Depression, medication, and 'bad blood'

Pia Natalya Reyes, MD, and Deborah Cross, MD

Clinicians find 2 antidepressants that reduce Mr. G's chronic depression. Unfortunately, each medication decreases his WBCs. What would you do?

CASE Sad and suicidal

Mr. G, age 44, has chronic depression with suicidality. At presentation he says he has felt sad and suicidal for 2 weeks. He also has no appetite and trouble sleeping at night.

Mr. G's depression has left him unable to work and has led to 4 hospitalizations over 10 years. He first attempted suicide in 1984 after his ex-wife took their child and left him. He endorses no suicide plan and has been sober for 7 years after 12-plus years of alcohol abuse, but says he has been tempted lately to resume drinking.

The patient was taking an antidepressant but stopped while at a homeless shelter, where he had been staying for several weeks. For more than 20 years, he also has been taking phenytoin, 300 mg/d, and phenobarbital, 30 mg bid, for a seizure disorder.

Mr. G is admitted with a working diagnosis of recurrent major depressive disorder. White blood cell count (WBC) at admission is 5.12×10^9/L and neutrophils are 3.6×10^9/L—both low-normal readings. Other laboratory results are normal.

We continue phenytoin and phenobarbital at the same dosages and start the selective serotonin reuptake inhibitor (SSRI) citalopram, 20 mg/d, which interacts minimally with both anticonvulsants.

After 2 weeks, Mr. G's seizures are well controlled and he is tolerating citalopram, but his depressive symptoms have not improved. We cross-taper citalopram to prevent SSRI-induced discontinuation syndrome and start the dopamine and norepinephrine reuptake inhibitor bupropion, 75 mg bid. We titrate bupropion over 2 weeks to 150 mg each morning and 300 mg at bedtime, and watch Mr. G closely for seizures. Although his seizure history contraindicates bupropion use, we think he can tolerate the medication because his seizure disorder is well controlled.

Mr. G's affect, appetite, and energy are improving with bupropion, but a routine complete blood count (CBC) 5 days after the medication is started reveals leukopenia (WBC 3.04×10^9/L) without neutropenia (neutrophils 1.9×10^9/L). Repeat blood tests 18 and 32 days after the first blood draw show continued low WBC. The gastrointestinal medicine team tests Mr. G's liver function but finds no abnormalities.

What is causing Mr. G's abnormal blood counts?

a) seizure medications
b) bupropion
c) undetected medical problem

Dr. Reyes is a clinical assistant instructor and fourth-year psychiatric resident, department of psychiatry, State University of New York Downstate Medical Center, Brooklyn.

Dr. Cross is director of adult ambulatory services, Westchester Medical Center, and associate professor of psychiatry, New York Medical College, Valhalla, NY.

continued

How would you handle this case?

Visit **CurrentPsychiatry**.com to input your answers and compare them with those of your colleagues

Clinical Point

When WBC and neutrophils are low, check medication history before ordering additional tests

The author's observations

Mr. G's low WBC and neutrophil counts coincided with bupropion use, suggesting medication-induced leukopenia. Phenytoin can cause neutropenia and other adverse hematologic effects,[1] but the patient had been using phenytoin and phenobarbital for years with no adverse reactions.

A medical cause also is unlikely. Mr. G's liver function is normal, and he shows no other signs or symptoms of a medical problem. Bone marrow biopsy and immunologic workup could rule out cancer, but the timing of Mr. G's abnormal blood readings strongly suggests bupropion intolerance.

TREATMENT Other medications

We immediately stop bupropion, start the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine at 37.5 mg bid, and titrate it over 5 days to 225 mg/d. Blood draws 3 and 5 days after bupropion discontinuation show slight increases in WBC.

Eleven days after venlafaxine is started, Mr. G's WBC and neutrophils are normal. However, he has become increasingly irritable and volatile, often arguing with a staff nurse and other patients. We cross-taper venlafaxine over 5 days, start the SSRI sertraline at 50 mg/d, and titrate sertraline over 1 week to 150 mg/d. Mr. G's irritability and depressive symptoms improve at the latter dosage.

Because Mr. G developed neutropenia while taking a medication not associated with this adverse effect, we start watching his WBC counts more closely than usual. WBC is 4.58×10^9/L 8 days after sertraline is started but falls to 3.4×10^9/L after another 8 days, with neutrophils at 1.5×10^9/L for both readings (***Table***).

We add lithium, 300 mg bid, to increase Mr. G's neutrophils and augment sertraline's antidepressant effects. Four days later, WBC is 5.8×10^9/L with neutrophils at 4.2×10^9/L.

We stop lithium briefly to see if WBC remains normal. After 3 days, WBC drops to 3.25×10^9/L with neutrophils at 1.5×10^9/L. We restart lithium, 300 mg/d, and Mr. G's WBC increases to 4.18×10^9/L 4 days later, with neutrophils at 2.1×10^9/L.

The authors' observations

For Mr. G, both bupropion and sertraline appear to have caused neutropenia on separate occasions.

To our knowledge, bupropion-induced leukopenia or neutropenia have not been reported in the literature. Neutropenia—a rare adverse effect of antidepressants[2]—and leukopenia were seen during bupropion's pre-marketing trials but were not definitely attributed to the drug.[1] According to pre- and post-marketing data, leukopenia was "infrequently" reported among 5,100 subjects who received bupropion.[3]

To our knowledge, sertraline-induced neutropenia has not been reported in nongeriatric patients, although sertraline-induced neutropenia[4] and agranulocytosis[5] have been reported in patients age >65. The Committee on Safety of Medicine in the United Kingdom has received 2 other reports of neutropenia and 1 report of leukopenia with sertraline.[5]

In one clinical trial, 2 of 1,304 patients taking unknown dosages of sertraline had low neutrophils (<15% of WBC). Incidence of abnormal hematologic readings did not differ significantly between the sertraline and placebo groups (data on file, Pfizer).

Medication is the second most common cause of acquired neutropenia, with infection being most common.[6] By definition, drug-induced neutropenia occurs within 4 weeks after starting the drug and usually resolves within 30 days after stopping it.

Neutropenia is an idiosyncratic reaction unrelated to pharmacologic action. Although overall neutropenia incidence is unknown, reported incidence of the rare, more severe agranulocytosis ranges from approximately 1 to 10 cases per million people annually, and medications have been implicated in 70% of these cases.[6]

Table

Mr G's white blood cell (WBC) and neutrophil counts (NC)* while taking bupropion and sertraline

Antidepressant	When measurements were taken	WBC	NC
None for several weeks	Baseline, first hospital admission	5.12x10^9/L	3.6x10^9/L
Bupropion, 75 mg bid	5 days after starting bupropion	3.04x10^9/L	1.9x10^9/L
Bupropion, 450 mg/d total	23 days after starting bupropion	3.14x10^9/L	1.6 x10^9/L
Bupropion, 450 mg/d total	2 weeks after previous test	2.73 x10^9/L	1.6 x10^9/L
Sertraline, 150 mg/d	8 days after starting sertraline (titration period)	4.58 x10^9/L	1.5 x10^9/L
Sertraline, 150 mg/d	16 days after starting sertraline	3.4 x10^9/L	1.5 x10^9/L
Sertraline, 150 mg/d, and lithium, 300 mg bid	4 days after lithium augmentation	5.8 x10^9/L	4.2 x10^9/L
None for 3 months	Baseline, second hospital admission	3.7 x10^9/L	2.1 x10^9/L
Sertraline, 150 mg/d	12 days after restarting sertraline	2.83x10^9/L	Not available

* Normal WBC values: 4.5 to 11x10^9/L; normal neutrophil values: 1.5 to 8x10^9/L

Conversely, only 2 of 97 incidental neutropenia cases studied by Lima et al[7] were medication-induced.

Drug-induced neutropenia can result from immune-mediated destruction of neutrophils by circulating antibodies or from direct toxic effects upon marrow granulocyte precursors. Whereas immune-mediated onset is acute and explosive, toxic effect is insidious (months to years) and asymptomatic.[8] Clozapine is thought to deliver a direct toxic effect, whereas the thyroid-regulating drug propylthiouracil generates anti-neutrophil antibodies.[9]

Mr. G's acute onset (within 5 to 16 days of starting bupropion or sertraline) and prompt return of neutropenia after stopping lithium suggest acute immune-mediated circulating neutrophil destruction.

Treating leukopenia

After 4 failed or intolerable antidepressant trials, lithium augmentation seemed reasonable and ultimately improved Mr. G's neutrophil count and his mood.

Lithium has helped resolve clozapine-induced neutropenia in case reports.[10-12] Well-controlled studies, however, have followed only patients with antineoplastic, drug-induced neutropenia.[1]

By acting on cyclic nucleotides, lithium prompts colony-stimulating factor production, which in turn stimulates neutrophil production by pluripotent stem cells. As with Mr. G, patients reach neutrophilia 3 to 7 days after starting lithium.

If the patient cannot tolerate lithium, try switching antidepressants or using growth factors to increase neutrophils.

Switching antidepressants. The SSRIs escitalopram or paroxetine, or the SNRI duloxetine are effective and do not necessarily cause neutropenia. Start at below-normal dosages to gauge tolerability, then titrate to normal dosages. Avoid tricyclics, which pose a higher risk of neutropenia than other antidepressant classes.

Case reports[13,14] associate fluoxetine and mirtazapine with neutropenia. The patient who received mirtazapine, 30 mg/d, later responded well to sertraline, 50 mg/d.[13]

If the new antidepressant is ineffective, consider adding the mood-stabilizing anticonvulsant lamotrigine, 12.5 mg/d. Increase lamotrigine to 25 mg/d after 1 week,

Clinical Point

Adjunctive lithium can improve mood and increase WBC in patients with medication-induced neutropenia

then titrate by 25 mg weekly to 100 to 400 mg/d depending on efficacy and tolerability.

Although lamotrigine has been associated with neutropenia in case reports,[1] it is safer than other anticonvulsants. Carbamazepine, oxcarbazepine, and valproic acid can cause blood dyscrasias, which can lead to serious infection, abnormal bleeding, or other complications.

Using growth factors. Although their efficacy is not proven, growth factors are minimally toxic and might have helped Mr. G. Granulocyte colony-stimulating factor and granulocyte macrophage colony-stimulating factor resolved neutropenia in uncontrolled studies, but results of one randomized controlled trial were equivocal.[8]

Clinical Point

Duloxetine, escitalopram, and paroxetine have not been reported to cause neutropenia

TESTING CT findings

Approximately 2 months after admission—shortly after a blood draw shows normal WBC and neutrophils—Mr. G complains of dizziness. He says he accidentally hit his head against a side table.

We order a full neurologic workup to check for traumatic brain injury or brain damage caused by long-term alcohol abuse:

- Head CT shows evidence of previous cerebrovascular infarcts in the bilateral frontal and cerebellar lobes and basal ganglia.
- MRI shows atrophied mammillary bodies, fornix, and corpus callosum.
- Magnetic resonance angiography reveals small cerebral vessel disease.

These findings and subsequent neuropsychiatric test results suggest an organic cause of depression, likely secondary to 12 years of alcohol abuse. In light of this new information, we change Mr. G's diagnosis to mood disorder with depressive features secondary to a general medical condition.

FOLLOW-UP Awaiting discharge

After 3 months of continuous hospitalization, Mr. G has become euthymic and nonsuicidal, though at times oversensitive and combative. We transfer him to an assisted-living center and continue sertraline, 150 mg/d; phenytoin, 300 mg/d; phenobarbital, 30 mg bid; lithium, 300 mg/d; and trazodone, 50 mg at night as needed for insomnia.

We also place Mr. G in a day treatment program for mentally ill chemical abusers. A psychiatrist sees him every 2 weeks, and staff supervise him daily.

When starting sertraline or bupropion, order blood tests:

a) at baseline and every 2 weeks
b) at baseline and every 4 weeks
c) 1 month after starting and every 6 months thereafter
d) would not order unless patient shows physical symptoms

The authors' observations

Mr. G's extended hospital stay allowed us to closely observe him and offered ready access to laboratory facilities while we cross-tapered medications. In outpatient treatment, however, a serious and life-threatening medication-induced complication could easily be missed.

If economically feasible, take CBCs for all patients before prescribing any medication that could cause neutropenia, such as an antidepressant or mood stabilizer. Make sure geriatric or medically ill patients have had a CBC ≤3 months before presentation and are seeing a primary care physician as needed. Order follow-up CBC for these patients 1 month after presentation, then every 6 months if CBC is normal.

For medically healthy outpatients, be sure CBC has been checked ≤6 months before presentation. Monitor CBC and urge the patient to see a primary care doctor if infection symptoms emerge. Watch for gingivitis, tooth abscess, and other oral cavity infections—which often are overlooked—and sore throat or fever.

Also check electrolytes and screen for

continued on page 106

highest dose of oral olanzapine (15±2.5 mg/d). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

Other Adverse Events: Dose-relatedness of adverse events was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (5±2.5, 10±2.5, or 15±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

In an 8-week, randomized, double-blind study in patients with schizophrenia, schizophreniform disorder, or schizoaffective disorder comparing fixed doses of 10, 20, and 40 mg/d, statistically significant differences were seen between doses for the following: baseline to endpoint weight gain, 10 vs 40 mg/d; incidence of treatment-emergent prolactin elevations >24.2 ng/mL (female) or >18.77 ng/mL (male), 10 vs 40 mg/d and 20 vs 40 mg/d; fatigue, 10 vs 40 mg/d and 20 vs 40 mg/d; and dizziness, 20 vs 40 mg/d.

Vital Sign Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (*see* PRECAUTIONS).

Weight Gain—In placebo-controlled 6-week schizophrenia studies, weight gain was reported in 5.6% of oral olanzapine patients (average 2.8-kg gain) compared to 0.8% of placebo patients (average 0.4-kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 56% of patients met the criterion for having gained >7% of their baseline weight. Average gain during long-term therapy was 5.4 kg.

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (*see* PRECAUTIONS). Asymptomatic elevation of eosinophils was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL (N=659), 0.5% experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean triglyceride increase of 20 mg/dL from a mean baseline of 175 mg/dL. In placebo-controlled trials, olanzapine-treated patients with baseline random cholesterol levels of <200 mg/dL (N=1034) experienced cholesterol levels of ≥240 mg/dL anytime during the trials more often than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In these same trials, olanzapine-treated patients (N=2528) had a mean increase of 0.4 mg/dL in cholesterol from a mean baseline of 203 mg/dL, which was significantly different compared to placebo-treated patients (N=1415) with a mean decrease of 4.6 mg/dL from a mean baseline of 203 mg/dL.

ECG Changes—Analyses of pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in incidence of potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

Other Adverse Events Observed During Clinical Trials—The following treatment-emergent events were reported with oral olanzapine at multiple doses ≥1 mg/d in clinical trials (8661 patients, 4165 patient-years of exposure). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. *Frequent* events occurred in ≥1/100 patients; *infrequent* events occurred in 1/100 to 1/1000 patients; *rare* events occurred in <1/1000 patients. ***Body as a Whole***—*Frequent:* dental pain, flu syndrome; *Infrequent:* abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt; *Rare:* chills and fever, hangover effect, sudden death. ***Cardiovascular***—*Frequent:* hypotension; *Infrequent:* atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, ventricular extrasystoles; *Rare:* arteritis, heart failure, pulmonary embolus. ***Digestive***—*Frequent:* flatulence, increased salivation, thirst; *Infrequent:* dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, tooth caries; *Rare:* aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, tongue discoloration. ***Endocrine***—*Infrequent:* diabetes mellitus; *Rare:* diabetic acidosis, goiter. ***Hemic and Lymphatic***—*Infrequent:* anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; *Rare:* normocytic anemia, thrombocythemia. ***Metabolic and Nutritional***—*Infrequent:* acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, upper extremity edema; *Rare:* gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, water intoxication. ***Musculoskeletal***—*Frequent:* joint stiffness, twitching; *Infrequent:* arthritis, arthrosis, leg cramps, myasthenia; *Rare:* bone pain, bursitis, myopathy, osteoporosis, rheumatoid arthritis. ***Nervous System***—*Frequent:* abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, schizophrenic reaction; *Infrequent:* akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, withdrawal syndrome; *Rare:* circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, tobacco misuse. ***Respiratory***—*Frequent:* dyspnea; *Infrequent:* apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, voice alteration; *Rare:* atelectasis, hiccup, hypoventilation, lung edema, stridor. ***Skin and Appendages***—*Frequent:* sweating; *Infrequent:* alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, vesiculobullous rash; *Rare:* hirsutism, pustular rash. ***Special Senses***—*Frequent:* conjunctivitis; *Infrequent:* abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, tinnitus; *Rare:* corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, pigment deposits lens. ***Urogenital***—*Frequent:* vaginitis*; *Infrequent:* abnormal ejaculation,* amenorrhea,* breast pain, cystitis, decreased menstruation,* dysuria, female lactation,* glycosuria, gynecomastia, hematuria, impotence,* increased menstruation,* menorrhagia,* metrorrhagia,* polyuria, premenstrual syndrome,* pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged,* vaginal hemorrhage*; *Rare:* albuminuria, breast enlargement, mastitis, oliguria. (*Adjusted for gender.)

The following treatment-emergent events were reported with intramuscular olanzapine for injection at one or more doses ≥2.5 mg/injection in clinical trials (722 patients). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. ***Body as a Whole***—*Frequent:* injection site pain; *Infrequent:* abdominal pain, fever. ***Cardiovascular***—*Infrequent:* AV block, heart block, syncope. ***Digestive***—*Infrequent:* diarrhea, nausea. ***Hemic and Lymphatic***—*Infrequent:* anemia. ***Metabolic and Nutritional***—*Infrequent:* creatine phosphokinase increased, dehydration, hyperkalemia. ***Musculoskeletal***—*Infrequent:* twitching. ***Nervous System***—*Infrequent:* abnormal gait, akathisia, articulation impairment, confusion, emotional lability. ***Skin and Appendages***—*Infrequent:* sweating.

Postintroduction Reports—Reported since market introduction and temporally (not necessarily causally) related to olanzapine therapy: allergic reaction (eg, anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, jaundice, neutropenia, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been reported.

DRUG ABUSE AND DEPENDENCE: Olanzapine is not a controlled substance.

Literature revised November 30, 2006

PV 5197 AMP PRINTED IN USA

Eli Lilly and Company
Indianapolis, IN 46285, USA

www.ZYPREXA.com

ZYPREXA® (Olanzapine Tablets)
ZYPREXA® ZYDIS® (Olanzapine Orally Disintegrating Tablets)
ZYPREXA® IntraMuscular (Olanzapine for Injection) PV 5197 AMP

continued from page 100

SSRI-induced hyponatremia at baseline for all at-risk patients.

Stop the offending drug when WBC reaches <2 x10^9/L or with absolute neutrophil count (ANC) <1.5 x10^9/L, then take a peripheral smear to confirm neutropenia. If the patient is asymptomatic, check ANC 2 to 3 times weekly, particularly if he or she recently had an infection or started a medication that can cause neutropenia. Neutropenia should resolve within 6 to 8 weeks of stopping the offending drug.

If neutropenia persists, order bone marrow biopsy in collaboration with an internist or hematologist to test for cancer. If the biopsy is negative, test for:

- HIV infection
- antinuclear antibodies to check for collagen vascular disease
- antineutrophil antibody to rule out immune neutropenia
- serum folate and B_{12} deficiency secondary to low WBC.

Also perform an immunoglobulins/immune evaluation to check for defects in cellular or humoral immunity, and bone marrow culture to test for infection.[8]

FOLLOW-UP Stressor and relapse

Seven months later, Mr. G is readmitted for depression. Three months earlier, he had stopped all medications and resumed drinking after a family member died. WBC at admission is 3.70x10^9/L

We restart sertraline, 150 mg/d. WBC falls to 2.83x10^9/L 12 days later, so we add lithium, 300 mg/d. Two days later, WBC returns to normal and he is discharged. His depression has been stable throughout this second admission, and he is euthymic at discharge.

We refer Mr. G to an outpatient psychiatrist, who sees him monthly. Several months later, the psychiatrist reports a WBC of 4.58x10^9/L.

Nearly 1 year later, Mr. G still lives at the assisted-living facility. He has not been rehospitalized for depression, is functioning well, and has a girlfriend.

The authors' observations

Mr. G's abnormal blood counts after sertraline rechallenge confirms that the SSRI probably was causing

leukopenia. If we had restarted bupropion and neutropenia recurred during that regimen, we could have more certainly established a bupropion-leukopenia connection.

References

1. McEvoy G, ed. *AHFS drug information*. Bethesda, MD: American Society of Health-System Pharmacists; 2005.
2. Nelson JC. Safety and tolerability of the new antidepressants. *J Clin Psychiatry* 1997;60:1101.
3. *Physicians desk reference, 61st ed*. Montvale, NJ: Thomson PDR; 2007.
4. Cohn CK, Shrivastava R, Mendels J, et al. Double-blind, multicenter comparison of sertraline and amitriptyline in elderly depressed patients. *J Clin Psychiatry* 1990;51(suppl B):28-33.
5. Trescoli-Serrano C, Smith NK. Sertraline-induced agranulocytosis. *Postgrad Med J* 1996;72:446.
6. Baehner RL. Overview of neutropenia. *UpToDate Online* (version 15.1); March 30, 2006. Available at: http://www.uptodate.com. Accessed April 16, 2007.
7. Lima CS, Paula EV, Takahashi T, et al. Causes of incidental neutropenia in adulthood. *Ann Hematol* 2006;85:705-9.
8. Holland SM, Gallin J. Disorders of granulocytes and monocytes. In: Kasper DL, Braunwald E, Fauci AS, et al, eds. *Harrison's principles of internal medicine, 16th ed*. New York: McGraw-Hill; 2005.
9. Baehner RL. Drug-induced neutropenia and agranulocytosis. *UpToDate Online* (version 15.1); June 8, 2005. Available at: http://www.uptodate.com. Accessed April 16, 2007.
10. Sporn A, Gogtay N, Ortiz-Aguayo R, et al. Clozapine-induced neutropenia in children: management with lithium carbonate. *J Child Adolesc Psychopharmacol* 2003;13:401-4.
11. Blier P, Slater S, Measham T, et al. Lithium and clozapine-induced neutropenia/agranulocytosis. *Int Clin Psychopharmacol* 1998;13:137-40.
12. Silverstone P. Prevention of clozapine-induced neutropenia by pretreatment with lithium. *J Clin Psychopharmacol* 1998;18:86-8.
13. Ozcanli T, Unsalver B, Ozdemir S, Ozmen M. Sertraline- and mirtazapine-induced severe neutropenia. *Am J Psych* 2005;162:1386.
14. Vilinsky FD, Lubin A. Severe neutropenia associated with fluoxetine hydrochloride. *Ann Internal Med* 1997;127:573-4.

Related Resources

- Neutropenia Support Association. www.neutropenia.ca.
- Baehner RL. Overview of neutropenia. *UpToDate Online* (version 15.1); March 30, 2006. www.uptodate.com.

Drug Brand Names

Bupropion • Wellbutrin
Carbamazepine • Tegretol, others
Citalopram • Celexa
Clozapine • Clozaril
Duloxetine • Cymbalta
Escitalopram • Lexapro
Fluoxetine • Prozac
Lamotrigine • Lamictal
Lithium • various
Mirtazapine • Remeron
Oxcarbazepine • Trileptal
Paroxetine • Paxil
Phenobarbital • various
Phenytoin • Dilantin
Propylthiouracil • various
Sertraline • Zoloft
Trazodone • Desyrel
Valproic acid • Depakene
Venlafaxine • Effexor

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Clinical Point

Make sure older or medically ill patients have had a CBC ≤3 months before starting medication that can decrease WBC counts

Bottom Line

Though infrequent, adverse hematologic effects can occur with antidepressant and mood stabilizer use. If possible, order CBCs at baseline for all patients before starting these medications. Repeat CBCs at regular intervals depending on medical history and test results.