and chlorothiazide reintroduced when plasma lithium falls to non-toxic concentrations.

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Maprotiline hydrochloride and grand-mal seizures

We report three cases in which grand-mal seizures occurred for the first time during treatment with maprotiline hydrochloride (Ludiomil).

Case reports

Case 1—A 28-year-old mother of two children had been subject to bouts of depression since the birth of her first child six years before and was prescribed maprotiline 150 mg at night. Four months later she had a grand-mal seizure, which was not preceded by any aura or partial seizure activity. There was no history of head injury or alcoholic excess and no family history of epilepsy. Her only other medication was the contraceptive pill (Ovranette). Physical examination and routine investigations, including skull radiography and biochemical tests, showed nothing abnormal. Maprotiline was stopped. Three weeks later electroencephalography (EEG) showed a post-central dysrhythmia, which became generalised with hyperventilation. EEG at six months showed no noticeable change, but the recording at 20 months showed only a mild, brief theta dysrhythmia. She experienced no further seizures during the follow-up period.

Case 2—A 37-year-old postmistress was taking maprotiline 75 mg at night during her third bout of depression. After four weeks of treatment she had a well-documented grand-mal seizure without aura or focal onset. She was also taking an oral contraceptive (Ovran) and trifluoperazine, which her general practitioner had prescribed for nervous tension. All medication was stopped after the seizure. There was no personal or family history of fits, and no other cause for her seizure was found. Results of routine biochemical investigations and skull radiography were normal. EEG 21 days after the seizure showed a raised-voltage paroxysmal theta dysrhythmia with rapid generalised epileptiform breakdown occurring on photic stimulation. The recording two months later showed only intermittent interruption of normal rhythms, and nine months after the attack it was entirely normal. No further seizures occurred during 18 months of follow-up but she became deeply depressed one month after stopping maprotiline and was admitted to a psychiatric ward. On this occasion she was successfully treated with a tricyclic preparation (amitriptyline).

Case 3—A 36-year-old housewife, recently separated from her husband, had been taking maprotiline 75 mg at night for one week when she experienced a well-documented grand-mal seizure. There was no aura or focal onset and no relevant personal or family history. She was taking no other medication. Results of physical examination, skull radiography, and biochemical investigations were normal. EEG two weeks after the seizure showed a theta dysrhythmia with raised voltage and a frequency of 4-6 c/s. These paroxysms were prolonged during hyperventilation. EEG 11 weeks later showed a return to normal with only a mild theta dysrhythmia. She had no further seizures during four months of follow-up.

Comment

Grand-mal seizures may occur after overdosage of maprotiline,[1] and convulsions in patients taking therapeutic doses have been noted[2–4] but not fully documented. In one series[5] 3-4% of patients taking tricyclic antidepressants in therapeutic doses had grand-mal seizures, but no figures are available for maprotiline, which is a tetracyclic compound.

When seizures occur during treatment with maprotiline the drug should be stopped. Investigation and close follow-up is required to eliminate another cause for the seizure. If an antidepressant is still required a tricyclic drug should be introduced with caution.

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SHORT REPORTS

Gold lung

In the past two years there have been three reports of unusual pulmonary reactions to gold treatment affecting six patients, which have all conformed to a similar pattern. We present a further case in which the histological appearance suggested adenocarcinomatous deposits, but the patient recovered when the gold was stopped and steroids were given.

Case report

A 41-year-old West Indian district nurse developed rheumatoid arthritis in 1964. Her symptoms were controlled by ibuprofen alone until April 1977, when she was started on sodium aurothiomalate injections 50 mg weekly. Her erythrocyte sedimentation rate was 60 mm in first hour (Westergren), Rose-Waaler 1/64, antinuclear factor 1/10, DNA antibodies < 10 units. The chest radiograph was normal, and radiographs of the hands and feet showed erosions of the metacarpophalangeal and metatarsophalangeal joints.

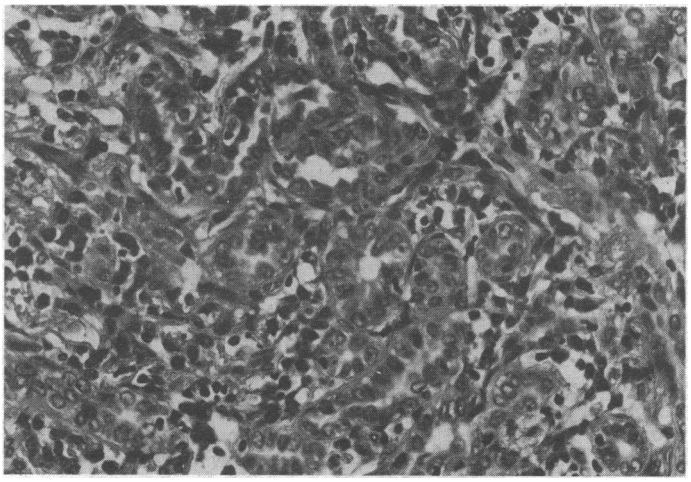
Eight weeks after starting treatment, having had 400 mg of gold, she developed pleuritic pain on the left and complained of shortness of breath. She did not have a cough. There was no rash or clubbing. There were coarse late inspiratory crackles at the left base anteriorly and laterally. A chest radiograph showed patchy consolidation in the region of the lingula, but a perfusion scan was normal. The patient refused admission. She was treated with ampicillin. One week later coarse inspiratory crackles were heard in all areas of both lungs and there were patchy, diffuse opacities in all areas on the chest radiograph. She was admitted for further investigation.

Investigations showed: white cell count $6{\cdot}4 \times 10^9$/l (neutrophils 65%, eosinophils 5%); P_{CO_2} 4·6 (4·6-6·0) kPa (34·5 (34·5-45) mm Hg); P_{O_2} 9·7 (12-15) kPa (72·7 (90-113) mm Hg); forced expiratory volume in one second (FEV_1) 1·0 l (predicted 2·8 l); vital capacity (VC) 1·1 l (predicted 3·6 l). Carbon monoxide transfer factor (T_{LCO}) could not be measured satisfactorily while the results of skin tests and precipitins were negative. An open lung biopsy was performed.

Histology—The sections showed numerous intra-alveolar inflammatory cells and macrophages. The alveolar walls were fibrotic and the alveolar

pattern was distorted. Type II cell hyperplasia was prominent. In the most cellular area (see figure) large cuboidal cells lined duct-like lumina. These cells were moderately pleomorphic, and, although mitoses were not seen and stains for mucin were negative, the appearances were interpreted as adenocarcinoma, probably metastatic rather than alveolar cell carcinoma. With hindsight the interpretation must be florid alveolar cell proliferation.

Progress—Despite the alarming histological appearances a trial of steroid treatment was started (prednisolone 60 mg/day) and the gold injections were stopped. After one month the chest radiograph had cleared and pulmonary function had improved: FEV_1 was 1·6 l, VC 1·7 l, T_LCO 11·7 mmol/kPa/min (predicted 26·4 mmol/kPa/min) (34·9 ml/mm Hg/min (78·8 ml/mm Hg/min)). After four months' follow-up the patient was still breathless on exertion but there were no abnormal physical signs. The dose of prednisolone had been reduced to 5 mg. The chest radiograph showed a high diaphragm and minimal reticular opacities in the mid-zones. The pulmonary function tests showed the same restrictive defect.



Photomicrograph showing grossly hyperplastic type II alveolar cells with duct formation mimicking adenocarcinoma. (H and E. ×270.)

Comment

In 1948 Savilahti[1] described pulmonary complications associated with a total dose of 1·06 g of gold which were successfully treated with dimercaprol. In 1976 Winterbauer *et al*[2] reported two similar cases: one of these patients had osteoarthritis and the other rheumatoid arthritis. There is no association between osteoarthritis and lung disease. The patient with rheumatoid arthritis was mistakenly given gold again after treatment of the lung disease and the symptoms reappeared. Geddes and Brostoff[3] described a patient with rheumatoid arthritis who developed fibrosing alveolitis after gold treatment. Lung function improved when the gold was stopped but deteriorated when gold was restarted. Gould *et al*[4] reported three further cases. In all six recent cases the onset of symptoms occurred five to 16 weeks after starting gold and after total doses of 400 to 800 mg.

We believe that our patient has suffered from "gold lung." She was left with a pronounced restrictive lung disorder, and would probably have died if gold treatment had been continued. The histological appearances were more striking than those previously illustrated,[2 4] the type II alveolar pneumocytes having reacted so vigorously as to have resembled adenocarcinoma, for which radiotherapy or cytotoxic treatment might have been prescribed.

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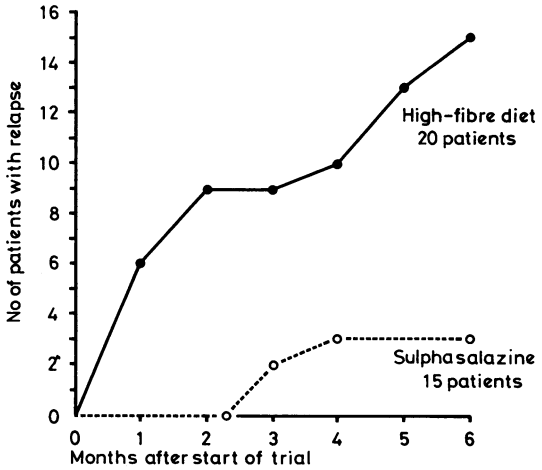
Maintenance of remission in ulcerative colitis with sulphasalazine or a high-fibre diet: a clinical trial

A high-fibre diet and cellulose preparations appear of value in patients with ulcerative colitis who develop colonic obstruction with clinical relapse of the disease. In recent years several of our patients who have been in remission with colitis have taken a high-fibre diet and spontaneously discontinued sulphasalazine but remained in remission. We questioned whether the high-fibre diet might prevent relapse, and in a controlled trial have examined the effect of replacing sulphasalazine treatment with the diet. Sulphasalazine maintains clinical remission in ulcerative colitis[1 2] and its withdrawal leads to relapse in up to 70% of patients within six months.

Methods and results

Thirty-nine patients in remission with colitis were divided into two similar groups; their mean age was 40, mean duration of disease 8·5 years, and mean interval since the last relapse 1·4 years. One group continued on sulphasalazine without a change in diet (15 patients) and the other (24 patients) increased their fibre intake by taking wholewheat bread, vegetables, and a supplement of 25 g of bran.* Four patients were unable to tolerate the diet and were withdrawn early from the study; additional patients were included to compensate for withdrawals. Patients who tolerated the diet discontinued sulphasalazine after two weeks. All patients were reviewed after one, three, and six months, and also if they had a recurrence of symptoms lasting over 48 hours—these symptoms consisted of three or more loose stools daily, usually with blood loss. At each interview the diet was reviewed, bowel symptoms were noted, and sigmoidoscopy was carried out.

The analysis is based on 35 patients who remained in the trial. In the sulphasalazine group three of the 15 patients relapsed, one with severe and two with mild symptoms. Of 20 patients given a high-fibre diet, four could not discontinue sulphasalazine because symptoms recurred when the dose was reduced. Five patients relapsed within three months after sulphasalazine was discontinued and a further six between three and six months. Only five of these 20 patients remained free from symptoms during the six-month period. Eleven patients on the high-fibre diet had been in remission for over one year and six of these relapsed when the sulphasalazine was withdrawn; four had been in remission for over three years, two of whom relapsed. The overall relapse rates for the sulphasalazine and high-fibre groups were 20% and 75%, respectively (fig).



Clinical relapse in patients who continued to take sulphasalazine compared with those who discontinued the drug and took a high-fibre diet.

Discussion

The high relapse rate in patients who discontinued or attempted to discontinue sulphasalazine is in keeping with other results, which have shown a relapse rate of 55 and 69% over six months[1 2]; relapses in the sulphasalazine group were also similar to those observed in these trials. The risk of relapse on withdrawal of sulphasalazine in our patients was independent of the duration of remission.[1] Our data lend

*The bran supplement was given as either Kellogg's All Bran or Allinson's Bran Plus.