function in determining the serum half-life of isoniazid (Bowersox et al., 1973). However, as the phenotype cannot be definitely established in patients with renal failure, these patients should be considered to be ‘slow acetylators’ and the dose of isoniazid reduced accordingly (Bowersox et al., 1973). PAS, however, although not a potent drug, is excreted mainly by the kidneys, and is an acceptable therapy, provided that the daily dosage is reduced and blood levels routinely monitored (Ogg et al., 1969).

Rifampicin has none of these toxic effects and may be given in normal dosages (450–600 mg daily) to patients with impaired renal function. The drug is excreted mainly in the bile and abnormalities of liver function tests have been reported after prolonged use (Jeannes et al., 1972; Lees, 1970). None was observed in this case. Blood levels need not be monitored but, as the drug is dialysable, it should be administered after dialysis. Multiple drug therapy has been conventionally recommended in the treatment of tuberculosis because of the rapid emergence of drug-resistant mutants of *M. tuberculosis*. Although such mutants are less likely to develop during therapy with rifampicin than with other agents (Canetti, 1968) and although the proportion of strains resistant to rifampicin is low (Grumbach and Rist, 1967), this potential problem must be considered and weighed against the known toxicity of the remaining agents. It is suggested that these drugs be administered only after a therapeutic trial of rifampicin has proved ineffective. Rifampicin should thus be considered as a drug of first choice in the treatment of pulmonary tuberculosis in patients on maintenance haemodialysis.

**References**


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