Agomelatine-Induced Maculopapular Rash: A Case Report

Agomelatinin İndüklediği Makülopapüler Döküntü: Bir Olgu Sunumu

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Dear Editor,

Agomelatine is a new antidepressant with a unique pharmacological profile, which includes the melatonergic agonistic (MT1 and MT2 receptors) and 5-HT(2C) antagonistic properties (1). Due to this mode of action, agomelatine is typically well tolerated and remarkably free from adverse side-effects at therapeutic dosages. The most common adverse effects reported with agomelatine use were headache, nasopharyngitis, and gastrointestinal complaints. Rarely skin rashes are reported during the treatment with agomelatine (1, 2). We also report a case of a 32-year-old woman with major depressive disorder (MDD) who has been treated with agomelatine and developed maculopapular rashes most prominent on the trunk. The rashes disappeared after cessation of the suspected drug.

Mrs A, a 32-year-old married woman, presented to us with a history of anhedonia, hopelessness, loss of energy, disturbed sleep and low self-esteem of 4 years duration. Her symptoms met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for MDD (3), and has been treated with venlafaxine 75 mg/day for the last six months. Although her depressive symptoms subsided to one point, no further substantial improvement has been observed. Subsequently, she was also prescribed oral mirtazapine 30 mg/day for her disturbed sleep but this medication was stopped after two weeks because of unusual disturbing restlessness and increased appetite. The venlafaxine dose was then increased to 150 mg/day over a period of 2 weeks. She tolerated this dose of the drug very well but did not show any improvement in her sleep disturbance. Upon her admission to the hospital, venlafaxine 150 mg/day was continued, and agomelatine

25 mg/day (taken at bedtime) was added to the treatment due to its proposed regulatory effects on circadian and sleep-wake cycles. No other new drugs had been introduced over the prior few days. After 10 days of agomelatine therapy, maculopapular rashes bright red in color and pruriginous appeared prominently on the trunk. The rashes blanch with pressure and showed signs of hypersensitivity reactions after the 8th day. No maculopapular rashes have been observed in any mucous membrane of the body. On admission, results of the clinical and laboratory examinations were unremarkable except for eosinophilia (14.4%; normal: 1-5%). The patient denied having used alcohol, smoke or illicit drug as well as having used new soap, cream or different kind of food. Also, there was no history of any endocrinological or dermatological disorder and allergy, preceding the administration of agomelatine therapy. She refused to give consent for a skin biopsy stating cosmetic reasons. Subsequently, agomelatine treatment was discontinued and it was replaced with quetiapine fumarate 25 mg/day (taken at bedtime). After termination of agomelatine treatment, skin rashes gradually subsided within a week. She is on regular follow-up with a good improvement in her clinical condition. She maintained her improvement with this treatment and no fresh skin lesions have appeared since then. The probability of an adverse drug reaction (ADR) was assessed using the Naranjo probability scale (4). This indicated a possible association (Naranjo scale scored; 8 points) between agomelatine and maculopapular rash. Maculopapular rash (maculopapular exanthem) is the most frequent (accounting for about 95%) clinical manifestation of non-immediate (type IV) hypersensitivity reactions, due to drugs (5). These hypersensitivity reactions can be caused by many medications (6). According to the report

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of European Medicines Agency (EMA), agomelatine-induced maculopapular rashes rarely occur (<1/10.000) (1). As regards cutaneous reactions, agomelatine appeared to be associated with different kinds of rashes; the incidence in the agomelatine group was 0.7% vs 0.4% for placebo (1, 7). The present case has demonstrated that, ADR of agomelatine may be depending on its effect of non-immediate type IV hypersensitivity reaction. It should be noted that, establishing causality between a medication exposure and the development of an ADR is a difficult process. In our opinion, agomelatine should be added to the list of drugs that can induce maculopapular rashes.

Consequently, ADRs can cause severe suffering, and are probably more frequent than many people think (6). Further studies are needed to determine the exact mechanism for the emergence of maculopapular rash due to agomelatine.

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