

A Case of Mirtazapine-Associated Hair Loss

To the Editor: Causes of hair loss include scalp disease, systemic disease, toxic agents, radiation exposure, trauma or pressure, psychiatric diseases, and other factors.^{1,2} Medication-induced hair loss usually presents as a diffuse, nonscarring, and reversible loss of hair that becomes clinically detectable a few months after medication treatment is started and is usually transient and reversible upon discontinuation of the medication.¹ The risk of hair loss might be higher in women,³ and it is suggested that alteration of hormones may contribute to the gender difference.² However, the underlying mechanism of drug-induced alopecia remains unclear.

An antimitotic effect of antidepressants has been regarded as a possible etiology,^{3,4} and the risk of hair loss may be different among agents.⁵ Sympathetic nerve fibers may be also involved, especially for dopaminergic agent-related hair loss.^{2,6,7} Hair growth in each hair follicle occurs in a cycle composed of 3 phases: anagen, catagen, and telogen. One mechanism for interrupting the hair growth cycle is *telogen effluvium*, which involves a premature interruption of growth with an early entry of anagen follicles into the resting phase.⁸

Many psychotropic drugs, including anxiolytics,¹ dopaminergic agents,^{2,9} mood stabilizers,^{1,10,11} and antidepressants,^{1,3,12-17} can lead to drug-induced alopecia. Among antidepressants, tricyclic/tetracyclic antidepressants,¹ selective serotonin reuptake inhibitors,¹²⁻¹⁵ a serotonin norepinephrine reuptake inhibitor,¹⁶ and serotonin modulators like trazodone¹ and nefazodone,¹⁷ but not yet a noradrenergic and specific serotonergic antidepressant (NaSSA), have been reported to cause temporary telogen hair loss. We report a female patient who lost hair during treatment with mirtazapine, the prototypical NaSSA. To our knowledge, this is the first report of hair loss associated with NaSSA therapy.

Case report. Ms A, a 50-year-old married and retired Han Taiwanese woman, began to experience menopause and related vasomotor symptoms (cold sweating, chills, hot flush) at the age of 48 years. Hormone replacement therapy was prescribed. Worried about the long-term risks of hormone replacement therapy, she turned to over-the-counter medication, isoflavones. She visited our hospital in July 2008 for anxiety, restlessness, insomnia, low mood, lack of energy, decrease of interest, preoccupation with death, psychomotor retardation, impaired concentration, multiple somatic discomforts, and vasomotor symptoms after her husband fell ill. Treatment with fluoxetine (20 mg/d) was started and then changed to paroxetine (10 mg/d) 2 weeks later because of Ms A's persistent poor appetite and weight loss. Because of treatment resistance, we subsequently tried citalopram (10 mg/d), escitalopram (10 mg/d), and venlafaxine (37.5 mg/d) for 4 to 5 weeks for each medication treatment. However, Ms A still suffered poor appetite and weight loss.

Treatment with mirtazapine (30 mg/d) was initiated, and 2 weeks later, she felt much improved in appetite and mood. After 3 months, her depressive symptoms were remitted, and she got a job. Hair loss was obvious after 6 weeks of mirtazapine treatment. Laboratory workup yielded no abnormalities in blood/urine routine, biochemistry, thyroid function, chest x-ray, or electrocardiogram. She had never experienced hair loss throughout her life, including during pharmacotherapy, except with mirtazapine.

Mirtazapine treatment was discontinued for this bothersome side effect, and paroxetine treatment was reinitiated. Ms A regained hair within 1 month. Two months later, her depressive symptoms relapsed, and she lost the job. She insisted on reinstitution of mirtazapine (30 mg/d) even with full awareness of the risk. Her depressive symptoms subsided, as in the antecedent scenario; however, hair loss recurred within 6 weeks.

The patient's hair loss occurred with mirtazapine use, subsided after discontinuation, and recurred after rechallenge with the drug. This series of events is the only reliable basis for a diagnosis of drug-induced alopecia.¹ Nonetheless, there are numerous other possible causes, which cannot be completely ruled out in this patient. Drug-induced hair loss is possibly dose related.^{1,5} It is a limitation of this report that mirtazapine was restarted at the original dose, 30 mg/d, because the patient preferred this dose (rather than a lower one) to treat her prominent depressive symptoms. Moreover, the patient had tried several antidepressants, each for 2 to 5 weeks, without hair loss. Because her hair loss with mirtazapine was evident after 6 weeks, treatment length may also have been a decisive element in this patient's hair loss. In addition, the risk of hair loss may differ among antidepressants.⁵ Due to its unique pharmacologic activities as a NaSSA, mirtazapine may pose a different risk for hair loss compared with other antidepressants. Further studies are warranted to elucidate this issue.

Hair loss is often overlooked due to difficult definition and measurement. Moreover, drug-induced hair loss, often troublesome, may have negative influence on life quality and discourage patients from continuing the therapy. Cheung et al¹⁸ surveyed the impact of antidepressant side effects on adolescent quality of life and found that hair loss was among the 5 side effects with the greatest negative impact. Clinicians should pay more attention to this troublesome side effect. Further systemic studies are also warranted.

To our knowledge, this is the first report of antidepressant-related hair loss in a patient of Asian ethnicity. An increasing number of studies indicate the importance of ethnicity in the psychopharmacologic treatment of depression.^{19,20}

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