CASE REPORT / OLGU SUNUMU

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Maculopapular Rash Related to Atomoxetine: Case Report

Atomoksetin ile İlişkili Makülopapüler Döküntü: Olgu Sunumu

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ABSTRACT

Exanthematous drug eruptions, also known as maculopapular drug eruptions, are the most common drug-induced hypersensitivity reactions. Pruritus, urticaria, exanthematous rash, fixed drug eruption, photosensitivity, pigmentation and alopecia are common skin reactions to psychotropic medications. Atomoxetine (ATX), a selective inhibitor of presynaptic norepinephrine transporters (SNRI), is classified as a non-stimulant and is commonly used in the treatment of attention deficit hyperactivity disorder (ADHD). It also binds to dopamine and serotonin transporters with a low affinity. Abdominal pain, loss of appetite, somnolence, irritability, fatigue, dizziness and dyspepsia are the most common side effects of ATX. Major cutaneous drug reactions with SNRIs are rarely reported in the literature. Here we present an eight-year-old girl diagnosed with ADHD who had a drug-induced skin reaction after an increase in the dosage of ATX treatment.

Keywords: ADHD, atomoxetine, maculopapular eruption

ÖZ

Makülopapuler ilaç erüpsiyonları; ekzantematöz ilaç reaksiyonları olarak da bilinen en sık ilaç hipersensitivite reaksiyonlarıdır. Kaşıntı, ürtiker, ekzantematöz döküntü, fiks ilaç erüpsiyonları, fotosensitivite, pigmentasyon ve alopesi psikotrop ilaçlara karşı gelişen en sık deri reaksiyonlarıdır. Atomoksetin (ATX) selektif norepinefrin geri alım inhibitörü (SNRI) olup dikkat eksikliği hiperaktivite bozukluğu (DEHB) tedavisinde Gıda ve İlaç İdaresi onayı alan non-stimülan bir ilaçtır. Düşük affinitede dopamin ve serotonin taşıyıcılarına da bağlanmaktadır. Karın ağrısı, iştah azalması, somnolans, irritabilite, halsizlik, baş dönmesi ve dispepsi ATX'in en sık bildirilen yan etkileridir. Literatürde SNRI ilaçlar ile ortaya çıkan majör deri reaksiyonları nadir olarak bildirilmiştir. Bizim çalışmamızda DEHB tanısı olan ve ATX tedavisi sırasında doz artışı ile birlikte ilaca bağlı deri reaksiyonu gelişen 8 yaşında bir kız olgu sunulmuştur.

Anahtar Kelimeler: DEHB, atomoksetin, makülopapüler döküntü

Introduction

"Adverse drug reactions" (ADRs), according to the World Health Organisation, consist of all unwanted, deleterious reactions to a drug used for diagnosis, treatment or prophylaxis at an appropriate dose.[1] ADRs may develop via immune or non-immune mechanisms, and cutaneous ADRs are the most common form, comprising 10%-30% of all reactions.[2] Clinically, cutaneous ADRs may lead to exanthema, urticaria/angioedema, drug eruptions, pustules, bullae, Stevens-Johnson syndrome/Toxic Epidermal Necrolysis or cutaneous lupus.[3]

Attention deficit/hyperactivity disorder (ADHD) is a neuro-developmental disorder characterised by impaired, persistent and age-inappropriate inattention, hyperactivity and/or impulsivity.[4] Atomoxetine, a selective norepinephrine reuptake inhibitor, is a non-stimulant agent frequently used to manage ADHD. The beneficial effects of atomoxetine are thought to be due to its actions in the prefrontal cortex and the absence of effects on serotonin or dopamine transporters.[4] The most frequent side effects are reported to include stomach aches, reduced appetite, nausea/vomiting, somnolence, irritability, weakness, vertigo and dyspepsia.[5] According to the manufacturer's information, cutaneous ADRs with atomoxetine may be observed in 2% of children.[6] According to web surveys, rashes may develop in 1.5% of patients using atomoxetine (https://www.ehealthme.com/ds/atomoxetine/rash/, accessed on 05.14.2019). Here, we report an 8-year-old female child with ADHD who developed maculopapular eruption while using atomoxetine. Informed consent was obtained from the parents.

Case Report

The patient was an 8-year-old female third grader who was brought to our department with complaints of "hyperactivity and non-compliance with chores and homework." The complaints, which were corroborated by her teachers, had been present for 6 years. She struggled academically, had poor spelling/writing

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and was rejected by her peers. Her developmental history was normal, except for having spoken her first words in her third year and forming sentences at 5 years. Her past medical history and family history were normal.

A baseline mental status examination revealed a hyperactive, inattentive female child with age-appropriate development. Parent and teacher forms supported ADHD, while a psychometric evaluation with the Wechsler Intelligence scale for Children-revised form revealed a total IQ of 76 with a 31-point difference between verbal and performance IQs. According to her history, examinations and tests, she was diagnosed with ADHD- hyperactive/impulsive presentation and a specific learning disorder (SLD) as per the DSM-5 criteria.[4] A 4-week trial of methylphenidate 20 mg/day in divided doses was not effective, and atomoxetine 25 mg/day was started. Titration to 50 mg/day was planned for the second week. However, the patient was brought to the department prior to titration due to a sudden eruption of diffuse, swollen rashes on her chest, back, shoulders and forearms. She was not using any other drugs at the time. Consultations from the Departments of Pediatrics and Dermatology were requested. Laboratory evaluations, including whole blood count, thyroid, renal and liver function tests, anti-nuclear antibodies, vitamin B12 and electrolytes, were within normal limits. The rashes were evaluated as exanthematous, maculopapular lesions (Figure 1) due to atomoxetine, and treatment was stopped. The rashes resolved spontaneously in the third week. Evaluation with the Naranjo et al.[7] revealed a score of 7 (probable adverse reaction). Due to continuing symptoms of ADHD and SLD, she was started on methylphenidate osmotic-controlled release oral delivery system 18 mg/day. Her symptoms benefited from this treatment, and she developed no adverse effects at the sixth month of treatment.

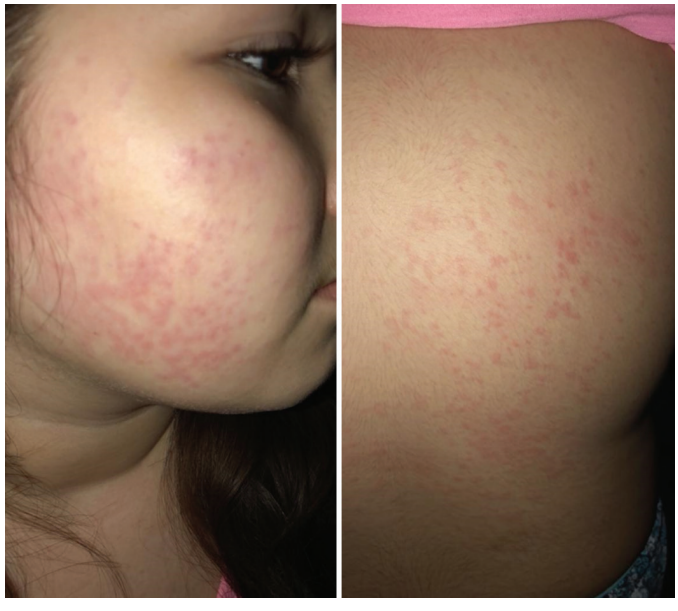

Figure 1. Exanthematous, maculopapular lesions on the face and body (an informed consent was obtained from the parents)

Discussion

Here, we report the development of diffuse exanthema (maculopapular rash) probably related to atomoxetine treatment in a prepubertal child with ADHD and SLD. Maculopapular eruptions due to drugs constitute the most common form of hypersensitivity reactions and may develop with anti-depressants, anticonvulsants, antipsychotics and other psychopharmacologic agents.[1,3,8,9]

Cutaneous ADRs with atomoxetine may be observed in 2% of patients.[6] This rate is also reported in web-based surveys. According to previous studies.[1,3,8,9], those reactions mostly occur in the first month of treatment, and many are thought to be due to delayed-type, T-cell-mediated immune reactions. Mild eosinophilia may be observed, and concomitant viral infections, co-medication with other drugs, disorders of the immune system and polymorphisms in the human leukocyte antigen alleles may increase the risk. In accordance with those reports, the rash developed at the end of the first week in our patient. However, neither eosinophilia nor any of the predisposing conditions were present. Evaluation with the Naranjo et al.[7] revealed a probable relationship between rash and atomoxetine. Post-marketing reports of cutaneous ADRs related to atomoxetine are rare.[10] Bilgiç and Bilgiç[10] reported a case of a female child with ADHD who developed localised depigmentation in the fourth week of treatment with atomoxetine. The authors posited that the depigmentation may be caused by catecholaminergic dysfunction leading to melanocyte destruction.

Our patient was deemed worthy of presentation due to the rarity of cutaneous ADRs with atomoxetine, which may even occur in the absence of predisposing risk factors.

Ethics

Informed Consent: Informed consent was obtained from the parents.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: N.K., Ç.Y., A.E.T., Design: N.K., Ç.Y., A.E.T., Data Collection or Processing: N.K., Ç.Y., A.E.T., Analysis or Interpretation: N.K., Ç.Y., A.E.T., Literature Search: N.K., Ç.Y., A.E.T., Writing: N.K., Ç.Y., A.E.T.

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