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Case Report

Clozapine-induced palilalia?

Azevedo JC, Lopes R, Curral R, Esteves MF, Coelho R, Roma-Torres A. Clozapine-induced palilalia?

Introduction: Palilalia is an acquired speech disorder characterised by involuntary and spontaneous repetition of words or phrases two or more times in a row. It can occur in a variety of disorders including postencephalic parkinsonism, pseudobulbar palsy, schizophrenia, Gilles de la Tourette syndrome and others.
Clinical Case: We describe a case of a 28-year-old man with refractory schizophrenia that developed palilalia with 300 mg of clozapine. In the patient evaluation we found unspecific alterations in the electroencephalogram, with normal blood tests and cerebral magnetic resonance imaging. Palilalia disappeared with lowering doses of clozapine.
Discussion: The appearance of palilalia induced by clozapine is a rare pharmacologic side-effect which physicians should be familiarised with when evaluating this symptom presentation.

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Introduction

Palilalia is an acquired speech disorder characterised by involuntary and spontaneous repetition of words or phrases two or more times in a row, during verbal output. It was described as a speech disorder distinct from aphasia by Souques (1908) (1). In a phenomenology's perspective, palilalia can be interpreted as a complex vocal tic with linguistic meaning of full or truncated words, or as a repetition of the individual's own words (2).

Reiterative speech disorders include palilalia, developmental stuttering, echolalia and coprolalia. The repetitions seen in palilalia are different from those in other speech disorders, as they tend to repeat longer linguistic units in a larger number (words and phrases rather than sounds and syllables). They involve the final words or phrases of utterances, which are different from those observed in patients with developmental stuttering. Patients with echolalia repeat the utterances of their interlocutors. The compulsive repetitions of patients with coprolalia are not context appropriate (3).

There are two types of palilalia, according to Sterling (1924). Type A, which he called 'palilalie spasmodique' or 'heterolalique', is characterised by compulsive reiteration of utterances with increasing rapidity and decreasing volume and by malfunctions in maintaining amplitude, rate and pitch parameters. Type A is a failure to terminate when the phrase has been successfully uttered. Type B, 'palilalie atonique' or 'homolalique', is characterised by reiteration of utterances at a constant rate alternating with periods of silence. Type B is a failure to terminate when the phrase has been successfully uttered. Syllabic iteration is predicted to occur as a result of a specific malfunction of initiation, that is, when the signal to initiate uttering a word is repeated, so that the beginning of the word is uttered more than once. These two types of reiterative speech suggest two separate malfunctions in the speech production system (1).

Palilalia is seen most often in patients with postencephalic parkinsonism and pseudobulbar palsy but can occur in association with a variety of disorders including encephalitis lethargica, postangiographic complications, carbon monoxide poisoning, fragile X syndrome, Pick's disease, Alzheimer's disease, advanced Parkinson's disease, progressive supranuclear palsy, traumatic or cerebrovascular lesions of the basal ganglia and thalamus, idiopathic cerebral calcinosis and epilepsia (4). It can occur in schizophrenia, in Gilles de la Tourette syndrome, in conversion disorders, in obsessive compulsive disorder and attention deficit hyperactivity disorder

(5). Palilalia has also appeared in stimulation experiments of left hemisphere sites and following stereotaxic thalamotomy as well as a side effect of neuroleptic medication (6).

The pathogenesis of palilalia is still unclear. Basal ganglia and extrapyramidal system involvement has been suggested as the cause of some cases and it has been proposed that palilalia reflects an inhibitory problem originated from a failure of subcortical inhibitory systems. It is hypothesised that there is a failure of the speech motor processing system after the formation of the phonetic plan, but before the level of the muscle action (4).

In the next section we describe a case of a patient with palilalia induced by clozapine. As we have mentioned before, palilalia has been associated with various disorders, but has seldom been reported as an antipsychotic side effect.

Clinical case

A 28-year-old Caucasian man, diagnosed as suffering from resistant paranoid schizophrenia, was admitted to acute inpatient treatment. The patient had auditory hallucinations and persecutory delusions that failed to respond initially to 160 mg of ziprazidone, and then to 8 mg of risperidone. For that, he was started on clozapine, and subsequently he developed palilalia when dosage reached 300 mg. His speech had several repetitions of his own words or phrases at a constant rate and amplitude. There was no history of illicit drug misuse. Physical examination was unremarkable as well as blood investigations. An electroencephalogram (EEG) revealed unspecific overactivity without point wave activity and a cerebral magnetic resonance (CMR) showed no alterations. The dose of clozapine was reduced to 150 mg and palilalia ceased.

Discussion

Palilalia may be a rare side effect. In this case report, there was a dose-dependent onset of palilalia with clozapine, which ceased when the dosage was reduced. As clozapine acts predominantly by blocking D2 and 5-HT2 receptors, possibly dopaminergic and serotonergic system may be involved in this phenomenon.

Causes of palilalia are many. The patient underwent investigation including CMR, which showed no alterations and EEG, which revealed unspecific alterations.

The usual explanation for palilalia is a disorder of motor speech which may be a possible counterpart of other pathological motor phenomena such as festination of gait or motor blocks (motor hypothesis). But some authors have pointed out that it is often linked to the production of propositional, effortful speech such as spontaneous speech, sentence formulation, picture description or naming. This suggests that palilalia can also receive input from a central, prearticulatory generator (cognitive hypothesis) (4). Other pathophysiologic mechanisms implicated could be neuron degeneration and neurotransmitter disturbances (7).

Language disturbances associated with clozapine are rare and generally assume the form of acquired stuttering (8).

One possible explanation for palilalia induced by clozapine is the disruption of the nigrostriatal dopaminergic pathways leading to basal ganglionic dysfunction.

Lesions selectively involving the medial *substantia nigra* producing anterior putaminal dopaminergic dysfunction can produce palilalia without motor symptoms in the extremities (9). Clozapine could produce this effect with D2 antagonism in basal ganglia.

This is related with the motor hypothesis of palilalia, which holds that repetitive speech phenomena are the result of a malfunction at the level of motor speech, probably resulting from a disintegration of subcortical–cortical interplay, whereby the basal ganglia stimulate speech activity in the cortex in an uncontrolled manner; alternatively, defective execution of pre-programmed motor sequences may result in an impairment of the duration and fluency of speech events (4).

Another possible explanation for palilalia induced by clozapine is related with the lowering of epileptic threshold and the emergence of epileptic activity that can culminate in major motor seizures, one of clozapine side effects. This is also the explanation for clozapine-induced stuttering (10). Finally, as clozapine shares some properties with other antipsychotics, we may expect to see palilalia as a side effect of this pharmacological group.

Comments

The above case report highlights clozapine as being possibly implicated in the pathogenesis of palilalia. To our knowledge no similar cases have been reported. Physicians should consider palilalia as a pharmacologic side effect in patients treated with clozapine. Further research is required to identify the neurophysiological and psychological basis of palilalia.

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