



## OLGU SUNUMU/CASE REPORT

### Cutaneous allergic reaction due to alprazolam in a child

Çocukta alprazolama bağlı kutanöz alerjik reaksiyon

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#### Abstract

Cutaneous allergic reactions due to drug intake may be triggered by many types of drugs such as atropine, anticonvulsants and benzodiazepines. But allergic reactions due to benzodiazepines are extremely rare. Alprazolam is a benzodiazepine which may be useful for refractory idiopathic urticaria due to antihistaminergic effect. Although antihistaminergic effect of alprazolam, a cold urticaria case and an angioedema case induced by alprazolam are known in the literature. In the case, we present a child suffering from cutaneous allergic reaction due to alprazolam at the first dose taken.

**Key words:** Allergy, alprazolam, child, cutaneous drug reactions

#### Öz

İlaça bağlı kutanöz alerjik reaksiyonlar atropin, antikonvulzanlar ve benzodiyazepinler gibi birçok ilaç türü ile ortaya çıkabilir. Fakat benzodiyazepinlere bağlı alerjik reaksiyonlar oldukça nadirdir. Alprazolam antihistaminergik etkisinden dolayı refraktör idiyopatik ürtiker tedavisinde faydalı olabilecek bir bezodiyazepindir. Alprazolamın antihistaminergik etkisine ragmen literatürde alprazolam ile tetiklenen bir anjiödem vakası ve bir de soğuk ürtikeri vakası bilinmektedir. Bu olguda tek doz alprazolamdan dolayı kutanöz alerjik reaksiyon gelişen bir çocuk sunulmuştur.

**Anahtar kelimeler:** Alerji, alprazolam, çocuk, cilt reaksiyonu

## INTRODUCTION

Drug reactions are frequently seen and the incidence of drug reactions is between 1-8 % in normal population. Of note, this proportion was reported to increase for non-steroid anti-inflammatory drugs, antibiotics and antiepileptic drugs<sup>1</sup>. Most of the drug reactions seen are cutaneous adverse effects<sup>2-4</sup>. Cutaneous reactions can be described as any undesired structural or functional changes in the skin, adnexa or mucous membranes caused by drugs<sup>5</sup>. Cutaneous reactions due to drug intake may be triggered by acetaminophen, antacids, atropine and benzodiazepines<sup>6-7</sup>.

The data regarding the frequency of drug reactions in children is limited; it has been reported as 9.5% in the children in pediatrics clinics while it's 1.5% on

polyclinic patient<sup>8</sup>. Moreover, it has been demonstrated that 39% of drug reactions seen in children can be life-threatening<sup>9</sup>. The drug reactions in children are frequently caused by antibiotics (penicillins, semi-synthetic penicillins, cephalosporins, trimethoprim-sulphomethoxazole) and anticonvulsants<sup>9</sup>. These are usually like exanthema, but they can be also urticarial, maculopapular (morbilliform), scarlatiniform, bullous or pustular<sup>9</sup>.

Allergic reactions due to benzodiazepines are extremely rare, and most have been associated with diazepam<sup>10</sup>. In the last decade, allergic reaction associated with alprazolam usage has not been reported except for an angioedema case and a cold urticaria case<sup>11,12</sup>. We hereby present a child suffering from cutaneous allergic reaction due to alprazolam at the first dose taken and also suffering

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from moderate mental retardation with attention deficit-hyperactivity disorder (ADHD).

## CASE

The case was admitted to our child and adolescent psychiatry out-patient clinic for the first time at the age of 10. He was born at 30 weeks of gestation by cesarean section. At the birth history, he suffered some asphyxiation, and his developmental skills were delayed relative to chronological age expectations. He could hear, but he could not speak any word.

He maintained eye contact, understood commands and displayed facial mannerisms. But, he also had poor communication with his sibling and peers beyond that expected by his mutism. He displayed nocturnal and diurnal enuresis, hyperactivity, screaming, biting, injuring and hitting himself and other people in addition to chronic significant sleep disturbances.

He had Moderate Mental Retardation according to DSM IV TR criteria. He could have attended only special education for five years. Initially, he was consulted to the pediatric urology department for the day and night wetting. His plain abdominal X-ray graphy, abdominopelvic ultrasound, hemogram, liver function enzymes, total protein, B12, Folic acid, T3, T4, TSH , complete urine analysis and urine culture results were normal. After all these detailed investigations, the pediatric urologist prescribed 1mg/day Tolterodin L-tartarat for the day and night wetting.

We evaluated the case after the child urology department's evaluation. He had harmful behaviors such as hitting, screaming. Furthermore, he had hyperactivity and sleep disturbance. He was diagnosed as Moderate Mental Retardation with ADHD according to DSM-IV criteria. We advised his mother to organize some social activities for him and we prescribed 0,5 mg/day risperidone for his disruptive behaviors. After 2 months, he came to our child and adolescent psychiatry outpatient clinic for a routine control. His behaviors got worse and his attachment to his mother was intensified. Additionally, his hyperactivity and irritability increased substantially. His symmetry and repeating compulsions began suddenly. We thought that akathisia developed due to risperidone, risperidone treatment stopped and 100 mg/day chlorpromazine was prescribed.

After one month, his harmful behaviors decreased due to taking chlorpromazine treatment, but his sleep disturbance and irritability still continued. Therefore, alprazolam 0.5 mg/day was added to chlorpromazine treatment for sleep disturbance and irritability.

Nearly twelve hours after adding alprazolam to the treatment, the patient developed generalized pruritic erythematous lesions especially localized on his face and dorsal parts of his hands. There was no mucosal, palmar or plantar involvement. He had no wheezing, dyspnea or intense cough. The dermatology department consulted the patient on the same day. An allergic drug reaction was presumed to be the cause and cetirizine hydrochloride was prescribed 10 mg BID. All skin lesions disappeared and cetirizine hydrochloride was quited in one week. Hydroxyzine hydrochloride 25 mg/day was initiated for sleep problems.

He is still being under follow-up in our child and adolescent outpatient clinic and he is using chlorpromazine 100 mg/day, hydroxyzine hydrochloride 25 mg/day, Tolterodin L-tartarat 1 mg/day and his symptoms have lessened.

## DISCUSSION

Although alprazolam is used widely in child and adolescent psychiatry clinics<sup>13</sup>, allergic skin reactions depending on alprazolam are rarely seen. As far as we know, allergic reaction due to alprazolam in treatment dosage has not been reported in the last decade except for an angioedema case and a cold urticaria case<sup>11,12</sup>.

Twelve severe refractory idiopathic urticarial cases were divided to two groups: one of them is alprazolam taken, and the other is rupatidine taken. All of alprazolam group treated whereas the 2 patients treated with rupatidine did not. Therefore, alprazolam may be an important agent on successful treatment of chronic drug-resistant urticaria<sup>14</sup>. Alprazolam has histamin H1 and H2 receptor antagonism in addition to increasing GABA receptor activity. This antihistaminergic effect is known to be responsible for successful treatment of drug resistant urticaria. Our case had mild allergic cutaneous reaction and no systemic complaints due to alprazolam allergy. Although antihistaminergic effect of alprazolam, allergic skin reaction is a rare clinical entity but may be encountered. On the other hand, severe conditions like angioedema could also

be seen, so clinicians should be aware of these rare complications of alprazolam treatment.

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