

of growing interest (5, 6). Ketamine is also a weak dopamine transporter antagonist and can be psychotomimetic. Its role as a primary anesthetic agent in ECT deserves more study. It may have its greatest use in patients with severe nonpsychotic depression.

#### References

1. Krystal AD, Weiner RD, Dean MD, Lindahl VH, Tramontozzi LA, Falcone G, Coffey CE: Comparison of seizure duration, ictal EEG, and cognitive effects of ketamine and methohexital anesthesia with ECT. *J Neuropsychiatry Clin Neurosci* 2003; 15:1:27–34
2. Berman RM, Cappiello A, Anand A, Oren DA, Henninger GR, Charney DS, Krystal JH: Antidepressant effects of ketamine in depressed patients. *Biol Psychiatry* 2000; 47:351–354
3. Kudoh A, Takahira Y, Katagai H, Takazawa T: Small-dose ketamine improves the postoperative state of depressed patients. *Anesth Analg* 2002; 95:114–118
4. Yilmaz A, Schulz D, Aksoy A, Canbeyli R: Prolonged effect of an anesthetic dose of ketamine on behavioral despair. *Pharmacol Biochem Behav* 2002; 71:349–352
5. Sanacora G, Rothman DI, Mason G, Krystal JH: Clinical studies implementing glutamate neurotransmission in mood disorders. *Ann NY Acad Sci* 2003; 1003:292–308
6. Paul IA, Skolnick P: Glutamate and depression: clinical and preclinical studies. *Ann NY Acad Sci* 2003; 1003:250–272

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### Sertraline- and Mirtazapine-Induced Severe Neutropenia

TO THE EDITOR: Neutropenia is a rare and reversible side effect of antidepressant treatment (1–4). Six cases of agranulocytosis in approximately 2 million exposures to mirtazapine have been reported (unpublished data from Organon, Inc., 1999). Because all of the patients had either a concomitant medication or disease that might have been related to agranulocytosis, it has been suggested that the association between mirtazapine and agranulocytosis might have been coincidental (5).

We report on a person with depression who developed severe neutropenia during treatment with mirtazapine and was safely treated with sertraline.

Ms. A, a 44-year-old woman with complaints of sleep disturbance, lack of energy, and unhappiness, was diagnosed with major depressive disorder and administered mirtazapine, 30 mg/day. Her medical history was negative, and the results of routine blood tests (WBC count of  $6.8 \times 10^9/\text{liter}$ ) were unremarkable except for a total cholesterol level of 204 mg/dl. Three weeks later, she came in with complaints of a severe sore throat, difficulty swallowing, a loss of appetite, and an aphthous ulcer in her oral mucosa, with a slightly elevated body temperature of  $37.7^\circ\text{C}$  during her physical examination. In subsequent blood counts, neutropenia (a WBC count of  $2.2 \times 10^9/\text{liter}$ ) was detected, and a blood smear revealed a granulocyte number of  $1.1 \times 10^9/\text{liter}$ . Mirtazapine was immediately discontinued, and sulfamethoxazole, 375 mg b.i.d., was started after consulting with the otorhinolaryngology department. Within 2 weeks, Ms. A's WBC count and granulocyte count had gradually increased to  $3.8 \times 10^9/\text{liter}$  and  $3.2 \times 10^9/\text{liter}$ , respectively. Four weeks after discontinuation of mirtazapine, sertraline was administered at 50 mg/day. Within 6

weeks, Ms. A's depression had responded to treatment, with more than a 50% reduction of her score on the Hamilton Depression Rating Scale, while her WBC count was  $6.1 \times 10^9/\text{liter}$ . Upon her final assessment, after 6 months of taking sertraline, her depression had remitted completely, without any adverse effects.

Since there was neither concomitant medication nor medical illness, an association between mirtazapine and severe neutropenia might be suggested. Neutropenia with cross-intolerance between two tricyclics has been described before (6), and there is evidence that patients may successfully be treated with another class of drug after such an incidence (4). Therefore, a selective serotonin reuptake inhibitor, sertraline, was administered and successfully used without an adverse effect. We may hypothesize that a different class of antidepressants might cause agranulocytosis by different mechanisms. Patients should be monitored closely for symptoms indicating agranulocytosis. An antidepressant from a different class might be considered after such an incident.

#### References

1. Albertini RS, Penders TM: Agranulocytosis associated with tricyclics. *J Clin Psychiatry* 1978; 39:483–485
2. Adams PC, Robinson A, Reid MM, Vishu MC, Livingston M: Blood dyscrasias and mianserin. *Postgrad Med J* 1983; 59:31–33
3. Nelson JC: Safety and tolerability of the new antidepressants. *J Clin Psychiatry* 1997; 58:26–31
4. Anghelescu I, Klawe C, Dahmen N: Venlafaxine in a patient with idiopathic leukopenia and mirtazapine-induced severe neutropenia (letter). *J Clin Psychiatry* 2002; 63:838
5. Davis J, Barkin RL: Clinical pharmacology of mirtazapine: revisited (letter). *Am Fam Physician* 1999; 60:1101
6. Draper BM, Manoharan A: Neutropenia with cross-intolerance between two tricyclic antidepressant agents (letter). *Med J Aust* 1987; 146:452–453

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### Clozapine-Induced Eosinophilic Colitis

TO THE EDITOR: Clozapine is an atypical antipsychotic with considerable efficacy compared to other antipsychotic medications (1). We report on a patient who developed fever and diarrhea while taking clozapine and was diagnosed with clozapine-induced eosinophilic colitis.

Mr. A was a 45-year-old man with schizophrenia who had psychotic decompensation in the setting of medication noncompliance and developed neuroleptic malignant syndrome when haloperidol and risperidone were restarted. He was treated with ECT. Concurrently, clozapine was started at a low dose and gradually increased. On the 14th day of clozapine therapy, he developed a fever of  $103.6^\circ\text{F}$  and profuse nonbloody diarrhea. His clozapine dose was 200 mg/day. His other medications at the time were lorazepam, aspirin, and metoprolol. His other vital signs were stable, and there was no muscle rigidity or elevation of creatine kinase to suggest recurrence of neuroleptic malignant syndrome.

His laboratory values showed mild elevation of his WBC count (to  $12,300/\text{mm}^3$ ). The results of multiple blood cul-