QUETIAPINE: A RARE CAUSE OF ANGIOEDEMA

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Background

Quetiapine is a dibenzothiazepine derivative that is used to treat patients with schizophrenia as well as for the treatment of acute manic episodes associated with bipolar I disorder. The antipsychotic effect of quetiapine is thought by some to be mediated through antagonist activity at dopamine and serotonin receptors. Specifically the D1 and D2 dopamine, the alpha 1 adrenoreceptor and alpha 2 adrenoreceptor, and 5-HT1A and 5-HT2 serotonin receptor subtypes are antagonized. Angioedema is the swelling of subcutaneous and deep dermal tissues that occurs on the face, tongue, extremities, genitals, and rarely, larynx. The late onset angioedema is a rare clinical condition that occurs months or years later, most of which is reported with use of ACEIs. Here, we report a male patient who developed late onset angioedema after treatment with quetiapine after two plus years.

Case Report

A 65 year old male was admitted to our facility for altered mental status. His past medical history includes schizophrenia (maintained on Haldol Decanoate 100mg IM every 4 weeks, quetiapine 600mg daily and valium 5mg thrice daily), blindness, hypertension, primary hyperparathyroidism, hypercalcemia and hepatitis C. At the admission time, patient was found to be afebrile, have AKI with hypernatremia, hypercalcemia, and leukocytosis. He was admitted with a working diagnosis of encephalopathy due to severe hypernatremia. On physical examination, the patient was lethargic and not responding to any questions. At baseline, he is withdrawn, preferring to be left alone and following some commands. All his oral home medications were held due to his inability to swallow. He had missed his monthly dose of Haldol decanote due to admission to the hospital. He was restarted on his home dosage of quetiapine 300mg twice a day on second day of his admission as he was more awake and responding to commands and passed swallowing evaluation. On the tenth day after starting quetiapine, facial swelling and lip edema were observed on his physical examination. He had no symptoms of pruritus and any infection. Angioedema secondary to quetiapine use was suspected at that time. He had no medical and family history of angioedema and allergy. There were no herbal drugs used by the patient. Hence, quetiapine was immediately discontinued at that time and patient was started on IV Methyl-prednisone 40mg every 6 hours along with Benadryl 20mg as needed. Facial and lip edema started to decrease within 2 days of discontinuation of quetiapine and steroids were slowly tapered down. Psychiatry was consulted who recommended continuing using Haldol 5 mg intramuscularly 2 times a day as needed during the hospital stay for his schizophrenia. The Naranjo probability scale was administered and a score of 5 was obtained, suggesting a probable adverse effect associated with quetiapine [1]. Since angioedema can become life-threatening if larynx becomes involved[2], drug rechallenge was not considered. Based on his symptoms and improvement after discontinuing the drug, the diagnosis was compatible with “quetiapine associated angioedema.” The swelling of the face and lips was completely resolved after 10 days of discontinuing the medication and steroids were discontinued as well.

Vitals

On admission:

Temp: 98.9 ^{0} F

BP: 110/70

Pulse: 112

RR: 22

SpO2: 71%

Labs

Admission Day

WBC AUTO	10*3/uL	**20.90***
HEMOGLOBIN	g/dL	13.6
HEMATOCRIT	%	43.0
PLATELETS AUTO	10*3/uL	251
SODIUM	mmol/L	**162***
POTASSIUM	mmol/L	3.6
CHLORIDE	mmol/L	**122***
CO2	mmol/L	29.0
BUN	mg/dL	**35.0***
CREATININE	mg/dL	**1.4***
GLUCOSE	mg/dL	88
CALCIUM UA	mg/dL	**16.5***
BILIRUBIN TOTAL	mg/dL	0.5
AST	U/L	**68***
ALT	U/L	**49***
ALK PHOS	U/L	**132***
ALBUMIN	g/dL	3.7

References

1. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30: 239–245.
2. Kaplan, Allen P. “Angioedema.” *The World Allergy Organization journal* vol. 1,6 (2008): 103-13. doi:10.1097/WOX.0b013e31817aecbe
3. Kalambay, Junior & Ghazanfar, Haider & Pena, Karen & Munshi, Ruhul & Zhang, George & Patel, Jay. (2017). Pathogenesis of Drug Induced Non-Allergic Angioedema: A Review of Unusual Etiologies. Cureus. 9. 10.7759/cureus.1598.
4. Muzyk AJ, Cvelich RG, Kincaid BR, Preud'homme XA. Angioedema occurring in patient prescribed iloperidone and haloperidol: a cross-sensitivity reaction to antipsychotics from different chemical classes. J Neuropsychiatry Clin Neurosci. 2012; 24 (2): E40
DOI: https://doi.org/10.1176/appi.neuropsych.11040094. PubMed PMID: 22772698
5. Tuman TC, Tuman BA, Şereflican B, Yildirim O. Quetiapine associated with angioedema. J Clin Psychopharmacol. 2016; 36 (3): 289- 90. DOI: https://doi.org/10.1097/JCP.0000000000000503

Discussion

Angioedema is characterized by painless, nonpruitic, nonpitting, and well-circumscribed areas of edema due to increased vascular permeability mediated by histamine, serotonin and bradykinins, causing the arterioles to dilate while inducing a brief episode of vascular leakage in the venules[2]. Complications of angioedema range from dysphagia to respiratory distress, complete airway obstruction, and death from laryngeal edema[2].

Drugs may induce two different types of angioedema: allergic and non-allergic angioedema. Allergic angioedema is a type I hypersensitivity, mediated by histamine[3]. Here, the medication cross links with IgE antibody bound on the surface of mast cells which results in the release of histamine[3]. Clinically, drug induced allergic angioedema will present with the rapid onset of swelling of mucosa and submucosa tissues and usually have urticarial rash present[3]. Symptoms will respond quickly to antihistamine, epinephrine and corticosteroid treatment. Drug induced non-allergic angioedema is mediated by bradykinin and the urticarial rash is absent as dermis is usually spared[3]. It usually occurs within first week of therapy and usually resolves within 24 to 48 hours after cessation of the drug[5].

Several cases of angioedema associated with drugs have been reported including the use of angiotensin converting enzyme inhibitors, insulin, nonsteroidal noninflammatory agents, sulfanomides, aspirin and beta lactam antibiotics. Antipsychotic agents causing angioedema reported cases include the use of clozapine, olanzapine, iloperidone, haloperidol, quetiapine, paliperidone, ziprasidone, risperidone, and chlorpromazine[4]. One case published in 2016 detailed a patient started on quetiapine who developed facial swelling and periorbital edema within 4 days of initiation of the drug[5]. However, in our case, the patient was on quetiapine for over two years and suddenly developed swelling of the lips and face.

Conclusion

Drug induced reactions may vary in severity and have to be closely monitored to prevent life threatening complications. The review of literature suggests that angioedema can develop at any time during the therapy with antipsychotics, and whenever it is suspected, clinicians should immediately stop the suspected agent and depending on the severity of the symptoms, appropriate treatment measures should be undertaken.