

A case of reversible aphasia-type speech disorders after treatment with quetiapine

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Summary

The study presents a case of a 64-year-old patient with diagnosed Parkinson's disease and coexisting REM sleep disorder (RBD) confirmed in a polysomnographic examination. In this patient, the use of supplementary therapy – quetiapine (50 mg/daily) – due to psychotic disorders, resulted in speech disorders with sensory-motor mixed aphasia type. Aphasia occurred on the fourth day after beginning the treatment with atypical neuroleptic. In MRI examination of the head, no “fresh” cerebral ischemia was found. No focal status epilepticus was reported in the video EEG trial.

Results. Complete cure occurred after discontinuation of quetiapine administration.

Conclusions. Due to the above, the side-effects of quetiapine treatment were assumed as the cause of focal neurological disorders.

Key words: aphasia, quetiapine, side-effects

Introduction

Quetiapine is a benzothiazepine derivative and an atypical antipsychotic drug that, according to the SPC (summary of product characteristics), is intended for the treatment of patients with schizophrenia and moderate to severe manic episodes in bipolar disorder. Thanks to its anti-dopaminergic activity [1], it is also used in delirium syndrome as well as psychotic disorders in the course of Parkinson's disease [2]. In Parkinson's disease, psychotic disorders are quite common, accounting for about 25–75% of cases. They usually occur in the form of visual hallucinations (20–25%) or delusions (5–15%). Adequate to the severity of the problem after excluding other causes (e.g., infections), they may only require correction of the list of medications: reduction/discontinuation: amantadine, selegiline, anticholinergic preparations, levo-

dopa agonists. However, it is not uncommon for additional pharmacotherapy to be required. Quetiapine or clozapine are used here. In addition, from April 2016, the FDA recommended the use of nuplazid (pimavanserin) in the case of hallucinations or delusions in the course of Parkinson's disease [3]. With quetiapine, a wide range of side-effects are often the cause of therapeutic dilemmas. The most significant side-effects within the aspect of neurological diseases, especially in the elderly with dementia, include: orthostatic decreases in blood pressure (in the mechanism of blocking alpha 1-adrenergic receptors), restless legs syndrome, epileptic seizures, neuroleptic malignant syndrome, nightmares, drowsiness, suicidal thoughts, tardive dyskinesias, dysarthria [4, 5]. The mechanism regarding increased risk of vascular events within the CNS is unknown. In randomized, placebo-controlled studies in dementia, patients treated with atypical antipsychotics were at an approximately 3-fold increased risk of cerebrovascular adverse reactions [6, 7].

In the summary of product characteristics for quetiapine, no information on the aphasiac side-effects of quetiapine can be found. In a review of literature, we find single or multiple cases of aphasia during the use of drugs such as ipilimumab, lamotrigine, vigabatrin, sulfasalazine, cyclosporin A, ifosfamide, phenylpropanolamine, naphthidrofuryl oxalate, cisplatin, and immunomodulatory drugs (thalidomide, lenalidomide, pomalidomide), contrast agents used in cardiac catheterization and metrizamide used in myelography [1, 8–19]. Aphasia-type speech disorders have not yet been documented in the case of other antipsychotics such as olanzapine or risperidone. However, there have been reports on the occurrence of hypotension due to circulatory failure in both the case of the analyzed quetiapine and other antipsychotics: olanzapine or risperidone [4, 5, 20–23]. We searched the Ovid Medline, PubMed, Cochrane CENTRAL and UpToDate databases for aphasia-type speech disorders during quetiapine pharmacotherapy. We extracted one work published in August 2017 by Chien et al. in *the Neuropsychiatric Disease and Treatment* journal, which describes the case of global aphasia during quetiapine treatment [1].

Case history

The 64-year-old patient with Parkinson's disease diagnosed 12 years earlier with coexisting REM sleep behavior disorder (RBD) – confirmed via polysomnography, and psychotic disorders, remained under regular neurological control in outpatient settings. This was done to optimize the pharmacological treatment of the underlying disease: manifested in both extrapyramidal – as well as extramotor disorders. It is known from the patient history that REM sleep behavior disorder (RBD) came approximately 30 years ahead of extrapyramidal symptoms in the course of the underlying disease. According to interview, the 28-year-old son of the patient has had REM sleep disorder for 2 years.

According to medical recommendations, the patient received levodopa in the total daily dose of 400 mg, a non-ergoline dopamine agonist – ropinirole, in the daily dose

of 4 mg. Because of REM sleep disorder (RBD), melatonin was implemented at a dose of 6 mg/day. Furthermore, the patient did not undergo chronic treatment or take any medication permanently. Also, the patient did not take any medication on a need-to-basis. Quetiapine (at a dose of 50 mg/day) was added to the non-modifiable pharmacological treatment during the neurological counseling visit due to increasing psychotic disorders in the form of visual hallucinations. The patient took the drug in the morning, at least 1 hour before breakfast. On fourth day after quetiapine implementation, approximately 60 minutes after taking the tablet, speech disorders of mixed sensorimotor aphasia-type occurred. The patient was suddenly unable to speak, the speech was not fluent, he also did not understand what was being said to him, he replaced the missing words with others. In the sentence, the patient entered incorrect grammatical forms, he also used words contrary to their meaning. Aphasia was diagnosed based on the result of a normalized aphasia scale – *the Western Aphasia Battery-R* (WAB-R), on which the patient obtained 74 points.

During neurological examination of the patient, apart from the features of the extrapyramidal syndrome, the features of moderate global sensorimotor apathy were found, without any other symptoms of focal brain damage or meningitis. During the episode of sudden speech disorders, the presence of ‘fresh’ cerebral ischemia and other organic changes, as well as the expansive process, were excluded based on the MRI scan of the head (Figure 1). Focal status epilepticus was also excluded using video EEG (Figure 2). The results of laboratory tests allowed to exclude infection, electrolyte disturbances and metabolic dysfunction. Based on the interview of both the patient and family members, the influence of external factors on the occurrence of mixed aphasia was also excluded.

Due to the unclear cause of isolated aphasia, a decision was made to discontinue the drug during the 6th day of treatment. Complete recovery occurred after termination of the drug. During the 2-week observation period without administering quetiapine,

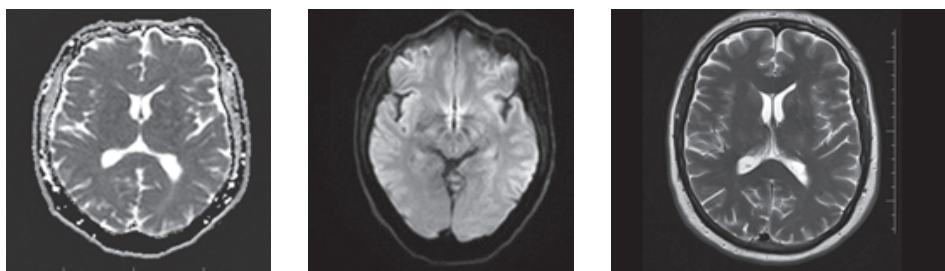


Figure 1. Head MRI

Normal white and grey matter signal. No restriction of diffusion was noted. After intravenous administration of the contrast agent, no abnormal signal increase was detected.

aphasia did not return. Due to the above, the side-effect of quetiapine treatment was recognized as the cause of focal neurological disorders.

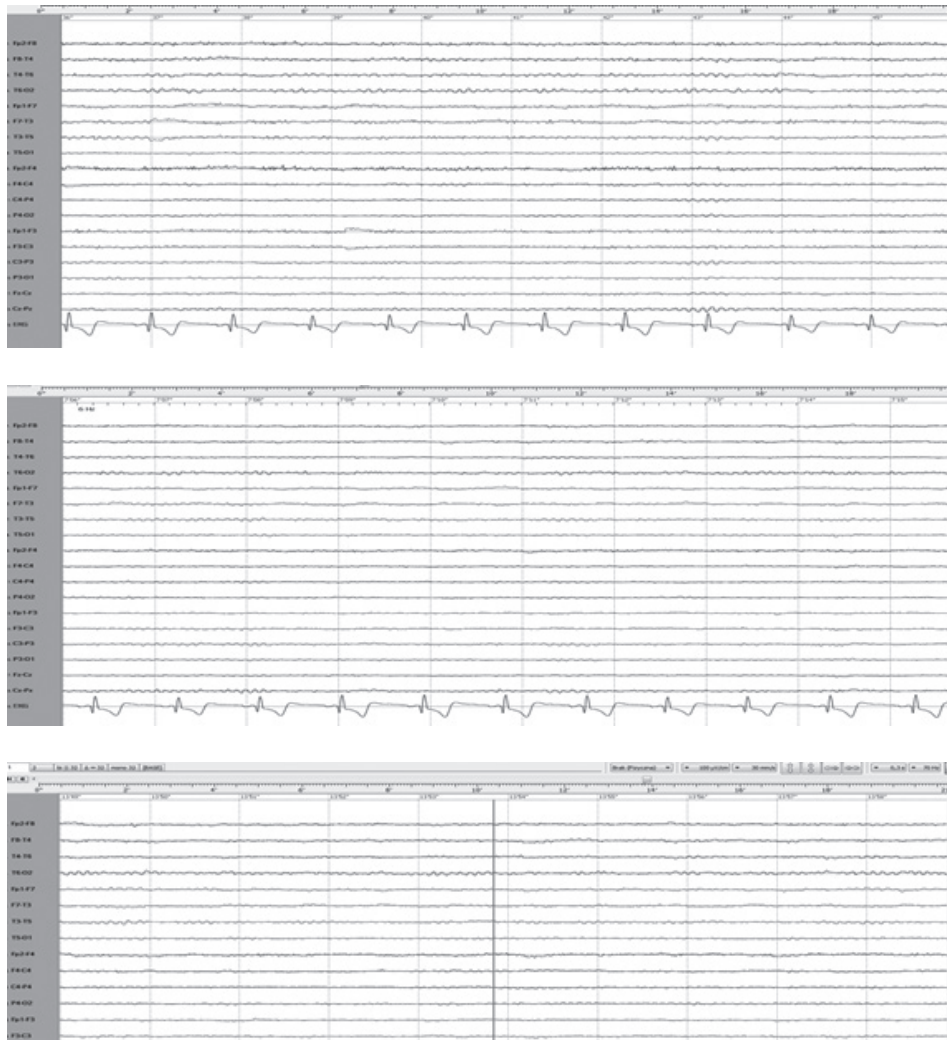


Figure 2. Video EEG test

Spatial differentiation of basic activity in the parietal-occipital region consists of an alpha frequency of 9–10 Hz and amplitude up to 40 μ V and beta waves with a frequency of 14–20/sec. Suppression – present. Photostimulation – does not activate the EEG record, tracing – present. Hyperventilation – without effect on the record. Record within norms.

Discussion

We present a case report of a 64-year-old man with long-term Parkinson's disease preceded by extra-motor REM sleep disorder with concomitant visual hallucinations. The patient was treated with quetiapine, after which acute global aphasia was observed, which subsided after drug discontinuation. The potentially acute adverse effect of quetiapine is the second case reported in literature to date.

Perhaps in the published description, aphasia had a different cause that could not be documented or in fact, it is only a side-effect of the used pharmacotherapeutic treatment. Based on an isolated case study, it is difficult to draw such far-reaching conclusions. The atypical psychoactive drug, a derivative of benzothiazepine – quetiapine, is a definitely more often chosen drug by practicing clinical neurologists than the dibenzodiazepine derivative – clozapine. In the case of many issues, this is probably due to the necessity for systematic monitoring of the morphological image of the blood regarding treatment with clozapine.

Quetiapine binds to many brain receptors. The antipsychotic effect is mainly due to the blockade of dopaminergic D2 and serotonergic 5HT2 receptors. It has the highest affinity with δ and $\alpha 1$ -adrenergic receptors, important for serotonergic 5HT-2, $\alpha 2$ -adrenergic, dopaminergic D2 receptors, and to a lesser extent – D1 and 5HT1A. It also has little predilection for benzodiazepine and cholinergic M1 receptors. Basically, main indications for the use of quetiapine include bipolar affective disorder, schizophrenia and other psychiatric disorders, e.g., in the course of Parkinson's disease.

Aphasia is a serious neurological symptom resulting from damage to the brain cortex responsible for speech. The most common etiology of aphasia is vascular. Other rarer causes are: brain tumors and brain injury or local inflammation. The analyzed case report presents a patient with acute moderate mixed aphasia, which occurred after quetiapine treatment. Aphasia was the only focal symptom and was not accompanied by other features of focal brain damage. Speech disorders did not increase, they were stationary and persisted throughout the antipsychotic treatment period. At present, the mechanism of this disturbance is not known in the current state of knowledge. However, orthostatic hypotension is a common, adverse reaction to quetiapine [4]. Nevertheless, low blood pressure was not noted in this patient. In contrast to the first case report from 2017 [1], the patient in this study had no diagnosed potential risk factors for vascular disease of the central nervous system, but nonetheless, neurological complications occurred. Aphasia can also occur in the course of organic changes, expansive processes in the central nervous system. In the analyzed patient, MRI examination of the head excluded the occurrence of focal lesions. Furthermore, neurodegenerative basis, epileptic seizure, poisoning, metabolic or infectious disorders were also excluded.

In the cases described in the literature, the course of affective speech disorders usually fluctuates, is unstable, different from that of the studied patient. Of course,

the impact of the implemented pharmacotherapy was not examined, but it is worth noting that it was unmodified for at least several months. It is obvious that there are a number of drugs that can cause aphasic adverse reactions [1]. Such adverse effects within the context of neurological clinical practice should be borne in mind in the case of lamotrigine or vigabatrin [10, 11]. Quetiapine may cause aphasia due to its anti-dopaminergic activity. Studies show that increased levels of dopamine can improve speech function in transcortical motor aphasia. The improvement of the speech function disappears as the level of dopamine decreases [24, 25]. The older age of the patient is also unfavorable in this case due to the decrease in the hepatic activity of CYP3A4, the main isoenzyme that metabolizes quetiapine in the elderly [4].

In the study, we assumed that due to the dose-dependent linear pharmacokinetics of quetiapine, aphasia-type side effects occurred while taking the drug as prescribed, without overdosing the substance. Perhaps, however, our patient needed slower introduction of quetiapine at a lower daily dose compared to the dose used in younger patients. Further analyses and clinical observations of patients during pharmacotherapy with this neuroleptic are needed.

Conclusions

From the presented case study, it may be presumed that aphasia can be a very rare side-effect of quetiapine implementation. During the treatment of elderly patients with psychotic disorders in the course of neurodegenerative diseases, special care should be paid to the selection of pharmacotherapy. It is necessary to find an optimal drug, with the least neurological complications.

The authors do not report a conflict of interest in this work.

The patient gave informed written consent for the publication of this work.

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