sistently ingested eight tablets (80 mg) daily without any side effects. Because he could not get metoclopramide without prescription while his regular doctor was away, he abruptly stopped taking the drug.

Ten days later he progressively developed severe persistent facial dyskinesia consisting of repetitive involuntary movements of the lips, jaws, cheeks, and tongue. The latter were mainly constant, forceful sucking, chewing, grimacing, and rapid protrusions of the tongue. Results of general physical and neurological examinations were otherwise normal. Blood count, sedimentation rate, and biochemical and serological examinations showed nothing abnormal. The patient had never received other drugs known to be associated with involuntary movements, such as phenothiazines or butyrophenones. Readministration of metoclopramide at a daily dose of 30 mg resulted in almost complete disappearance of the involuntary movements. Another attempt to withdraw the drug was associated with recurrence of the dyskinesia, which subsided when metoclopramide was given again.

Comment

The severe involuntary movements developed by this patient after chronic use of high doses of metoclopramide are identical to the syndrome of tardive dyskinesia. The latter is commonly reported in psychiatric patients after long-term administration of phenothiazines or butyrophenones, particularly when these agents are abruptly withdrawn or their dosage reduced.⁵ Similarly, our patient developed this extrapyramidal syndrome after long-term ingestion of metoclopramide and sudden discontinuation. Phenothiazines and butyrophenones are potent dopamine-receptor antagonists, and tardive dyskinesia may be caused by a hypersensitivity of central dopamine receptors induced by neuroleptics.⁶ Metoclopramide may block cerebral dopamine receptors,⁷ and a similar mechanism may have operated in our patient. Paradoxically, tardive dyskinesia sometimes improves after readministration of neuroleptics.^{5, 6} Similarly, the involuntary movements in our patient also subsided after reinstitution of metoclopramide. This report should alert doctors to the risk that patients may develop serious and potentially irreversible extrapyramidal side effects after long-term use of metoclopramide.

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Dapsone and renal papillary necrosis

This paper records a case of renal papillary necrosis in a patient with dermatitis herpetiformis treated for many years with dapsone in high dosage. Dapsone, which resembles phenacetin in its effect on red blood cells, was probably responsible for the renal disease.

Case report

A 51-year-old machine assembly supervisor had had attacks of rheumatic fever while in his teens and developed dermatitis herpetiformis in 1957, for which he took dapsone 100 mg three times a day for the first five years, decreasing to 100-200 mg daily more or less continuously without specialist supervision. In 1966 he presented with attacks of acute gouty arthritis, which were treated initially with various drugs and then completely controlled with allopurinol 100 mg thrice daily. During 1972-7 he had about six attacks of renal colic, during one of which he passed some debris.

He first presented at this hospital in March 1977 with an attack of renal colic. Repeated questioning elicited nothing to suggest analgesic abuse. Examination showed a tall, thin (height 188 cm, weight 61 kg), clinically anaemic man with the rash of dermatitis herpetiformis (DH). Blood pressure was 130/80 mm Hg. There were signs of well compensated mitral and aortic

Retrograde pyelogram showing papillary necrosis.

valvular heart disease. Changes of bilateral renal papillary necrosis were seen on intravenous pyelography and confirmed by retrograde pyelography, which was carried out (Dr P M Bretland) to exclude possible ureteric obstruction (see figure).

Results of investigations were as follows: haemoglobin 10.6 g/dl; reticulocytes 6%, occasional fragmented cells and spherocytes; urinary haemosiderin absent; glucose-6-phosphate dehydrogenase screen normal; serum creatinine 180 μ mol/l (2.0 mg/100 ml); creatinine clearance 35 ml/min; plasma urea 10.5 mmol/l (63.3 mg/100 ml); serum urate 0.27 mmol/l (4.5 mg/100 ml). Glycosuria was not detected, and several random blood glucose measurements were normal.

Skin biopsy with immunofluorescence confirmed the diagnosis of DH (Dr C M Ridley). Circulating immune complexes containing IgG were found (Dr J F Mowbray). There was biochemical evidence of small-bowel malabsorption, and jejunal biopsy showed subtotal villous atrophy.

The patient was treated with a gluten-free diet and only topical applications for the DH.

Comment

There is no recognised association between papillary necrosis and either DH or its treatment with dapsone¹ and no published evidence incriminating gout or allopurinol. Over the years, however, this patient ingested an estimated 1.25 kg of dapsone, which is more than is normally taken in either DH or leprosy. Like phenacetin, the most likely cause of analgesic nephropathy, dapsone induces a chronic haemolytic anaemia often associated with Heinz body formation.² This patient's anaemia was at least partly haemolytic—a condition often found in patients with analgesic nephropathy³—and hence the unusually large dapsone intake probably caused the renal damage.

The mechanism by which phenacetin in analgesic mixtures produces renal disease is uncertain. Papillary necrosis is probably the primary lesion but whether the major effect is on the blood supply or due to direct toxicity is controversial.⁴ A recent review⁵ suggests that vascular mechanisms are the more likely. The papillary necrosis of sickle-cell disease and trait is generally attributed to local ischaemia due to increased blood viscosity. By analogy, this case suggests that alteration in the mechanical properties of red cells may play a part in analgesic- and dapsone-induced papillary necrosis. This tentative hypothesis lends itself to experimental study.

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