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Tremor and Other Hyperkinetic Movements

Case Reports

Tardive Akathisia with Asymmetric and Upper-body Presentation: Report of Two Cases and Literature Review

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Abstract

Background: Akathisia is an inner urge to move a body area with an objective motor component of restlessness. Tardive akathisia (TA) is usually bilateral with a predominant lower-body presentation. We report two patients with an asymmetrical predominantly upper-body involvement.

Case Report: Two young men with history of psychiatric problems and neuroleptic use revealed atypical TA, characterized by asymmetrical and predominantly upper-body involvement. Their main manifestations were rubbing the face, mostly with one hand, accompanied by an inner sensation of restlessness.

Discussion: Our patients are proof that TA can present with asymmetrical and upper-body involvement even with normal brain imaging.

Keywords: Tardive akathisia, akathisia, tardive, unilateral, phenotype

Citation: Shahidi G, Rohani M, Munhoz RP, Akhoundi FH. Tardive akathisia with asymmetric and upper-body presentation: report of two cases and literature review. Tremor Other Hyperkinet Mov. 2018; 8. doi: 10.7916/D8224B00

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Editor: Elan D. Louis, Yale University, USA

Received: April 7, 2018 **Accepted:** April 30, 2018 **Published:** May 29, 2018

Funding: None.

Financial Disclosures: None.

Conflict of Interest: The authors report no conflict of interest.

Ethics Statement: All patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

Introduction

Akathisia, defined as a sense of inner unease and urge to move a body area accompanied by an objective motor component of restlessness, may be seen in the setting of a number of disorders such as Parkinson's disease and brain injuries but is more commonly a drug-induced phenomenon, mostly related to dopamine receptor blockers, such as neuroleptics.[1] Acute, persistent, and tardive akathisia (TA) and pseudoakathisia may follow neuroleptic intake although this classification is not globally accepted. TA, one of the most common neuroleptic-induced tardive syndromes, is also one of the most disabling.

TA syndromes described to date are usually bilateral with predominant lower-body involvement including repeated knee crossing, plantar and dorsiflexion of the toes and feet, changing the body position when sitting, walking on the spot, and body swaying, which vary in severity.[1]

Herein we present two patients considered to have atypical TA due to their asymmetrical and markedly predominant upper-body involvement.

Case reports

Case 1

A 44-year-old male with a 3-year history of bipolar mood disorder was admitted to a specialized psychiatric center 2 years earlier because of an episode of mania and psychosis. Unfortunately, we do not have full access to the patient's medical records, but he was discharged on fluvoxamine 100 mg twice a day (BD) and haloperidol decanoate 50 mg intramuscular injection (IM) monthly. During the past year he had developed abnormal movements characterized by repeated jaw opening and tongue thrusting. He was also continuously rubbing his forehead, both eyes, and the perioral area with his left hand accompanied by unceasing flexion and extension movements in the neck. He reported a general inner feeling of restlessness Video 1.

During the past year, haloperidol was stopped, and he was started on tetrabenazine 25 mg three times a day, trihexyphenidyl 2 mg three times a day, and clonazepam 1 mg every night at bedtime (QHS) in an attempt to control his abnormal movements but with poor results.

Except for the abnormal movements, his neurological examination was unremarkable. Table 1 shows his scores on the Barnes Akathisia Rating Scale (BARS).[2] There were no trophic changes in his upper extremities, and deep tendon reflexes, strength, and coordination were normal. In addition to the abnormal movements described above, he had parkinsonian features in the form of axial and appendicular rigidity and mild hypokinesia. He had no tremor. Brain magnetic resonance imaging (MRI) and electroencephalography were within normal limits.

He was diagnosed with TA plus tardive dyskinesia and drug-induced Parkinsonism. Trihexyphenidyl and tetrabenazine were tapered and eventually discontinued, and the clonazepam dose was increased to 2 mg two times a day. Clozapine was also added, up to 150 mg. Symptoms improved markedly but did not completely disappear. Later, lamotrigine 100 mg BD and gabapentin 300 mg three times a day (TDS) were added in an attempt to achieve full recovery Video 2.

Video 1. **Case 1.** Akathisia characterized by ceaseless rubbing of the eyes, periorbital, and forehead areas with upper extremity and repetitive side-to-side swaying of the head. Dyskinetic movements characterized by abnormal jaw opening and blepharospasm are also seen.

Case 2

A 30-year-old male was referred to our unit by his psychiatrist with a diagnosis of generalized anxiety disorder (GAD) and panic attacks for the past year. Symptoms were only partially responsive to the usual anti-anxiety medications and he was eventually started on trifluoperazine 3 mg per day. After 3 months of therapy, his psychiatric symptoms resolved but he developed an abnormal movement characterized by excessive rubbing of his eyes and the periorbital and frontal areas using both hands, with a marked predominance of the left hand associated with a sensation of facial tingling and an urge to move his left upper extremity Video 3.

In addition to trifluoperazine, he was taking clonazepam 1 mg QHS. There were no personal or family histories of abnormal movements, and he denied any substance abuse.

On examination, the patient clearly seemed restless and was constantly touching and rubbing the skin over his forehead and the periorbital area with his left hand. He also displayed repetitive forward flexion of the trunk, excessive blinking, and minor dyskinetic movements of the neck. Table 1 summarizes the severity of his symptoms using the BARS scale. His general and neurologic examination—other

Video 2. **Case 1**. This video shows the first case in another visit. Jaw and eye dystonia are much less because of botulinum toxin injections. This video shows that the trunk and lower limbs are grossly not involved.

Table 1. **Severity of Tardive Akathisia over the Right and Left Sides of the Patients' Bodies Based on the Barnes Akathisia Rating Scale**

	Objective		Subjective: Awareness of Restlessness		Subjective: Distress Related to Restlessness		Global Clinical Assessment of Akathisia	
	Right	Left	Right	Left	Right	Left	Right	Left
Patient 1	0	2	1	3	0	3	0	5
Patient 2	1	2	1	3	1	3	1	5

Video 3. **Case 2**. Akathisia characterized by non-stop rubbing of the eyes and face with the upper extremities with a significant left predominance. Blepharospasm and neck dystonia are also noted.

than the involuntary movements—were intact. He had normal brain MRI and routine laboratory examinations.

The diagnosis of TA accompanied by mild blepharospasm was established and an attempt to ameliorate symptoms by stopping trifluoperazine and increasing clonazepam to 1 mg BD was trialed. The symptoms improved but did not disappear completely. Panic attacks and GAD symptoms recurred, and he reported excessive daytime sleepiness. He was then started on clozapine 25 mg a day while clonazepam was discontinued, with striking satisfactory results.

Discussion

The term akathisia has a Greek background meaning "not to sit". It was first described in 1902 in hysteric and neurotic patients and later in 1923 in idiopathic Parkinson disease and post-encephalitic Parkinsonism. It was not until 1947 that akathisia was reported as an extrapyramidal complication of neuroleptic drugs.[3]

There is no definite diagnostic criteria for akathisia, but in its typical presentation it usually consists of two components.[3] The subjective aspect of akathisia implies feelings of inner restlessness and mental unease, distress, and having a particular sense of tension, pain, or even paresthesia in the limbs. The objective component is defined by restlessness, in the form of complex, repetitive, and seemingly purposeful movements of the limbs, the most characteristic of them being rocking from foot to foot or pacing on the spot while standing.

Akathisia is the most common neuroleptic-induced movement disorder.[2] Drug-induced akathisia is classified into acute, persistent, tardive, and pseudoakathisic forms. The acute form occurs within days of starting the medication, and tends to subside on dose reduction or especially discontinuation of the responsible drug.[3] If it does not disappear on drug discontinuation and requires specific therapy, it is called persistent akathisia. TA usually develops with a latency of months to years of chronic medication use. The definition of a tardive syndrome requires a minimum of 6 weeks of drug intake, but it has also been reported with shorter periods. In pseudoakathisia, the complex and repetitive movements are present but the patient seems unaware of the urge to move. In other words the subjective component of akathisia is absent.[4]

Although akathisia has been described in frontal lobe injury[5] and subthalamic nucleus (STN) abscess,[6] its central pathways have not been anatomically localized so far. The ultimate responsible biochemical mechanism of akathisia has still to be identified. It has been proposed that patients with defective iron metabolism are probably more prone to develop neuroleptic-induced akathisia.[7]

As akathisia is a very common side effect of dopamine blockers and dopamine depletor agents, dopaminergic pathways have also been proposed as a possible pathophysiologic mechanism. This could explain why both akathisia and Parkinsonism may occur as a complication of the dopamine blocker or dopa depletory medications. Interestingly the two pathophysiologic etiologies explained above are related. It has been shown that iron distribution in the human brain follows the distribution of dopaminergic neurons, and D2 receptor density is decreased in iron-deficient animal models.[8]

Different reviews have estimated the incidence of drug-induced akathisia as between 20% and 75%[3] and depends on the type of the offending drug, dose and duration of drug intake, and probably genetic backgrounds. Akathisia is most commonly seen as a complication of typical and atypical neuroleptics, but it also occurs following antiemetics, dopamine depletors, and antidepressant medications including Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and mono amino oxidase inhibitors (MAOIs).

The clinical features of neuroleptic-induced akathisia are virtually always bilateral and more often with lower-body involvement.[9] In the present article we present two TA patients with a unilateral and predominant upper-body involvement. There are sparse reports of unilateral akathisia. Carrazana et al.[6] reported unilateral akathisia in a patient with acquired immune deficiency syndrome and subthalamic toxoplasmosis abscess. Hermesch and Monitz[10] reported four patients with unilateral neuroleptic-induced akathisia. They mentioned that both the subjective and the objective components of akathisia in these patients had a unilateral predominance. But the neuroleptic-induced akathisia in all those patients was acute and, in addition, only two of these four patients had normal brain computed tomography scans. They hypothesized that the "akathisia area" is different in the two hemispheres.

Neuroleptic-induced akathisia is not actually a benign condition. It causes major distress to the patient, may result in aggressive and suicidal behavior, and impairs adhesion to treatment in psychiatric diseases. This highlights the importance of diagnosing and treating akathisia, which despite its high incidence is commonly underdiagnosed or misdiagnosed as agitated depression or neurosis. The atypical presentations of akathisia are much more prone to be overlooked by specialists, which motivated us in reporting our experience here. Additional evaluation of these patients such as functional MRI could probably lead us toward the anatomical localization of akathisia and its pathophysiology.

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