mhc
MENTAL HEALTH CLINICIAN

CASE REPORT Open Access

Cross-reaction of angioedema with clozapine, olanzapine, and quetiapine: A case report

Gabriela D. Williams, PharmD, BCPS, BCPP[1]

How to cite: Williams GD. Cross-reaction of angioedema with clozapine, olanzapine, and quetiapine: A case report. Ment Health Clin [Internet]. 2019;9(5):315-7. DOI: 10.9740/mhc.2019.09.315.

Abstract

Angioedema is characterized by marked swelling of the subcutaneous or submucosal tissue and may affect various parts of the body, including the face, mouth, and extremities. Angioedema has specifically been associated with the use of several antipsychotic agents, including clozapine, olanzapine, iloperidone, haloperidol, quetiapine, paliperidone, ziprasidone, risperidone, and chlorpromazine. A 67-year-old African American male with a past medical history significant for hypertension, coronary artery disease requiring stent placement, mitral insufficiency, hyperlipidemia, tobacco use disorder, and schizophrenia presented with altered mental status and disorientation in the setting of clozapine nonadherence, which prompted acute hospitalization for clozapine reinitiation. During clozapine titration, the patient developed edema, erythema, and pruritus on his face and arms along with lip swelling characteristic of angioedema. Upon discontinuation of clozapine, the patient was trialed on several other antipsychotic medications to help manage acute psychosis and subsequently developed angioedema symptoms with trials of both olanzapine and quetiapine. Following these 3 distinct events of angioedema, the clinical decision was made to no longer trial atypical antipsychotics for the patient, and loxapine was cautiously initiated. The patient responded well to loxapine and continued to tolerate loxapine therapy for years. This case report identifies angioedema cross-reaction linked with 3 second-generation antipsychotics. Given the potentially life-threatening nature of angioedema, awareness of recurrent angioedema should be undertaken when trialing antipsychotics following an episode of angioedema correlated to antipsychotic use, particularly when trialing antipsychotics from the same generation and with similar chemical structures.

Keywords: angioedema, antipsychotic agents, clozapine, cross-reactivity

[1] (Corresponding author) Clinical Pharmacy Specialist – Psychiatry, Eskenazi Health, Indianapolis, Indiana, gabriela.dimitrievski@gmail.com, ORCID: https://orcid.org/0000-0001-8768-8706

Disclosures: The author has no actual or potential conflicts of interest related to the content of this article.

Background

Angioedema is an event characterized by marked swelling of the subcutaneous or submucosal tissue and may affect various parts of the body, including the face, mouth, and extremities. This reaction is often mild and overall self-limiting but can be life-threatening, particularly in cases in which airway patency is threatened.[1,2] Angioedema has been linked to a variety of medications and has specifically been associated with the use of several antipsychotic agents, including clozapine, olanzapine, iloperidone, haloperidol, quetiapine, paliperidone, ziprasidone, risperidone, and chlorpromazine.[2-8]

Limited prior case reports have identified angioedema cross-reactivity among antipsychotic medications. In one published case,[2] a 27-year-old female taking clozapine for 5 years presented with facial swelling and periorbital eruption, prompting a diagnosis of acute angioedema. Clozapine therapy was discontinued, and upon resolution of angioedema, olanzapine was initiated; however, angioedema symptoms recurred within several days of initiation of olanzapine. Similarly, a 24-year-old male patient presented with tongue and facial swelling 24 hours after the initiation of haloperidol, prompting haloperidol

discontinuation.[3] Iloperidone was then initiated, also leading to the formation of an erythematous rash, lip swelling, shortness of breath, and speech difficulty within 3 days.

The following case report details the development of angioedema following trials of clozapine, olanzapine, and quetiapine in a patient with a long-standing history of schizophrenia. This patient case prompts a need for further awareness of and caution for recurrent angioedema following an initial episode linked to antipsychotic medication.

Case Report

The patient is a 67-year-old African American male with a past medical history significant for hypertension, coronary artery disease requiring stent placement, mitral insufficiency, hyperlipidemia, tobacco use disorder, and schizophrenia. The patient was initially brought in for hospitalization by family secondary to altered mental status and disorientation. Upon presentation, an extensive medical workup was undertaken, including laboratory analysis (basic metabolic panel, complete blood count, urinalysis, urine drug screen, ammonia concentration, vitamin B12 concentration, folate concentration, thyroid stimulating hormone, liver function tests, and venereal disease research laboratory), computed tomography of the head, and electroencephalography. All workup for a general medical cause of that patient's acute presentation was negative, and a psychiatric consult was subsequently requested given the patient's chronic history of schizophrenia. Upon consultation and assessment by psychiatric services, the patient endorsed nonadherence to clozapine therapy, with which he had been effectively treated for numerous years. As a result of the negative medical workup and medication nonadherence, the patient was subsequently transferred to the acute care psychiatric unit for reinitiation of clozapine. Concurrent scheduled medications at this time included aspirin 81 mg by mouth daily, atorvastatin 80 mg by mouth at bedtime, buspirone 10 mg by mouth every morning and 20 mg by mouth every night, clopidogrel 75 mg by mouth daily, metoprolol succinate 25 mg by mouth daily, and thiamine 100 mg by mouth daily.

Clozapine was titrated up to a dose of 375 mg by mouth nightly over a 14-day period with the ultimate goal of achieving the previously prescribed dose of 450 mg by mouth nightly; however, it was at this time the patient developed edema, erythema, and pruritus to his face and arms along with lip swelling characteristic of and concerning for angioedema. Clozapine was discontinued upon development of this reaction, and the patient was symptomatically treated with hydroxyzine and ranitidine for suspected angioedema. A single 40-mg dose of prednisone was also given to the patient; however, due to resolution of symptoms, further glucocorticoid treatment was not found to be warranted. A complete blood count was drawn and noted to be significant for increased eosinophils to 1.1 10×3/uL, consistent with an inflammatory response. A probability score for this reaction was calculated utilizing the methods described by Naranjo et al,[9] which identified the described as a probable drug reaction to clozapine.

All scheduled antipsychotic therapy was held for 8 days, during which all allergic sequelae improved; all other nonpsychotropic medications were continued without change. Given resolution of the allergic reaction and continued symptoms of uncontrolled psychosis, the decision was made to initiate olanzapine 10 mg by mouth nightly with plans to cautiously increase the dose as tolerated. Two days following the initiation of olanzapine, the patient had a re-emergence of facial edema, and olanzapine was immediately discontinued. Treatment with an antihistamine was again initiated, and the patient was transitioned to haloperidol 5 mg by mouth twice daily for continued treatment of schizophrenia symptoms. A repeat complete blood count indicated a continued increase in eosinophils to 2.9 10×3/uL. Over the next week, haloperidol was titrated to a dose of 5 mg by mouth every morning and 10 mg by mouth nightly, which was well tolerated and appropriately controlled the patient's psychosis, allowing for discharge.

Fifteen days after discharge, the patient presented to acute care services again, this time with complaints of disorganization, confusion, and substantial extrapyramidal symptoms. Haloperidol was promptly discontinued and replaced with quetiapine 100 mg by mouth nightly in an attempt to minimize extrapyramidal symptoms. Yet again, following 2 days of quetiapine therapy, the patient re-experienced facial edema. Following this reaction, the decision was made by the treatment team to no longer trial atypical antipsychotics, and loxapine was cautiously initiated. Over the next 2 weeks, loxapine therapy was maintained and slowly titrated to a final dose of 25 mg by mouth each morning and 50 mg by mouth at bedtime. The patient responded well to loxapine, so much so that, at the time of discharge, he was logical, organized, and had a sustained reduction in auditory hallucinations. Additionally, the patient continued to tolerate loxapine therapy with no further emergence of allergic sequelae. A review of the patient's medical record identified continued treatment with loxapine for an additional 2 years following the events reported above, at which time the patient was transitioned to paliperidone due to a sustained unavailability of loxapine at local pharmacies.

Discussion

Drug-induced angioedema has been reported[1,10,11] with numerous medications and is thought to promote edema via inflammation caused by immunoglobulin E-related hypersensitivity, kinin-dependent processes, or C_1-esterase inhibition deficiencies. Angioedema presents as swelling of the subcutaneous and/or submucosal tissue, and although, in many cases, it is mild and self-limiting, it has the potential to cause severe complications, particularly when swelling involves compromise to airway structures.[1,2] In various cases, symptoms of angioedema present within the first several weeks of drug therapy; however, cases of angioedema developing after months or years of medication use have also been previously reported.[2]

Published reports[2-8] have identified cases of angioedema related to antipsychotic use, particularly related to clozapine, olanzapine, iloperidone, haloperidol, quetiapine, paliperidone, ziprasidone, risperidone, and chlorpromazine. Although cases of angioedema have been fairly well documented with a number of antipsychotic medications, very limited information is available regarding the potential cross-reactivity of antipsychotics as it relates to angioedema events. To date, only 2 other cases of cross-reactivity have been published, 1 documenting cross-reactivity between clozapine and olanzapine[2] and the other between haloperidol and iloperidone.[3] In the case report of cross-reactivity between clozapine and olanzapine,[2] the patient presented with a delayed angioedema reaction to clozapine after 5 years of therapy, followed by a similar reaction to olanzapine several days after initiation; similarly, the case report identifying cross-reactivity between haloperidol and iloperidone[3] noted reactions within several days of drug initiation. The course of these previously published reports is consistent with the currently presented case in which the patient developed angioedema following years of clozapine therapy with similar reactions occurring several days after the initiation of olanzapine and quetiapine. At the present time, angioedema cross-reaction among 3 antipsychotic medications has not been described elsewhere in the literature.

A potential explanation of the recurrent swelling seen with trials of clozapine and quetiapine, both dibenzodiazepine antipsychotics, and olanzapine, a thienobenzodiazepine antipsychotic, may be related to the structural similarities shared by these 3 medications although this does not explain the lack of reaction seen when the patient was trialed on loxapine, another dibenzodiazepine antipsychotic medication structurally similar to clozapine. Additionally, one cannot rule out other unknown confounding factors that may have contributed to the occurrence of angioedema related specifically to the trials of clozapine, olanzapine, and quetiapine within this patient's course of treatment.

Conclusion

The presented case report identifies angioedema cross-reaction linked with three atypical antipsychotics: clozapine, olanzapine, and quetiapine. Although usually mild, angioedema may result in life-threatening complications and warrants further awareness regarding the potential recurrence and cross-reactivity of medications. Awareness of and caution for recurrent angioedema should be undertaken when trialing antipsychotics following an episode of angioedema correlated to antipsychotic use, particularly when trialing antipsychotics from the same generation and with similar chemical structures.

References

1. Salih I, Thomas S. Causes and management of drug-induced angioedema. Prescriber. 2006;17(7):14-8. DOI: 10.1002/psb.358.
2. Tatar ZB, Oflaz S, Baran B. A case of late-onset angioedema associated with clozapine and redevelopment of angioedema with olanzapine. J Clin Psychopharmacol. 2014;34(4):523-5. DOI: 10.1097/JCP.0000000000000153. PubMed PMID: 24911442.
3. 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):E40-1. DOI: 10.1176/appi.neuropsych.11040094. PubMed PMID: 22772698.
4. Tuman TC, Tuman BA, Şereflican B, Yildirim O. Quetiapine associated with angioedema. J Clin Psychopharmacol. 2016;36(3):289-90. DOI: 10.1097/JCP.0000000000000503. PubMed PMID: 27035491.
5. Yucel A, Yucel N, Ozcan H, Saritemur M. Dose-dependent paliperidone associated with angioedema. J Clin Psychopharmacol. 2015;35(5):615-6. DOI: 10.1097/JCP.0000000000000368. PubMed PMID: 26125544.
6. Mohan T, Bastiampillai T, Dhillon R. Ziprasidone-induced angioedema. J Clin Psychiatry. 2009;70(7):1054. DOI: 10.4088/JCP.07lo4657. PubMed PMID: 19653983.
7. Cooney C, Nagy A. Angio-edema associated with risperidone. BMJ. 1995;311(7014):1204. DOI: 10.1136/bmj.311.7014.1204c. PubMed PMID: 7488898.
8. Hine FR. Severe angioneurotic edema during chlorpromazine therapy. Am J Psychiatry. 1958;114(10):942. DOI: 10.1176/ajp.114.10.942. PubMed PMID: 13508935.
9. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30(2):239-45. DOI: 10.1038/clpt.1981.154. PubMed PMID: 7249508.
10. Lamer V, Lipozencic J, Turcic P. Adverse cutaneous reactions to psychopharmaceuticals. Acta Dermatovenerol Croat. 2010;18(1):56-67. PubMed PMID: 20361889.
11. Inomata N. Recent advances in drug-induced angioedema. Allergol Int. 2012;61(4):545-57. DOI: 10.2332/allergolint.12-RAI-0493. PubMed PMID: 23183389.