Modafinil-induced Fixed Drug Eruption

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ABSTRACT
Modafinil is a stimulant drug widely used to promote wakefulness in a variety of psychiatric and neurological conditions. Modafinil-induced severe dermatologic reactions are uncommon but serious side effects. We report a patient who developed fixed drug eruption after exposure to a single dose of modafinil. On assessment using the Naranjo scale, the score was five, which made us conclude that modafinil was the "probable" cause of the patient’s adverse drug event. This case report highlights the need to be alert toward the emergence of dermatologic side effects among patients taking modafinil.

Key words: Adverse drug reaction, fixed drug eruption, modafinil

INTRODUCTION
Modafinil is a stimulant drug approved for the treatment of excessive daytime sleepiness associated with narcolepsy, shift-work sleep disorder, and obstructive sleep apnea syndrome by the US Food and Drug Administration (FDA). It promotes wakefulness by increasing the level of glutamate, serotonin, and histamine; activating the orexinergic system; and decreasing gamma amino butyric acid in the brain. Modafinil-induced severe dermatologic reactions are uncommon but serious side effects. In this report, we describe a patient who developed a fixed drug eruption (FDE) after exposure to a single dose of tablet modafinil.

CASE REPORT
A 29-year-old man reported itchy, painful patches of mucosal erosion with hyperpigmentation on the right half of upper lip and left half of lower lip. The patient was a student preparing for competitive examinations. He was prescribed tab modafinil 200mg in the morning by a psychiatrist to improve his daytime wakefulness and alertness for few days prior to his examinations. Within 12 h after taking a single dose of the tablet, the patient experienced numbness in his right upper lip and left lower lip. The patient discontinued the tablet. Over the next 24 h, he developed painful erosion and hyperpigmentation over the same area that persisted over the next 4-5 days [Figure 1]. There were no complains of fever, difficulty in breathing, or erosion or hyperpigmentation in other body parts. The patient had no history of similar complains or any allergic reaction in the past.

A differential diagnosis of herpes zoster or an FDE was considered, and tablet acyclovir 400mg 3 times a day for 2 weeks was prescribed; however, there was no relief in the symptoms. His complete blood count was normal; the viral DNA test and Tzanck test of the oral erosions were negative for herpes simplex virus. Following this, the lesions were diagnosed as an FDE. The patient was prescribed becomethasone ointment for local application 3 times a day and tablet fexofenadine 60mg twice daily for 2 weeks. The ulcers
healed completely within a week and the discoloration resolved completely over the next 4-6 weeks.

**DISCUSSION**

The term FDE describes the development of one or more annular or oval erythematous patches as a result of systemic exposure to a drug; these reactions normally resolve with hyperpigmentation and may recur at the same site with reexposure to the drug. Common locations are the lips, oral mucosa, hands, genitals, and perianal area. Treatment includes stopping the offending drug with topical steroids, emollients, and oral antihistamines. In this case, FDE developed after consumption of a single dose of tablet modafinil. When the above-mentioned adverse drug event (ADE) was adjudged on the Naranjo scale, the score was 5, which made us conclude that modafinil was the probable cause of the patient’s ADE. The patient refused to undergo subsequent oral challenge test or a patch test for the fear of cosmetic disfigurement.

Modafinil has a rapidly expanding list of off-label uses. It is widely used for treatment of unipolar and bipolar depression, attention deficit hyperactive disorder, Parkinson’s disease, schizophrenia, and disease-related fatigue.[5,6] Its use as a neuroenhancer to improve wakefulness, attention capacity, and vigilance in healthy volunteers is also on rise.[7]

There are very scanty reports in the literature about modafinil causing dermatologic reactions. Cases of severe cutaneous adverse reactions including erythema multiforme, Stevens–Johnson syndrome, toxic epidermal necrolysis, and drug rash with eosinophilia and systemic symptoms involving adult and pediatric patients have been received by FDA.[8]

Although modafinil-induced ADE was not life-threatening in our patient, the painful oral ulcers caused discomfort and pigmentation of lips led to cosmetic problem. This case report highlights the need to be alert toward the emergence of dermatologic side effects among patients taking modafinil, as the drug has been known to be associated with serious life-threatening cutaneous adverse reactions.

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