Angioedema associated with atomoxetine: a case report

Merve ÇIKILI UYTUN,1 Esra DEMİRCİ2

ABSTRACT
Angioedema can be occur a drug adverse reaction. Drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), antihypertensive drugs, antibiotics, proton pump inhibitors, fibrinolytic agents, estrogens, calcium channel blockers, beta blockers, and psychotropic drugs (such as serotonin reuptake inhibitors-SSRIs) can induce this reaction. In the literature, there are few case reports about angioedema induced by SSRIs and there is no case report related to atomoxetine. Herein we report a case of angioedema which occurred after initiation of atomoxetine in a 9-year-old girl being treated for attention deficit and hyperactivity disorder; the side effect disappeared after discontinuation. (Anatolian Journal of Psychiatry 2016; 17(Suppl.3):35-37)

Keywords: atomoxetine, angioedema, ADHD

INTRODUCTION
Angioedema (AE) is defined as a deep dermal, subcutaneous and/or mucous swelling.1 The pathogenesis of AE is related to an activation of the contact phase system, which leads to bradykinin that is known as the main vasopermeabilizing substance.2 Because of its rapid and potentially life-threatening clinical progress, angioedema of the pharynx and larynx require emergency treatment.3 There are different clinical forms of AE such as hereditary AE, which is due to a genetic defect of the complement C1 inhibitor (C1-inh) with an autosomal transmission. The other type of AE is acquired AE, which is associated with malignancies, lymphoproliferative disorders, monoclonal gammopathies, or other conditions.4 Angioedema may also occur due to the adverse effects of drugs. Drug-induced angioedema has been reported to result from several drugs, including non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor antagonists, antibiotics, radiocontrast media, proton pump inhibitors, statins, fibrinolytic agents, estrogens, diuretics, calcium channel

---

1 Kayseri Research and Training Hospital, Emel-Mehmet Tarman Child Hospital, Department of Child and Adolescent Psychiatry, Kayseri, Turkey
2 Erciyes University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, Kayseri, Turkey
Correspondence address / Yazışma adresi:
Uzm. Dr. Merve ÇIKILI UYTUN, Kayseri Eğitim ve Araştırma Hastanesi, Emel-Mehmet Tarman Çocuk Hastanesi, Çocuk ve Ergen Psikiyatri Kliniği, Kayseri
E-mail: mervecikili@yahoo.com
Received: 27.02.2016, Accepted: 31.03.2016, doi: 10.5455/apd.220072

Anadolu Psikiyatri Dergisi 2016; 17(Ek.3):35-37
Angioedema associated with atomoxetine: a case report

Blockers, beta blockers, and psychotropic drugs (such as serotonin reuptake inhibitors-SSRIs). Atomoxetine is a selective norepinephrine reuptake inhibitor and the first nonstimulant medication for the treatment of attention-deficit/hyperactivity disorder (ADHD). Although there are reported cases of allergic reactions such as urticaria and rash, which were induced by atomoxetine, we were unable to find any case of angioedema associated with atomoxetine (we searched the terms atomoxetine and angioedema together) via PubMed and Google Scholar.

We report herein a case of angioedema which occurred after initiation of atomoxetine in a 9-year-old girl being treated for attention deficit and hyperactivity disorder; the angioedema disappeared after discontinuation and antiedema therapy.

CASE

A 9-year-old girl who was referred to our outpatient clinic with complaints of inattention, gradually decreased academic performance, difficulty in doing homework, forgetfulness, and not being organized. She had normal level of psychomotor development and had no disorder in her medical history, allergy history or family history. At the time of the evaluation in our hospital, her body weight was 34 kg and she had no abnormality in her physical examination. She had been treated previously with OROS-methylphenidate (MPH) and the OROS-MPH dosage was increased to 27 mg/day (1.5 mg/kg). It was used for 2 months for a diagnosis of ADHD. Because of inadequate response with OROS-MPH, it had been discontinued. Atomoxetine was initiated at a dosage of 18 mg/day and the dosage was increased to 25 mg/day after 2 weeks. After the increase in dose the patient, developed angioedema on the lips and tongue. Physical examination did not show any relevant sign such as 37rticarial. The patient was referred to the dermatology department for differential diagnosis and to exclude other etiologic factors for angioedema. Laboratory investigation showed normal levels of C1- inh and inflammatory markers. The patient had no allergy history and skin test was negative. There was no angioedema history in the patient’s family and normal levels of C1-inh excluded hereditary angioedema. However, we did not find any disorder in the patient which was related with angioedema.

Based on the clinical examinations and analyses that were performed, angioedema was thought to have developed due to atomoxetine. Atomoxetine was discontinued and an antihistamine and prednisolone were started within two hours. The patient’s symptoms resolved completely three days after atomoxetine treatment was stopped.

Written informed consent was obtained from the patient’s parents for publication of this case report and any accompanying images.

DISCUSSION

Atomoxetine is a well-tolerated drug in children and adolescents with ADHD. The most frequent adverse events are gastrointestinal symptoms, reduced appetite, sleep problems, increased heart rate and blood pressure. Serious but uncommon side effects of atomoxetine include hepatotoxicity, with an increase in hepatic enzymes, bilirubin and jaundice, suicidal ideation and attempts.

Drug-induced angioedema is related with 37 articular in approximately 50% of cases and possibly complicated by life-threatening anaphylaxis. Even though the combination of 37rticarial and/or angioedema with systemic symptoms is typical for IgE mediated allergic reactions, some drugs induced isolated angioedema by a kinin-dependent mechanism, which is particular to angioedema but not urticarial.

Drug-induced angioedema, like other cutaneous drug reactions, has been reported to most frequently occur following the use of beta-lactam antibiotics and NSAIDs, though epidemiologic data studies are limited. In the literature, there are few case reports about angioedema induced by SSRIs. There are two case reports for angioedema related with fluoxetine use, and there is only one case report about AE induced by 37rticarial and paroxetine. Although they have been shown to be uncommon, allergic reactions including anaphylactic reactions, angio-neurotic edema, 37rticarial, and rash, have been reported in patients taking atomoxetine, however, atomoxetine-induced angioedema has not been reported in the literature.

In our case, angioedema developed on the lips only; she had no 37rticarial. We thought that atomoxetine may have induced angioedema by the quinine-dependent pathway. She had no allergy or any disease that could cause angioedema. Because of a lack of family history for similar reactions or allergy and normal C1 levels, coinciding with use of atomoxetine, the latter was

Anatolian Journal of Psychiatry 2016; 17(Suppl.3):35-37
thought to be the offending agent. We used the Naranjo ADR Probability Scale for adverse reaction assessment and the score was 7 (5-8 probable).16 As a conclusion, we believe that clinicians should be aware of angioedema associated with atomoxetine treatment, and should assess dermatological/allergy history before beginning to atomoxetine treatment.

**Yazarların katkıları:** M.Ç.U.: Literature, the assessing the patient, and writing the article; E.D.: The assessing the patient, and revising the article.

**REFERENCES**