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Case Report

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The Possibility of the Second Generation Antipsychotic-Olanzapine to Cause Severe Akathisia in a Drug Naive Patient -A Case Report

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Summary

Here we are presenting this case of 26 years old gentleman with no past psychiatric history who presented initially to the emergency department with anxiety and depressive symptoms in the context of ongoing stressors, diagnosed as a case of severe anxiety and started on neuroleptic medication.

A few days later, it was reported by the family that the patient was moving around and only sit for a few minutes before starting to move again in response to an urge to keep moving. Barnes Akathisia-Rating Scale was administered and indicated severe akathisia.

The patient started on Mirtazapine 15 mg and Propranolol 20 mg twice daily, and he dramatically improved in a few days.

Background

Akathisia is a very distressful condition that can be easily misdiagnosed, especially in emergency department settings. In neuroleptics, naïve patients, the risk might be higher, which can affect their future compliance and adherence to medications. Given the low profile for the second-generation antipsychotics to cause extrapyramidal side effects, including akathisia, this should not be a reason to have a low suspicion index. This case highlights the possibility of encountering severe akathisia with the use of Olanzapine, a second-generation antipsychotic, Only few cases were reported describing akathisia with olanzapine usage[1,2].

Olanzapine is a thienobenzodiazepine derivative that is known for its efficacy and fewer side effects in treating patients with schizophrenia and psychosis [3]. Typical or first-generation antipsychotics and atypical or second-generation antipsychotics are effective for positive symptoms. However, as a class, FGAs cause more extrapyramidal motor symptoms and tardive dyskinesia than SGAs, whereas SGAs generally cause more weight gain and adverse cardiometabolic effects [4].

Case Presentation

26-year-old male, with no previous psychiatric history, brought by his mother after he was urgently referred to the psychiatry department following severe anxiety and restlessness.

The patient was doing perfectly well until three weeks before the current presentation when he started to feel severely worried and anxious about his coming medical school exams.

He is in the second year of medical school, although he did well on his first-year exams and he was not feeling anxious as such, he reported the feelings of agitation this time, something that he cannot find a reason for it.

However, he managed to take his exams, and he did well, but his anxiety persisted and started to feel low mood and sleeping difficulties, he had problems in initiating and maintaining sleep, he was able to sleep for only two to three hours daily without taking nabs during the day. His baseline sleep was between 7-8 hours daily. Accordingly, he started to feel fatigued and tired most of the time. His concentrations decreased as well.

He reported less appetite but no weight changes.
The patient reported no death wishes or suicidal ideations, intentions, or plans.
The patient denies bad ideas or intrusive and persistent thoughts.

He denies hearing voices or other forms of abnormal perception, denies the feeling of being followed or under surveillance by others. Until this point, he did not seek any medical help.

One week before the current presentation to the psychiatry hospital, he went to emergency with the symptoms mentioned above, basic labs were done, and they were all within normal limits, he was reassured and discharged with no medications prescribed.

Four days later, he could not tolerate his current symptoms, especially the sleeping difficulties and not being able to sleep more than a few hours per day.

His low mood symptoms became more evident, so he was retaken by the family to the emergency department.

He was given the diagnosis of severe anxiety and was prescribed Olanzapine 10 mg daily at bedtime-there was no clear justifications for Olanzapine use in the patient notes.

He was discharged with an urgent appointment at the psychiatry hospital.

Second day after discharge from the emergency, the patient and his family noticed that there is no improvement, although they were told that his sleep would improve after the use of the Olanzapine, subsequently the patient himself increased the dose of Olanzapine to 20 mg daily hoping that it will have faster effect in a shorter time. The following day the patient became extraordinarily restless and fidgety, developed the inability to sit still and was constantly moving around, when asked by the family to sit down he wasn't able to do so for more than two to three minutes before starting moving again and he told them about the irresistible urge to keep moving.

At this point, he presented to the psychiatry hospital, and the above-mentioned history was collected and confirmed by his mother, who brought him.

Mental state examinations; young male, average weight and height, appears as stated age. Looks anxious and irritable, was not able to sit down, and when asked to do so, he could not tolerate to remains seated for more than two to three minutes and was crossing-uncrossing his legs constantly before he stands up again and start pacing. The patient reported low mood with congruent affect, denies abnormal perceptions, no evidence of delusions or obsessions noted during the interview; he denies death wishes and suicidal ideations.

Memory and cognitive functions were grossly intact.
Barnes Akathisia-Rating Scale was administered and indicated severe akathisia.

The diagnostic impression changed to major depressive episode with severe Olanzapine induced akathisia. Akathisia was a prominent problem.

Propranolol 20 mg twice per day prescribed.
Mirtazapine 15 mg at bedtime was started simultaneously as an antidepressant, but at the same time, it was specially selected to address akathisia as well, according to several studies. All medications given via oral administration.

Investigations

Complete blood count (CBC) and compressive metabolic panel did reveal any abnormalities.

Levels of thyroid-stimulating hormone and free thyroxine were within range. CT and MRI of the head were unremarkable for any acute or chronic brain insult.

Differential Diagnosis

Initial impression in the emergency department was of severe anxiety; however, when the patient was seen and assessed in the psychiatry department, the assessment reflected the presence of major depressive episode as the patient described low mood, insomnia, excessive worries, tiredness, decreased concentration, and appetite.

Subjective and objective symptoms and signs of akathisia were present as well. Furthermore, the Barnes akathisia rating scale indicated severe akathisia.

At this point, the diagnosis of Olanzapine induced severe akathisia was added.
Given the symptoms of motor agitation, the diagnosis of agitated depression was considered, Mania as a diagnosis was excluded due to the presence of low mood and low energy level, other differential diagnoses such as restless leg syndrome, attention deficit hyperactivity disorder and psychotic illness, were inconsistent with the patient presentation.

Treatment

On the patient first encounter to emergency department he was discharged without medications, few days later on the second encounter with the same initial presentation of anxiety and insomnia he was started on Olanzapine 10 mg and discharged home, the dose was increased by the patient himself to 20 mg daily on the following day, next morning he presented again to emergency with severe anxiety, insomnia and new development of severe restlessness , Olanzapine was stopped by the emergency department and the patient provided with urgent referral to psychiatry hospital in three days where he was started on Mirtazapine 15 mg and propranolol of 20 mg twice a day [5].

Outcome and Follow up

The patient was seen one week after prescribing propranolol and Mirtazapine.
He was dramatically improved, was able to sit down with no objective evidence of akathisia, subjective feeling of restlessness, or the urge to keep moving.

Although he still has the depressive symptoms in terms of low mood, decreased concentration and fatigability but he described his mood as much better than when he came one week ago, giving the fact that antidepressant effect of medication will need between four to six weeks for possible improvement to be evident we didn't judge the improvement on his depressive symptoms at this point but at the same time there was a dramatic improvement in akathisia symptoms. Propranolol was discontinued at this point.

Discussion

The term akathisia is of Greek derivation and, translated literally into English, means 'not to sit.' It was first used by Lad Haskovec (1902) to describe two patients with restlessness and an inability to

sit still, there are many hypotheses describing the pathophysiology of akathisia but the most interesting one was suggesting that its due to the blockade of dopamine receptors in the mesocortical and mesolimbic regions of the brain[6,7].

It is known that the second-generation antipsychotics have a lower incidence of extrapyramidal side effects like dystonia, parkinsonism and tardive dyskinesia in comparison to first-generation but this does not remain valid for akathisia, Although a very limited number of cases were reported on Olanzapine inducing akathisia [1,8,9].

A number of issues can be identified that have led to the confusion with regard to definition. First, while most investigators have emphasized two components of akathisia - a subjective or psychological or cognitive component and an objective or movement component - there is disagreement about the relative importance of these two aspects [10]. In other words, is akathisia a mental disorder or a movement disorder or both? Is the subjective report of akathisia without any observational features enough to make the diagnosis? Is it valid to diagnose akathisia in the absence of a subjective report of distress? No clear answers to these questions are available, and operational criteria have only recently been proposed. Second, no general agreement exists regarding which clinical features are specific to akathisia. Clinical judgment is called on to decide if the patient's movements are manifestations of akathisia, anxious restlessness, dyskinesia or some other abnormality, and whether the distress is akathisia or anxiety, depression, agitation, exacerbation of psychosis or has some other psychiatric cause. Third, a number of subtypes of DIA have been identified [10].

On the other hand, on the further literature review, we can find that akathisia is defined as a movement disorder described as the subjective sensation of inner restlessness and the objective observation by clinicians of fidgeting movements. It is most often associated with antipsychotic drugs, which antagonize dopamine receptors [11].

The subjective component can be characterized by the aforementioned restlessness, as well as tension, panic, irritability, and impatience. Objective signs include increased motor activity, such as complex, repetitive movements. The urge to move appears to be a core feature, with the abnormal movements being a method used to calm this urge. Several subtypes exist, with classification based on timing, duration, and clinical presentation. Categories include the following [8].

- **Acute:** develops soon after starting medications; lasts less than six months; intense dysphoria; awareness of restlessness; and complex, semi-purposeful fidgetiness
- **Chronic:** persists for more than six months; tends to have milder dysphoria; has stereotyped movements, often with presence of limb/orofacial dyskinesia
- **Tardive:** delayed in onset; not related to medication changes; associated with tardive dyskinesia
- **Withdrawal:** associated with switching/stopping antipsychotic medications; onset usually within six weeks of discontinuation, dosage decreases, or stoppage of anticholinergic medication

According to the above categories of clinical presentation of akathisia, the case that we are presenting fall under the acute category, which develops soon after starting the medication and lasts for less than six months and presented with the typical subjective and objective symptoms and observations

The latest research supports an increased role for Mirtazapine as the preferred treatment method due to its marked 5-HT2a/c antagonism. In a 90-patient, double-blind, controlled trial, Mirtazapine was shown to be as effective as propranolol in controlling akathisia when given at low doses (15 mg/day) over the course of 7 days and had better tolerability and more convenient dosing than propranolol [11-13].

In our case, we used both propranolol, which was primarily used to address akathisia symptoms and the Mirtazapine, which used to treat the depressive symptoms putting in mind the effect of Mirtazapine on akathisia as well according to the literature review.

Learning Points

- Akathisia is a common side effect of the first-generation antipsychotics, but it should be considered when using second-generation antipsychotics as well.
- Concise use can cause severe akathisia, as in the described case, special attention should be paid to drug-naive patients.
- Emergency and family physicians to be aware of the risk of akathisia in patients receiving neuroleptic medications.

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