Azotaemia Aggravated by Tetracycline

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Summary : Oxytetracycline given to two patients with impaired renal function produced clinical deterioration and increasing azotaemia. Both patients improved when oxytetracycline was stopped. In general tetracycline should not be used in patients with poor renal function, but if it is necessary the blood urea level should be checked frequently.

Introduction

Although it is well established that tetracycline given to patients with diminished renal function may raise the blood urea (Bateman *et al.*, 1952; Wray *et al.*, 1965; Hanson, 1968), the dangers of using this drug under such circumstances do not seem to be sufficiently widely known. We therefore report two further instances in which tetracycline caused a rise in blood urea accompanied by pronounced deterioration in the patients' clinical state, the reason for which was not immediately appreciated.

Case 1

A 50-year-old man was admitted to hospital with a six-week history of left-sided loin pain and haematuria. For six months he had had increasing frequency of micturition and nocturia. Three weeks before admission he developed a cough productive of brownish blood-streaked sputum. On examination he was found to have malignant hypertension; his blood pressure was

FIG. 1.—Effect of tetracycline in Case 1, showing the rise in blood urea and blood pressure, and the fall in weight when the antibiotic was started. Note the weight gain and fall in haematocrit value attributable to rehydration when tetracycline was stopped and the associated fall in the blood urea concentration.

180/110 mm.Hg; there was papilloedema, with retinal haemorrhages and exudates. Neither kidney was palpable or tender. Coarse crepitations were heard over both lung bases, more on the right than the left.

The blood urea on admission was 91 mg./100 ml. (Fig. 1). An intravenous pyelogram showed two calculi in the left ureter which subsequently were passed and consisted of calcium phosphate. A chest radiograph showed patchy bronchopneumonia at both bases. *Haemophilus influenzae*, sensitive to tetracycline, was cultured from the sputum. Treatment was started with oxytetracycline 250 mg. four times daily (Fig. 1), and this was associated with a striking deterioration in the patient's condition. He became anorexic and dehydrated; the blood pressure and blood urea continued to rise. He developed a mild left hemiparesis and became confused; his deterioration was attributed to progression of the malignant hypertension.

On transfer to the Metabolic Unit on 21 May tetracycline was stopped and there was an immediate improvement in the patient's condition and a reduction in the blood urea. Bethanidine was started on 26 May and this reduced the blood pressure without significant worsening of the azotaemia or further reduction in the glomerular filtration rate as judged by creatinine clearance. The patient's subsequent course was uneventful. At the time of writing he was back at work, his blood pressure was controlled with bethanidine, the grade IV hypertensive retinopathy was regressing, and the blood urea was 123 mg./100 ml.

Case 2

A 67-year-old man was admitted to hospital with a two-months history of thirst, polyuria, breathlessness, and failing vision. Examination revealed congestive cardiac failure with a blood pressure of 175/110 mm.Hg. and grade III hypertensive retinopathy. His urine contained sugar.

The fasting blood glucose was 135 mg./100 ml. and the blood urea on admission 98 mg./100 ml. Three weeks later he developed a pyrexia and a productive cough. Oxytetracycline 250 mg. four times daily was given. His condition deteriorated; he became disorientated and dehydrated. His blood urea rose strikingly (Fig. 2).

FIG. 2.—Effect of tetracycline on the blood urea level in Case 2. Note the precipitous rise in the blood urea when tetracycline was given in a dose of 250 mg. four times daily.

When tetracycline was stopped his condition improved and the blood urea fell. He made progress for the next five days and then developed rapidly progressive renal failure, found at necropsy to be due to thrombosis of the left renal artery. Both kidneys showed histological changes of benign hypertension with additional tubular atrophy attributable to ischaemia in the left kidney and acute pyelonephritis in the right kidney.

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Discussion

Tetracycline may affect renal function in several ways. (1) Degraded tetracycline produces renal tubular abnormalities resembling those found in the Fanconi syndrome (Gross, 1963), and experimental studies suggest that anhydro-4-epitetracycline is the toxic compound (Benitz and Diermeier, 1964). (2) In some normal subjects tetracycline has a natriuretic and diuretic action (Shils, 1963; Roth *et al.*, 1967). Although the mechanism for this action is not understood, dehydration in patients with pre-existing renal disease will lead to increasing azotaemia. (3) In normal subjects tetracycline has an anti-anabolic effect, and failure to utilize ingested proteins causes a rise in the blood urea (Shils, 1963). (4) Intravenously administered tetracycline, usually but not always in a dose exceeding 1 g. daily and particularly in pregnancy, may cause hepatic necrosis, and this may be accompanied by renal failure (Kunelis *et al.*, 1965). In animals the toxic effects of tetracycline are related to the blood level, which is higher when renal disease impairs urinary excretion of the drug (Farhat *et al.*, 1958). Hyperbilirubinaemia, myoglobinaemia, haemoglobinaemia, and dehydration render the kidney vulnerable to the development of acute tubular necrosis in appropriate circumstances, such as postoperative shock. In animals a combination of haemoglobinaemia and tetracycline may produce renal tubular necrosis, whereas neither alone has this effect (Tapp and Lowe, 1966). In man tetracycline may perhaps have a similar action on an already vulnerable kidney.

In the present two cases the tetracycline was of recent manufacture and the drug was not given intravenously. Which of the other possible mechanisms was responsible for the increased azotaemia is uncertain. There is evidence in Case 1, judging by the patient's weight loss and the development of dehydration, that tetracycline caused a natriuresis and diuresis. This is supported by the negative sodium balance and subsequent sodium retention, the weight gain, and the fall in haematocrit that occurred when the tetracycline was stopped (Fig. 1). We have no evidence as to the effect of tetracycline on nitrogen metabolism in these two patients. In retrospect we accept that, in view of the initial impairment of renal function in both patients, the dosage of tetracycline used was too high or an alternative antibiotic should have been given.

Conclusions

Treatment with tetracycline merits wider recognition as a possible cause of deterioration in a patient with pre-existing azotaemia or occult renal disease. We suspect that, in more instances than the literature indicates, a rise in blood urea and clinical deterioration occurring during treatment of renal infection with tetracycline is ascribed to progression of the pyelonephritis rather than to the tetracycline. Present evidence suggests that tetracycline should not be used in patients with impaired renal function, but if this is ever necessary the dosage should be reduced and the blood urea level checked frequently as recommended by Kunin *et al.* (1959). This antibiotic should not be prescribed for patients predisposed to renal tubular necrosis by hyperbilirubinaemia, haemolysis, or postoperative shock. Intravenous tetracycline should be avoided in a dose exceeding 1 g. daily and should never be given to pregnant women. Outdated degraded tetracycline must never be used.

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Results of Anterior Transposition of the Ulnar Nerve for Ulnar Neuritis

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Summary: A clinical and electrophysiological follow-up study was done on 23 patients with ulnar neuritis treated by surgical transposition of the nerve at the elbow. Pain was relieved in all those affected and other sensory symptoms showed some degree of improvement in most. Weakness tended to persist, but recovery of full use of the hand followed operation in 74%. Muscle wasting was the least likely to improve. The chance of recovery after operation was greatly reduced in patients in whom preoperative symptoms had been present for more than one year.

Introduction

Anterior transposition of the ulnar nerve is considered to be the treatment of choice for established cases of ulnar neuritis in which the lesion can be shown to be at the elbow (Sunderland, 1968).

Most reports of the results of surgical treatment of ulnar neuritis have been optimistic (Richards, 1945; McGowan, 1950; Nigst, 1953; Jensen, 1959). Few cases, however, have been followed over a long period and few results have been analysed in detail. In particular little is known of the factors affecting the prognosis after transposition, though both McGowan (1950) and Jensen (1959) were able to show that the slighter the paralysis the greater the chance of recovery.

We have recently completed a follow-up study of a group of cases operated on at the National Hospital, Maida Vale, in which particular attention has been paid to the degree of recovery and to the factors which affected it.

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