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OLGU SUNUMU / *CASE REPORT*

A Rare Adverse Effect of Cetirizine in a 7- Month-Old Infant: Dystonic Reaction

Yedi Aylık Bebekte Setirizin'in Nadir Bir Yan Etkisi: Distonik Reaksiyon

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ABSTRACT

Cetirizine is a selective H1 histamine receptor antagonist derived from piperazine. Piperazine is a cyclic moiety molecule located in the structure of many drugs, including anxiolytics, antidepressants, and antipsychotics. Drug-induced dystonia is reported mostly due to antipsychotic and antiemetic drugs. It occurs due to the disruption of dopamine and acetylcholine balance in favor of acetylcholine. Although cetirizine is a relatively safe drug, it has rarely been reported to cause a dystonic reaction. To the best of our knowledge, there is no reported case of dystonia due to cetirizine in infancy. Here, we present a 7-month-old patient who developed a dystonic reaction after cetirizine administration.

Keywords: Acute dystonia, cetirizine, infant

ÖZ

Setirizin, piperazinden türetilen seçici bir H1 histamin reseptör antagonistidir. Piperazin, anksiyolitikler, antidepresanlar ve antipsikotikler dahil olmak üzere birçok ilacın yapısında yer alan siklik bir moleküldür. İlaca bağlı distoni, çoğunlukla antipsikotik ve antiemetik ilaçlara bağlı olarak bildirilmektedir. Dopamin ve asetilkolin dengesinin asetilkolin lehine bozulması sonucu oluşur. Setirizin nispeten güvenli bir ilaç olmasına rağmen, nadiren distonik reaksiyona neden olduğu bildirilmiştir. Şimdiye kadar süt çocukluğu döneminde setirizine bağlı olarak bildirilmiş bir distoni vakası yoktur. Burada setirizin uygulaması sonrası distonik reaksiyon gelişen 7 aylık bir hasta sunulmuştur.

Anahtar Kelimeler: Akut distoni, setirizin, sütçocuğu

INTRODUCTION

Cetirizine is a derivative of piperazine. It acts as a highly selective antagonist of the histamine H1 receptor and is classified as a second generation, non-sedative antihistamine (1). Piperazine is a cyclic molecule and component of many antipsychotic, antidepressant, and anxiolytic drugs (1). Piperazine containing drugs, such as clozapine, quetiapine, and trifluoperazine, exertsits central pharmacological activity and antipsychotic effects mainly through dopamine receptor blockade (1,2). Generally, second-generation antihistamines are characterized by their lack of access to the central nervous system and the absence of central side effects (3); however, recent studies have highlighted that cetirizine also exerts histamine receptor blocking activity in the central nervous system (4). Therefore, a new classification was made based on the effect on cerebral H1 receptors for antihistaminic agents, and cetirizine has been included among the less sedative antihistaminic agents (4,5).

Dystonia is a movement disorder characterized by continuous or intermittent muscle contractions, causing abnormal posture and or movement. Drug-induced dystonia typically may occur with antipsychotic and antiemetic drugs due to the dopamine receptor blockade effect. Calcium channel blockers and selective serotonin reuptake inhibitors have been rarely reported as the cause of drug-induced dystonia (6).

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There are few reported cases of dystonia due to cetirizine (7-10). To the best of our knowledge, there are no reported cases of dystonia due to cetirizine in infancy in the literature. Herein, we present a 7-month-old patient who developed the drug-induced dystonic reaction after the first dose of cetirizine.

CASE REPORT

An 7 month-old male patient had a history of contraction in his neck for 20-30 minutes after the administration of 5 ml oral cetirizine. In this period, his neck rotated to the right, chin deviated to the same side, and the right half of his lips contracted. This half-hour episode was completely regressed with midazolam. He had no runny nose, nasal congestion, cough, or fever.

He was not taking any other medication other than vitamin D replacement. The neuromotor developmental stages of the patient were appropriate for his age. He has been followed up for egg allergy since he was 6 months old . There was no history of a movement disorder in his family.

At his first examination, body temperature was 36.8°C, the respiratory rate per minute was 14/min, heart rate was 85/min, weight was 6.9 kg (90-95 p), height was 63 cm (90-95 p), and head circumference was 42 cm (90-95p). The examinations of the oropharynx, ear, and eye were regular. There were no other pathologic findings in system examinations. His reflexes were normoactive, and no pathological reflex was observed.

Laboratory tests

In complete blood count, hemoglobin was 12 g/dL, leukocyte count was 8770/mm^3, platelet count was 434,500/mm^3, and total eosinophil count was 400/mm^3. The liver and kidney functions were normal. The blood calcium level was 9.4 mg/dL. Other electrolytes and glucose were within normal limits. Erythrocyte sedimentation rate was 10 mm/h, immunoglobulin (Ig) E level was 37 IU/mL, IgG level was 987 mg/dL, IgA level was 112 mg/dL, and IgM level was 95 mg/dL. Sleep electroencephalography (EEG) and cranial magnetic resonance imaging (MRI) were normal. Naranjo score was 7 for cetirizine.

Detailed history revealed that the patient could use nebulized salbutamol and budesonide due to recurrent cough and wheezing without any side effects during the one-year follow-up period. He did not use any cetirizine containing preparation again and did not experience any similar reaction.

DISCUSSION

Although it is accepted that the second-generation antihistaminic agents have the low transition to the central nervous system because of their high molecular weight, hydrophilic groups and high peripheral H1 receptor affinity, *positron emission tomography (PET)* studies on cetirizine showed that it binds to H1-receptors at the rate of 20-50% in the cerebral cortex (4,5).

Drug-induced dystonia usually occurs due to typical antipsychotic and antiemetic drugs as a result of the imbalance between dopaminergic and cholinergic activity and blockage of dopamine (D) receptors. Although not fully elucidated, gamma-aminobutyric acid (GABA) is thought to contribute to the development of dystonia (9,11).

A limited number of pediatric patients with dystonia due to cetirizine has been reported. One of them developed dystonia 10 hours after taking a single dose of cetirizine for upper respiratory tract infection and successfully treated with clonazepam. No recurrence was reported during follow-up (7). Another patient, a four-year-old boy, had acute dystonia after 18 days of use of cetirizine. His mother had dystonia due to promethazine in infancy, and his grandfather had akathisia due to metoclopramide. It was reported that the patient was observed for 8 weeks, and it was repeated once after expectorant syrup without a known trigger (9). There are two cases of cetirizine induced dystonia reported from our country. The first case was a 6-year-old boy who had dystonia after 3 days of cetirizine treatment and did not recur after treatment with biperiden (8). The second was a three-year and 5-month-old patient who developed dystonia 20 hours after taking a single dose of albendazole and cetirizine together and recovered in 6 hours after treatment with biperiden (10). In most of the cases reported in the literature, dystonia developed after the first dose of the drug, as seen in our patient. To our knowledge, there is not any patient identified as acute dystonia due to cetirizine in infancy. Therefore, we believe that our case is unique in being the first case reported in the literature. Our patient's symptoms started within 30 minutes. The time interval between drug intake and onset of symptoms is in fact consistent with the maximum reported plasma concentration (T max) as reported 0.5 hours for oral cetirizine (11). It was shown that cetirizine binds to histamine receptors in the central nervous system (1,2,4,5). In our opinion, cetirizine caused central nervous system side effects in this patient due to high intake at double the usual recommended dose.

We diagnosed our patient with cetirizine-induced acute dystonia because cetirizine use was temporally related to the adverse event. The findings were recovered with benzodiazepine, which is used in the treatment of dystonia. Naranjo score (Adverse drug reaction probability score) was calculated as 7 points, suggesting a possible adverse drug event (12). A seizure was also excluded with EEG and MRI, which is the differential diagnosis of drug-induced acute dystonia.

CONCLUSION

As a result, cetirizine is widely used in pediatric patients considering that it is safe. However, it should be kept in mind that it may cause drug-induced dystonia during infancy.

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