Prolonged dystonic reaction to chlorpromazine in myxoedema coma

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Summary
A case of myxoedema coma is reported where the administration of chlorpromazine resulted in a prolonged dystonic reaction. A similar challenge with a butyrophenone when the patient was on thyroxine caused a similar but much abbreviated response.

Introduction
Hypothyroidism is associated with a decreased rate of metabolism of a number of commonly used drugs (Evered, 1976). Side effects of such drugs, therefore, may be prolonged. Dyskinetic reactions can result from the administration of phenothiazines and the authors report here a prolonged dystonic reaction to a single dose of chlorpromazine in a patient with myxoedema coma.

Case report
A 75-year-old woman was admitted to another hospital because of self-neglect. She was known to be hypothyroid and supposedly taking 0.2 mg L-thyroxine daily but her general practitioner had found a large quantity of these tablets in her house.

On the first evening she received 50 mg of chlorpromazine i.m. for sedation. The following evening she was transferred to Wharfedale General Hospital where, on admission, she was hypothermic (rectal temperature 33°C), confused and unresponsive with delayed tendon reflexes.

Muscle spasms of all 4 limbs, neck retraction and myoclonic twitches of the facial muscles suggested an acute dystonic reaction. Thyroid function tests at that time showed: serum total thyroxine 50 nmol/l (normal range 62–166); triiodothyronine resin uptake (T3 resin) 127% (normal range, 177–92); free thyroxine index 3.6 (normal range, 3.5–12.5); serum thyroid stimulating hormone (TSH), 110 µu./ml (normal range, up to 7). Lumbar puncture revealed: red cells < one/mm³; white cells < one/mm³; no organisms on microscopy or culture; protein 0.33 gm/l; glucose 3.6 mmol/l.

She was treated with triiodothyronine 10 µg i.v. 8 hourly and hydrocortisone acetate 100 mg i.v. 6 hourly. Two mg of benztpoline were administered i.v. for the dystonia and repeated 3 hr later with initial improvement of the dystonic signs on each occasion. However, she was still showing dyskinetic movements the next morning, 40 hr after the chlorpromazine had been given. A third injection of benztropine (2 mg i.v.) was administered and the dystonia had fully recovered after a further 8 hr.

Two weeks later she was clinically much improved and re-established on oral L-thyroxine (serum total thyroxine 61 nmol/l; T3 resin, 117%; free thyroxine index, 4.1; serum TSH 50 µu./ml).

However, one night she became agressive and confused and was sedated with 5 mg of haloperidol i.m. For the next 15 hr she again showed dystonic signs, this time of minor degree.

Discussion
Chlorpromazine is normally metabolized in the liver and excreted in the urine and faeces. Although metabolites can be found in the urine 6 months after the last dose has been administered, the plasma half-life of chlorpromazine is about 6 hr (Goodman and Gilman, 1975). Dystonic reactions have been described in association with phenothiazines and usually occur soon after the drug has been started (Richter, 1969). The syndrome is characterized by involuntary tongue movement, facial grimacing, oculogyric crises, retrocollis and opisthotonos. The signs disappear when the drug responsible is withdrawn (Davies, 1977). Benztropine can be used to expedite recovery, beneficial effects becoming apparent 10 min after administration. Chlorpromazine is not usually associated with such reactions, only 5 such cases being listed in the Committee on Safety of Medicines’ Register of Adverse reactions, 1962–1977.

The patient showed typical features of an acute dystonic reaction but myoclonic twitching was still occurring 40 hr after a single dose of chlorpromazine and 3 doses of benztropine. Whilst others have reported the occasional need for a second dose of benztropine or similar drug the present authors can find no record of a dystonic reaction lasting this length of time (Dundee, Clark and Carruthers, 1975).

It is presumed that the prolonged response was due
to the decreased rate of metabolism which occurs with hypothyroidism and hypothermia and that the second episode was shorter because of the patient’s improved thyroid status. This report adds further evidence that great caution should be used in prescribing drugs for patients suffering from hypothyroidism as adverse drug reactions may be prolonged.

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References

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