

Reversible global aphasia as a side effect of quetiapine: a case report and literature review

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Abstract: Quetiapine is an atypical antipsychotic agent which is also prescribed for delirium due to its anti-dopaminergic effects; aphasia is an unusual side effect associated with the drug. Here, we report the case of an 83-year-old woman who was prescribed quetiapine (50 mg per day) for delirium. Unexpected, global aphasia occurred 3 days after treatment began. Complete recovery occurred following discontinuation of the drug. A brain computed tomography scan excluded intracranial hemorrhage and the laboratory results confirmed that no exacerbation of infection or electrolyte imbalances were present. During the aphasic episode, the patient's condition did not deteriorate and no new neurological symptoms occurred. We suspect that the occurrence of aphasia was directly due to an adverse reaction to quetiapine. To our knowledge, this is the first case report of reversible, global aphasia as a side effect of quetiapine. We propose that this occurrence of aphasia may be due to the action of quetiapine as a dopamine receptor antagonist. Clinicians should use quetiapine with caution, especially in elderly patients. On observation of aphasia, a review of the patient's medical history is required to assess for the usage of quetiapine.

Keywords: aphasia, quetiapine, insomnia, delirium

Introduction

Quetiapine is a new, atypical antipsychotic medication, and its usage has become more frequent due to its excellent disease control and the presence of fewer extrapyramidal side effects compared to other atypical antipsychotics. It is predominantly used for the treatment of schizophrenia and bipolar disorder. It is also used to treat delirium due to its anti-dopaminergic effects. Although it is generally well-tolerated, several adverse reactions have been associated with the usage of Quetiapine, especially in elderly patients.¹ These include ischemic stroke, orthostatic hypotension, seizure, drowsiness, Stevens–Johnson syndrome, and suicidal ideation. Aphasia is rare side effect associated with quetiapine. Here, we present a case of global aphasia as a side effect of quetiapine usage. We go on to discuss the possible mechanisms behind this adverse reaction.

Case history

An 83-year-old, right handed, Chinese female patient presented at our clinic with a medical history of diabetes, hypertension, and an old ischemic stroke in the left cerebral hemisphere (corona radiata and lentiform nucleus) with sequelae of right mild hemiparesis. On presentation, no aphasia was observed. According to her medical history, the patient had been prescribed with low dose Risperdal® (risperidone; Johnson & Johnson, New Brunswick, NJ, USA) (0.5 mg per night) for the past 3 months. She was

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conscious, alert and spoke fluently. The patient was partially dependent due to right hemiparesis. She was admitted to the infection ward via the emergency department with suspected urinary tract infection, hyperglycemia, and hyponatremia. During hospitalization, the infection and hyponatremia were treated and controlled; however, the patient still maintained mild delirium as well as insomnia. On the 7th day of hospitalization, to treat the delirium, the clinician prescribed extended-release quetiapine at 50 mg per day in replacement of risperidone. Following the administration of quetiapine, the patient presented with acute global aphasia and an inability to follow instructions. Upon neurological examination, no new symptoms or signs were detected. The patient's systolic blood pressure was around 120–160 mmHg during hospitalization. Complete laboratory studies, including complete blood count and biochemistry profiles, confirmed that no further exacerbations of infection, electrolyte imbalances or other metabolic problems were present. Emergent brain computed tomography indicated that there was no intracranial hemorrhage. On the 7th day of hospitalization we prescribed quetiapine, but the unexpected aphasia persisted for 3 days, so we then ceased quetiapine on the 10th day of hospitalization. We suggested the need for further brain imaging to exclude a new cerebral ischemic infarction or seizure disorder; however, the patient asked to be discharged before we could undertake these studies. In the outpatient follow-up, 1 week after discharge, no recurrent aphasic episodes had occurred. Despite the lack of a complete brain survey, we strongly suspected that the unexpected, reversible, global aphasia was a direct adverse reaction to quetiapine.

Written informed consent has been provided by the patient to have the case details published.

Discussion

Here, we describe an 83-year-old, delirious female who presented with acute global aphasia following quetiapine administration, which completely recovered following discontinuation of the drug. To the best of our knowledge, this is the first case report of reversible global aphasia as a side effect of quetiapine.

The atypical antipsychotic drug quetiapine is a dibenzothiazepine derivative, with a similar chemical structure to clozapine. It shares characteristics with dopaminergic (D1, D2, D3, D4 receptor) antagonists, adrenergic (α 1, α 2 receptor) antagonists, 5-HT1A partial agonists, high affinity 5-HT2A partial antagonists, and potentially shares properties with histamine (H1 receptor) antagonists.^{2–4} The main indications for quetiapine are schizophrenia, bipolar disorder, and delirium.

A lesion blocking the language network can result in aphasia, hence the most common etiology of aphasia is a

vascular event.⁵ As the patient had a previous history of ischemic stroke, the probability of recurrent stroke and transient ischemic attack (TIA) increased. In this patient, no further deterioration or new neurological symptoms and signs occurred during the aphasic episode and the aphasia fully recovered following the discontinuation of quetiapine. TIA typically presents with new neurological signs that resolve within 24 hours. In our patient, aphasia persisted for 3 days, which is not compatible with the definition of TIA. Upon brain magnetic resonance imaging, no new lesions were observed. We concluded that in this patient TIA or a recurrent stroke involving language function was unlikely to have occurred. Although one of the side effects of quetiapine is orthostatic hypotension, which may cause ischemic stroke, the patient's blood pressure remained in the normal to mildly hypertensive range during hospitalization.

Aphasia can also result from degenerative diseases, seizure disorders, or medication usage. The course of degenerative disease is often slowly progressive and irreversible. Our case was not compatible with the clinical presentation of degenerative disease. Both the ictal and post-ictal phases of a seizure can manifest with aphasia.^{6–7} During hospitalization, we did not witness any limb convulsions or focal tremor in the patient. Therefore, a seizure disorder diagnosis was not favored.

So far, several medications have been reported to cause aphasia, including: ipilimumab; immunomodulatory drugs (thalidomide, lenalidomide, pomalidomide); lamotrigine; vigabatrin; sulfasalazine; cyclosporine A; ifosfamide; phenylpropanolamine; naftidrofuryl oxalate; and some contrast mediums (Table 1). In the reported cases of medication-associated aphasia, aphasia completely recovered following discontinuation of the medication. Medication induced central neurotoxicity can lead to aphasia. However, other mechanisms leading to aphasia are unclear. Previous studies have concluded that increased dopamine levels can improve speech function in transcortical motor aphasia. The improvements in speech function gradually disappeared when dopamine levels decreased.^{8,9} Acetylcholine is known to be involved in the verbal memory process and can have benefits in the treatment of aphasia. The influence of amphetamine and serotonin on language is still controversial. Risperidone has a stronger affinity for dopaminergic receptors than quetiapine. It is reasonable to hypothesize that risperidone usage would result in similar symptoms in this patient. The patient had a history of taking low dose, short-acting risperidone (before sleep), which achieved peak plasma levels within 1 hour and had a half-life of 3 hours. We removed risperidone from the patient's regime and instead prescribed extended-released

Table I Reported medication causing aphasia in literature review

Drug	Symptoms	Mechanism	Level of evidence
Ipilimumab ¹⁰	Aphasia, tremor and ataxia, myocloni, hallucinations, anxiety and agitation in turns with somnolence	Unclear, suspect related to anti-thyroid antibodies	Case report
Immunomodulatory drugs ¹¹ (thalidomide, lenalidomide, pomalidomide)	Reversible coma, amnesia, expressive aphasia, and dysarthria	Central neurotoxicity	Case series
Lamotrigine ¹²	Global aphasia	EEG showed continuous spikes and waves	Case report
Vigabatrin ¹³	Aphasia disorder	Unclear	Case report
Sulfasalazine ¹⁴	Dysphasia, seizures, rash	Unclear	Case report
Cyclosporine A ¹⁵	Aphasia	Central neurotoxicity	Case report
Ifosfamide ¹⁶	Confusion, aphasia, hallucinations, and coma	Central neurotoxicity	Case series
Phenylpropanolamine ¹⁷	Acute memory loss and nominal aphasia	Unclear	Case report
Contrast (cardiac catheterization) ¹⁸	Encephalopathy, motor and sensory disturbances, vision disturbance, ophthalmoplegia, aphasia, and seizures	1. Disruption of the BBB and direct neuronal injury; 2. Transient vasoconstriction	Case series
Metrizamide myelography ¹⁹	Expressive dysphasia	Neurotoxic reaction	Case series
Naftidrofuryl oxalate ²⁰	Aphasia	Unclear	Case report
Cisplatin ²¹	Aphasia, confusion, and agitation	Central neurotoxicity	Case report

Abbreviations: EEG, electroencephalography; BBB, blood–brain barrier.

quetiapine. Quetiapine usage resulted in prominent aphasia. We proposed that quetiapine may result in aphasia through its anti-dopaminergic activity. We also suspected that old age and the presence of a previous ischemic stroke (which interfered with the adjacent nigrostriatal pathway) contributed to the development of aphasia in this case.

Conclusion

We reasoned that aphasia occurred as a rare adverse reaction of quetiapine, through its anti-dopaminergic activity. When treating delirium, clinicians should use quetiapine with caution, especially in elderly patients. On observation of aphasia, the medical history should be reviewed and quetiapine induced side effects should be kept in mind. These side effects may be reversible following the discontinuation of quetiapine.

Disclosure

The authors report no conflicts of interest in this work.

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