

Mania or Hypomania After Withdrawal from Antidepressants

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Depression is a common psychiatric disorder seen in primary care practice.¹ In one study 9.2% of patients presenting for the first time to three primary care clinics were found to be depressed.² Although some patients with depression are treated by psychiatrists or other mental health professionals, many are treated by primary care physicians. In fact, about 70% of tricyclic antidepressants are prescribed by nonpsychiatric physicians, mainly those in primary care.³ It is important, therefore, for primary care physicians to be cognizant of the possible side effects and complications of the use of antidepressants.

This report describes the development of mania after withdrawal from amitriptyline, and hypomania after withdrawal from phenelzine in a 24-year-old woman with a history of longstanding depression. Switching from depression to mania or hypomania during antidepressant therapy has been described.⁴ There is some controversy as to whether the switch is due to the antidepressant therapy or is spontaneous and coincidental.⁵ Nevertheless, Wehr and Goodwin⁶ have recently reviewed the data and conclude that antidepressants can precipitate mania or hypomania.

Less commonly identified are cases of hypomania or mania precipitated by the withdrawal of antidepressants, as in this case. There are case reports and one prospective study of mania or hypomania after the withdrawal of either tricyclic antidepressants or monoamine oxidase inhibitors.⁷⁻¹⁰ This case report is the first to describe the development of hypomania after withdrawal from phenelzine, and is more interesting because the patient became hypomanic despite being on lithium.

CASE REPORT

A 24-year-old woman with recurrent depression was admitted to a psychiatric inpatient unit with suicidal ideation. She was on amitriptyline 150 mg at bedtime. The patient abruptly stopped the amitriptyline and in four days developed mania for the first time in her life. There was no family history of bipolar disorder. Her mania was successfully treated with lithium carbonate 600 mg twice a day.

She was maintained on lithium after discharge. Her serum levels ranged from 0.6 to 1.1 mmol/L (mEq/L). Twenty-two months later she developed major depression again. She was treated with phenelzine 60 mg/d. She was on phenelzine for a total of 16 months, when it was tapered over 7 days. Within 72 hours she developed hypomania despite being on lithium carbonate (serum level 0.7 mmol/L [mEq/L]). Her irritability, sleeplessness, and racing thoughts resolved with fluphenazine 2 mg/d in 2 weeks. There has been no recurrence of depression, mania, or hypomania in the 4 months since that time.

DISCUSSION

This is a case of the development of mania or hypomania after withdrawal from antidepressants. It is a unique case in three respects: (1) the same patient developed the switch response with two different classes of antidepressants (tricyclic antidepressants and monoamine oxidase inhibitor); (2) the patient developed hypomania upon withdrawal despite being on lithium carbonate; and (3) it is the only report of hypomania following withdrawal from phenelzine.

The mechanism for the development of mania or hypomania after withdrawal of antidepressants is not known. Some researchers have proposed that withdrawal of antidepressants can cause "behavioral activation on a continuum to frank mania" due to cholinergic overdrive.¹¹ The manic switch has occurred, however, after use of isocarboxazid,⁸ trazodone,¹² and, in this case, phenelzine,

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which have only mild anticholinergic activity. Thus, cholinergic rebound as a primary explanation is made somewhat less likely by this case report.

Other proposed mechanisms, such as noradrenergic¹³ or dopaminergic hyperactivity,¹⁴ have been suggested. Further research is needed to clarify the role, if any, of these mechanisms.

In summary, this case supports the hypothesis that mania or hypomania may occur after withdrawal from antidepressants. Also, it demonstrates that hypomania may occur after withdrawal despite lithium therapy. Physicians should be alert for this switch process while withdrawing their patients from antidepressants.

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