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Movement disorder in a 56-year-old woman

A 56-YEAR-OLD WOMAN is brought to the emergency department by her husband because of “depression,” which began approximately 4 months ago after her aunt died. Her mother-in-law died 2 days ago.

The patient often feels overwhelmed by any request and has been unable to perform her routine homemaking tasks. She has not been sleeping well, and describes being “up much of the night.” Her appetite is reduced, and she has lost 10 pounds. She has not been interested in tennis or golf this spring, as she has been in the past. She feels guilty about getting behind with the grocery shopping, mailing the bills, and other chores, for which her husband who works full-time has started to assume responsibility. She forgets where she left her purse, billfold, and glasses. Names of familiar persons are difficult to remember.

Several weeks ago the patient went to see a psychiatrist, who started her on paroxetine in a low daily dose and lorazepam for sleep as needed. However, her symptoms have not improved. When her son came home for spring break, he was amazed at how much she had deteriorated and convinced his father to bring her to the emergency department for a second opinion.

The patient describes herself as physically healthy and does not have hypertension, diabetes, or renal disease. She has been taking estrogen and medroxyprogesterone for 6 years as postmenopausal hormone replacement therapy.

As you talk with the family, you notice the patient moving her hands to her face or her hair quickly and without a clearly defined purpose, and rapidly and abruptly shifting her feet and legs. When you ask her about these movements, she says she just “feels like it.”

The patient and her husband are not sure when these movements began, but the son says they have gradually been increasing since last summer. He adds that his mother has always been a nervous person and the family had not thought about it very much until this spring, when the depression and the movements both seemed to increase.

■ WHAT FURTHER INFORMATION IS NEEDED?

1 At this point, which of the following would you would like to find out?

- ☐ If anyone else in the family ever had these movements
- ☐ If these movements changed when she started taking paroxetine
- ☐ Whether she can stop the movements and sit perfectly still
- ☐ All of the above

This patient displays akathisia—motor restlessness characterized by an urge to move about constantly and an inability to sit still. In assessing this physical sign, all of the above questions are pertinent.

Family history. According to the patient’s son, the patient’s mother has dementia and a movement disorder but has not been given a specific diagnosis. These symptoms increased over a 10-year period until the family finally had to place her in a nursing home approximately 3 months ago. The patient’s paternal grandmother died of “dementia” and also had some abnormal movements.

Akathisia and selective serotonin reuptake inhibitors. The patient’s involuntary

TABLE 1

Causes of chorea**Hereditary**

Huntington disease
 Hereditary nonprogressive chorea
 Neuroacanthocytosis
 Wilson disease
 Ataxia-telangiectasia
 Lesch-Nyhan syndrome

Secondary

Infectious or immunologic
 Sydenham chorea
 Encephalitis
 Systemic lupus erythematosus
 Drug-induced
 Levodopa
 Anticonvulsants
 Anticholinergic
 Antipsychotics
 Metabolic and endocrine
 Chorea gravidarum
 Hyperthyroidism
 Birth control pills
 Hyperglycemic nonketotic encephalopathy
 Vascular
 Hemichorea-hemiballism
 Periarteritis nodosa

Unknown etiology

Senile chorea
 Essential chorea
 Tardive tremor

**All SSRIs
 increase the
 likelihood of
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 akathisia**

jerking and general restlessness have increased since she started taking paroxetine. All of the selective serotonin reuptake inhibitors (SSRIs) are known to increase the likelihood of developing akathisia, especially in patients with preexisting movement disorders, brain injury, or concomitant use of metoclopramide, prochlorperazine, or antipsychotics (such as the phenothiazines and the butyrophenones).^{1,2}

Drug-induced akathisia can present either acutely (within a few months of starting a drug), or chronically (with long-term use). Patients feel restless or an aversion to being still, and exhibit frequent and repetitive stereotyped movements such as pacing or repeatedly rubbing the scalp. Acute akathisia resolves when the responsible drug is withdrawn; in contrast, the chronic form becomes worse.

Voluntary control of akathisia. Our patient tries to control the rapid, jerking movement of her neck and extremities, and can sit still for a few seconds, but not for a longer period (several minutes).

Physical examination

Deep tendon reflexes are all brisk (+4). The Babinski reflex is negative bilaterally. The patient has a wide gait and finds it difficult to walk in a tandem fashion.

Mental status examination

The patient has difficulty recalling what hospital she is at, or the date. She generally gives one-word or two-word answers in a telegraphic style. Although she can repeat three words easily, she does not remember any of them 5 minutes later. Asked to count backward from 100 by sevens ("serial sevens"), she misses three out of five. She can spell "world" forwards, but not backwards. She can consistently repeat six digits in forward order and three in reverse order.

When asked, the patient says she has not been thinking of suicide. However, she expresses several paranoid delusions about her husband, family finances, and a mental healthcare worker. These are reliably reported as untrue by multiple sources.

■ WHAT IS THE DIAGNOSIS?

2 At this point, what is the most likely diagnosis?

- ☐ Simple major depression, first episode, nonpsychotic, moderate in level of severity
- ☐ Generalized anxiety disorder
- ☐ Depression and dementia, secondary to a medical condition (ie, Huntington disease)
- ☐ Drug-induced akathisia
- ☐ Vascular dementia

The findings are consistent with both an affective disorder (depression) and a cognitive disorder (dementia), in association with a movement disorder. The patient needs a full workup, especially oriented to diseases that could cause these three conditions (TABLE 1). Specifically, the workup should include:

- An imaging study of the brain (by

computed tomography or magnetic resonance imaging)

- A genetic blood test for Huntington disease, specifically looking for increased copies of the cysteine-alanine-glycine sequence (CAG trinucleotide repeats) in the chromosomes associated with Huntington disease³

- The thyroid-stimulating hormone level
- Antinuclear antibody titers
- A peripheral blood smear

In a younger patient, antistreptolysin O titers might be added to rule out Sydenham chorea, and the ceruloplasmin level to rule out Wilson disease.

Given the patient's age, the most likely diagnoses are Huntington disease, drug-induced chorea, hyperthyroidism, hemichorea-hemiballism, and senile chorea. The other causes of chorea listed in **TABLE 1** are more common in younger people.

Examining the abnormal movements

The patient's brain imaging studies and thyroid-stimulating hormone level were normal, and the patient was not taking levodopa, anticonvulsants, or other medications that typically produce choreiform movements. While awaiting the results of the test for CAG trinucleotide repeats, the best way to differentiate Huntington disease from hemichorea-hemiballism and senile chorea is to examine the involuntary movement in detail.

In Huntington disease, the movement disorder can include choreiform jerking, tremors, tics, or rigidity. Pseudopurposeful movements (parakinesia) are common in attempts to mask the involuntary jerking. Typically, the choreic movements are involuntary, purposeless, and abrupt, but less rapid and lightning-like than those seen in myoclonus. The somatic muscles are affected in a random fashion, and involuntary movements flow from one part of the body to another. Proximal, distal, and axial muscles are involved.

In the early stages and in less severe forms, patients grimace slightly, move their eyebrows and forehead, shrug their shoulders, and have jerking movements of the limbs. As the disease progresses it affects walking, causing a dancing, prancing, stuttering type of gait. The choreic movements

are worsened by emotional stimuli, disappear during sleep, and become superimposed on voluntary movements. In the terminal stages of Huntington disease, choreic movements may disappear and be replaced by muscular rigidity and dystonia.

In hemichorea, the involuntary movements are confined to the arm and leg on one side of the body. Ballistic movements are a more violent form of chorea: continuous uncoordinated activity of the axial and proximal appendicular muscles, so vigorous that the limbs are forcefully and aimlessly thrown about. The movements tend to have a sudden onset, which suggests a vascular basis, and indeed they may be preceded by focal neurologic deficits.

This condition is the result of a destructive lesion of the contralateral subthalamic nucleus or its connections, most often secondary to a vascular event, either hemorrhagic or ischemic. However, hemiballism has also been described in association with tumors in the subthalamic nucleus and with thalamotomy.

In senile chorea, which is often hard to distinguish from Huntington disease, the choreic movements begin insidiously, are mild, and usually involve the limbs. However, involuntary movements of the lingual-facial-buccal region have also been described. No particular mental disturbances are associated with it, nor do patients have a family history of movement disorders. In general, the symptoms are mild and often do not need treatment.

The cause of this disorder is unknown, but degenerative changes in the caudate nucleus and the putamen have been described. A recent article reported a small group of patients with senile chorea having the CAG trinucleotide repeat.⁴

■ HUNTINGTON DISEASE

Huntington disease is an autosomal-dominant disorder with complete penetrance. Hence, children born to a parent with this disorder have roughly a 50% chance of being affected.

The dementia of Huntington disease differs from that of Alzheimer disease. Alzheimer disease arises from changes in the

Children of Huntington patients have a 50% chance of inheriting the disease

TABLE 2

Neuroleptic-induced movement disorders

Acute dystonic reaction
 Oculogyric crisis
 Acute akathisia
 Drug-induced parkinsonism
 Neuroleptic malignant syndrome
 Withdrawal emergent syndrome
 Persistent dyskinesias
 (tardive dyskinesia syndromes)
 Classic oral-buccal-lingual dyskinesia
 Tardive dystonia
 Tardive akathisia
 Tardive tics
 Tardive myoclonus

**Up to 30% of
 depressed
 Huntington
 disease
 patients
 attempt suicide**

cerebral cortex, whereas the dementia of Huntington disease is subcortical, arising from changes in deeper structures. Typical Huntington patients show poor recall, impaired visual-spatial abilities, slowed thinking, a depressed and apathetic mood, and low motivation. In contrast, Alzheimer patients have difficulties with recognition, calculation, and speech. Patients with subcortical dementias can often recall with cueing, while those with Alzheimer disease still find that difficult.

Increased irritability may be noted before the onset of dementia. Alcoholism, conduct disorder, and antisocial traits have been described. Occasionally, paranoid delusions or other positive symptoms resembling schizophrenia are noted and were certainly present in our case.

Depression, behavioral changes, and insomnia can appear before abnormal movements appear.⁵⁻⁸ One group⁹ reported the prevalence of major depression following diagnosis of Huntington disease to be 41%. The risk of suicide is two to three times higher for these patients than for age-matched controls. Up to 30% of depressed persons with Huntington disease may attempt suicide, and 2% to 7% of them succeed.¹⁰ Extreme vigilance and attention to the patient's mood and communication are important.

WHAT IS THE TREATMENT?

3 The treatment options for this patient include which of the following?

- ☐ Increasing the dose of paroxetine
- ☐ Adding an antipsychotic agent for the choreiform movements
- ☐ Starting a beta-blocker
- ☐ Trial of a tricyclic antidepressant
- ☐ Family counseling

Adding an antipsychotic medication and a trial of a tricyclic antidepressant are appropriate options at this point.

Antipsychotic medications. Dopamine antagonists, such as haloperidol in starting doses of 0.5 to 1.0 mg, are often helpful in controlling choreiform movements and psychosis. However, Folstein¹¹ advocates using fluphenazine instead of haloperidol because it may be less likely to produce dysphoria in this group.

Of note: Most neuroleptic or antipsychotic medications can induce movement disorders such as those listed in TABLE 2. These adverse reactions are due to their blocking effect on dopamine D2 receptors. The "atypical" neuroleptic clozapine, a drug that predominantly blocks the D4 receptor, is free of these complications except for acute akathisia. As yet, no adequate controlled trials have compared the various choices to reduce abnormal movements in patients with Huntington disease.

Antidepressive medications. Very few studies have assessed the various treatments for depression in these patients. Whenever an organic or medical disorder is producing a secondary depression, treatment is often less effective.¹² Although this patient took only a low dose of paroxetine for a brief period of time, akathisia may have limited the option of increasing the dose to therapeutic levels of this medication. Therefore, switching to a tricyclic is a reasonable option.

Folstein^{9,11} found electroconvulsive therapy and tricyclics to offer benefit, particularly nortriptyline, which has a lower propensity to produce orthostasis than other tricyclics. Ford¹³ treated three patients with monoamine oxidase inhibitors. SSRIs are also used if

movements do not increase for any particular patient.⁵ Neurovegetative symptoms may improve more than subjective mood. Lithium, carbamazepine, or neuroleptics may be used to treat manic symptoms.

Beta-blockers can be helpful for irritability and aggression associated with severe acute anxiety. Metoprolol, pindolol, or propranolol in small doses with increments as needed can be prescribed. However, paradoxical responses occasionally occur, producing greater agitation.¹⁴

Counseling. Helping the family cope may be one of the most important aspects of care. As the patient becomes increasingly disabled, he or she will become increasingly unable to keep up with work, household tasks, management of finances, and eventually with social relationships and self-care. The family should be offered help in planning for these circumstances beforehand. The family also needs genetic counseling.

The family's grief and anxiety around the loved one and often their own personal fears, anger, or depression will benefit from the extension of a helping hand and open heart. Psychotherapy and counseling are particularly helpful when symptoms are great and supports are few.

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Helping a family cope with Huntington disease is a key to care

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