An Isotretinoin-Induced Manic Episode in a Patient with a Family History of Bipolar Disorder

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Dear Editor,

Isotretinoin, also known as 13-cis-retinoic acid, is a derivate of vitamin A and has been used in mild and severe cases of acne for more than 30 years. Isotretinoin is lipid-soluble and easily passes the blood–brain barrier; thus, it can affect the central nervous system (1). A causal relationship has been reported between the use of the drug and various psychiatric side effects, including suicidal ideation and depressive, psychotic, and affective symptoms (1-3). Despite the risk of serious psychiatric side effects, the use of isotretinoin has increased in patients with dermatologic diseases (1,2). In the present case, we reported on an isotretinoin-induced manic episode in a patient with a family history of bipolar disorder and aimed to add to this growing body of data.

The 19-year-old male patient was admitted to hospital by his relatives due to decreased need for sleep, increased psychomotor activity, rapid speech, irritability, flight of ideas, and grandiosity. His symptoms had started about 15 days previously. In the past medical history of the patient, dermatological drugs had been used for acne vulgaris over the past few years, but the treatment was not effective. Therefore, the patient had started taking isotretinoin 1 month prior. After only 2 weeks of treatment, psychiatric symptoms began to emerge. The patient had no history of psychiatric disease, substance abuse, or other medical conditions. He had a family history of bipolar disorder in second-degree relatives (uncle and aunt). On dermatological examination, dry skin (xerosis) on his face due to isotretinoin use and cheilitis on his lips were visible.

Mental status examination showed decreased self-care; open conscious and normal orientation; increased amount and speed of speech, decreased concentration and attention; persecution, grandiose and mystical delusions; dysphoric mood; irritability and psychomotor agitation; aggressive and hostile behavior toward his father and the doctors; lack of insight; and decreased appetite and sleep. The patient fulfilled the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria for a manic episode and scored 35 on the Young mania ratingscale. The results of laboratory investigations of parameters such as hemogram, liver and kidney function tests, thyroid hormones, vitamin B12, and folate levels were normal.

Dermatologists recommended azithromycin 500 mg per day and clindamycin gel for acne vulgaris. Olanzapine was started at 10 mg/day and increased to 20 mg/day. Because there was no significant reduction in his symptoms, lithium carbonate 900 mg/day was added on the 11th day. After this treatment, the patient’s symptoms markedly decreased and returned completely to premorbid status after 24 days of hospitalization.

Previous works and the present case show that there is a strong link between isotretinoin and psychopathology. Barak et al. (2005) reported a case series that suggested an association between exposure to isotretinoin and manic psychosis (1). In addition, they described family and/or personal history of psychiatric disorders as a risk factor. Moreover, Ersoy et al. (2014) presented a case with attention deficit hyperactivity disorder who developed manic symptoms during isotretinoin and methylphenidate combination treatment (2). This patient had no personal or family history of bipolar disorder. These findings indicate that isotretinoin use may present a high risk, particularly in individuals who had previous psychiatric disease, and could result in the emergence of new symptoms or the exacerbation of previous ones (2,3).

Although the mechanism of action for isotretinoin is not exactly known, a few studies have attempted to identify pathogenic processes. Animal studies have demonstrated high expression of retinoid receptors and cellular retinoid binding proteins in dopamine innervated pathways, including the limbic system,
especially the hippocampus and hypothalamus; the cingulate gyrus and subregions of the thalamus; and the medial prefrontal cortex, striatum, and nucleus accumbens (4,5). It has also been found that retinoic acid changes the expression of serotonin in the developing hindbrain. High-dose exposure can cause a decrease or complete loss of serotonergic neurons (5). Finally, the current knowledge indicates that isotretinoin can affect the central nervous system, particularly neuronal development and neurotransmitter systems that are involved in the pathogenesis of different psychiatric disorders.

This case suggests that dermatologists should take care in prescribing isotretinoin in patients who have a family history of psychiatric disorder, and if needed, psychiatric consultation should be provided. Clinicians also have a duty to warn patients and their relatives about potential adverse psychiatric events.

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