sensory loss might have made her particularly vulnerable to the seizure threshold lowering effects of clomipramine. To our knowledge there has been only one other report that MH began in two patients shortly after the initiation of an antidepressant (amtriptyline 75 mg and nortriptyline 75 mg) (Wegel *et al*, 1989).

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Crossover reaction between haloperidol and amoxapine for NMS

SIR: Neuroleptic malignant syndrome (NMS) is a potentially fatal complication of neuroleptic treatment. This syndrome has also been reported in association with antidepressants (Baca & Martinelli, 1990; Halman & Goldbloom, 1990). We report a crossover reaction between a neuroleptic (haloperidol) and an antidepressant (amoxapine), which has not previously been reported.

Case report. The patient was a 68-year-old woman (body weight 41 kg) suffering from major depression with psychotic features. Nine days before admission, amitriptyline (30 mg/day) was introduced. On admission, the prescription was switched to haloperidol 1 mg and mianserin 10 mg, daily. Haloperidol was gradually increased, and from the 12th day of admission the daily dose was fixed to 10 mg. On the 17th day, the following clinical symptoms and laboratory findings were observed: stupor, lead-pipe muscle rigidity, a fever of 38.9°C axillary, autonomic disturbances (hypertension, tachycardia, profuse diaphoresis, and dysuria), an elevated serum creatine phosphokinase (CPK) level (640 IU/l: normal value, 30–170 IU/l), leucocytosis (12 100/mm^3), and a low serum iron level (14 μg/dl: normal value, 50–170 μg/dl). A diagnosis of NMS was made, and all medication was discontinued. All symptoms of NMS disappeared by dantrolene and subsequent levodopa treatment. During the next 14 months, several antidepressants, such as mianserin (10–20 mg/day, 23 weeks), maprotiline (10–30 mg/day, 4 weeks), and clomipramine (10–50 mg/day, 4 weeks) were prescribed with no significant improvement in depression. Finally, amoxapine (25 mg/day) was introduced. On the 21st day, the development of NMS was unequivocal. The following clinical symptoms and laboratory findings were observed: stupor, lead-pipe muscle rigidity, a fever of 39.0°C, autonomic disturbances, an elevated serum CPK level (1090 IU/l), and a low serum iron level (10 μg/dl). Amoxapine was withdrawn, and all symptoms of NMS disappeared with levodopa treatment. Blood analysis including serum iron level was normal except in the NMS episodes.

Some investigators have postulated facilitative roles of increased noradrenergic (Baca & Martinelli, 1990) or serotonergic (Halman & Goldbloom, 1990) activity in the pathogenesis of NMS. However, in the present patient, who was apparently very susceptible to NMS, of the antidepressants prescribed, only amoxapine, which has a significant dopaminergic blockade property (Cohen *et al*, 1982), caused NMS, while the remaining antidepressants which all potentiate noradrenergic and/or serotonergic activities did not. Thus, the present report suggests that dopaminergic blockade sufficiently explains the pathogenesis of NMS (Otani *et al*, 1991), and that facilitative roles of noradrenalin and serotonin are minute. Although the cause(s) of dramatic fall in serum iron level in NMS remains obscure, this may further facilitate hypodopaminergic states as suggested by Rosebush & Stewart (1989), since iron deficiency diminishes central dopaminergic activity.

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