Neuropsychiatric Phenomena Associated With Movement Disorders

Joshua L. Roffman, M.D.; Todd Eisenberg, M.D.; and Theodore A. Stern, M.D.

Have you ever encountered a patient whose progressive movement disorder and constellation of affective, behavioral, and cognitive symptoms do not easily lend themselves to classification? Has uncertainty surrounding the underlying diagnosis complicated medical management of these symptoms? If so, then the following case vignette of an elderly man with progressive motor and cognitive decline should shed some light on these and other questions related to neuropsychiatric sequelae of movement disorders.

Case Presentation

Mr. A was a 74-year-old widowed economist with a 1-year history of tremor and bradykinesia but no history of psychiatric problems. He was admitted to the hospital with a fractured hip following a mechanical fall, which occurred when he slipped in the bathroom. According to his primary care physician, Mr. A was recently started on levodopa-carbidopa for his motor symptoms, with little effect. The primary care physician was also concerned about cognitive decline over the last year. In the emergency room, Mr. A appeared mildly confused, with a Mini-Mental State Examination score of 24 (points were lost for short-term memory recall, figure construction, and calculation) and poor executive function as indicated by his performance on the Draw-A-Clock test. His affect was flat, and he was noted to have increased speech latency, paucity of speech production, and decreased prosody. The initial neurologic examination also indicated ataxia, bilateral tremor, and increased muscle tone in his upper and lower extremities. While awaiting surgery on the orthopedics service, Mr. A developed worsening confusion and combativeness, with concomitant tachypnea and oxygen desaturation. A chest X-ray revealed the presence of aspiration pneumonia, which was treated with intravenous antibiotics. His agitation was well controlled with twice-daily administration of risperidone (1 mg); however, his stiffness and tremor worsened. Neurologic consultation was ordered, and a detailed neurologic examination revealed bilateral vertical gaze palsy in addition to the previously documented motor symptoms. A diagnosis of progressive supranuclear palsy (PSP) was made.

What Are Movement Disorders?

Abnormalities in the extrapyramidal motor system can cause impaired regulation of voluntary motor activity, manifesting clinically as movement disorders. Depending on the specific disorder, as well as the clinical stage, patients can present with a variety of motor symptoms. These symptoms fall into the categories of hypokinetic and hyperkinetic signs (Tables 1 and 2). Although treatment may improve symptoms early in the course of the illness, most movement disorders are progressive and ultimately lead to significant morbidity and incapacitation. While the dis-
Table 1. Hypokinetic and Related Signs in Movement Disorders

<table>
<thead>
<tr>
<th>Sign</th>
<th>Description</th>
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<tbody>
<tr>
<td>Akinesia</td>
<td>A tendency not to move</td>
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<tr>
<td>Bradykinesia</td>
<td>A tendency to move slowly</td>
</tr>
<tr>
<td>Freezing</td>
<td>A sudden inability to move</td>
</tr>
<tr>
<td>Rigidity</td>
<td>Increased tone in a muscle group</td>
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<tr>
<td>Mask-like facies</td>
<td>Decreased tone in facial muscles, giving the impression of flat affect</td>
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<tr>
<td>Aprosodia</td>
<td>Speech lacking in normal intonation, rhythm, and intensity of expression</td>
</tr>
<tr>
<td>Abulia</td>
<td>Reduced spontaneity of speech, motion, and goal-directed behavior in the absence of sadness</td>
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</table>

*Based on Flaherty et al.*

Table 2. Hyperkinetic Signs in Movement Disorders

<table>
<thead>
<tr>
<th>Sign</th>
<th>Description</th>
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<tbody>
<tr>
<td>Chorea</td>
<td>Rapid jerking movements</td>
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<tr>
<td>Athetosis</td>
<td>Slow, writhing, dance-like movements</td>
</tr>
<tr>
<td>Festination</td>
<td>Tiny accelerated steps associated with difficulty stopping</td>
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<tr>
<td>Hemiballism</td>
<td>Sudden flinging movements of a limb</td>
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<tr>
<td>Tics</td>
<td>Brief stereotyped muscle contractions</td>
</tr>
<tr>
<td>Tremor</td>
<td>An involuntary oscillatory movement, occurring with action or rest</td>
</tr>
</tbody>
</table>

*Based on Flaherty et al.*

ease course varies, progression usually occurs over a 5- to 15-year period after initial symptoms present. Incidence increases with age, and movement disorders are a common problem in the elderly.

There are several types of movement disorders; each type corresponds to a different pattern of neurodegeneration with a separate cluster of symptoms. The prototypic disorder, Parkinson’s disease, involves loss of pigmented dopamine neurons in the substantia nigra, with resultant tremor, rigidity, and bradykinesia. Levodopa relieves symptoms, especially in the initial stages of illness, by providing replacement of dopamine. Huntington’s disease, an autosomal dominant disorder, is associated with progressive chorea and destruction of the head of the caudate nucleus. Wilson’s disease is an autosomal recessive disorder of copper metabolism that leads to neurologic (e.g., dysarthria, tremor, and spasticity) and sometimes hepatic (hepatitis, cirrhosis) symptoms.

Progressive supranuclear palsy, with which Mr. A was ultimately diagnosed, shares symptoms with Parkinson’s disease, but it is uniquely associated with a vertical gaze paralysis. Patients with PSP are also especially prone to falls (due to postural instability) and to swallowing difficulties, both of which caused significant morbidity for Mr. A.³ While levodopa treatment may initially improve symptoms in Parkinson’s disease, patients with PSP may not benefit³ (as was the case with Mr. A). No treatment has yet been identified that stops the progression of PSP.

What Cognitive Symptoms Are Associated With Movement Disorders?

Many movement disorders, including PSP, are associated with progressive cognitive decline and psychosis. The underlying pathophysiology of this process has not been fully established, but it very likely reflects the degeneration of cholinergic neurons (as is seen with Alzheimer’s disease).⁶ Lewy body dementia, which shares clinical and pathologic features of Parkinson’s disease and Alzheimer’s disease, renders patients especially susceptible to visual hallucinations. As with dementia patients, patients with movement disorders are also especially predisposed to delirium in the setting of comorbid medical illness (e.g., infections, stroke, and cardiovascular events).⁷ Formal neuropsychological testing can be useful in determining whether cognitive symptoms reflect localized brain pathology; for Mr. A, neuropsychological testing may have further delineated a frontal lobe problem (as suggested by his performance on the Draw-A-Clock test).

It is also important to note that medications that treat the motor symptoms of some movement disorders can worsen psychotic features. These medications include indirect dopamine agonists (e.g., levodopa), direct dopamine agonists, and anticholinergic medications. Clinicians who treat these patients are faced with the dilemma of balancing intact motor function with preserved mental status.³ Prior to initiating treatment with antipsychotic medication (which may worsen motor symptoms as discussed below), clinicians should rule out other etiologies for psychotic symptoms, e.g., effects of other medications or other medical illness. The next step is to reduce or eliminate antiparkinsonian medications (i.e., starting dopamine agonists, and anticholinergic medications, then levodopa).

What Affective and Behavioral Symptoms Are Associated With Movement Disorders?

Depression and anxiety occur with high frequency in patients with movement disorders. In Parkinson’s disease, depression is seen in nearly 50% of cases.⁹ At the same time, depression is severely underrecognized by clinicians who treat patients with movement disorders,¹⁰ quite possibly owing to the significant clinical overlap between these conditions. Symptoms common to movement disorders and depression are as follows⁸¹⁰¹¹:

1. Movement: bradykinesia, restricted affect, stooped posture.
3. Vegetative: decreased energy, fatigue, impaired sleep, appetite changes.

Symptoms of depression and anxiety have been found to correlate with “on-off” effects of many antiparkinsonian drugs, but not necessarily with the overall course of the movement disorder. In the case of Mr. A, several symptoms (flat affect, increased speech latency, paucity of speech production, and decreased prosody) suggest the possibility of comorbid depression. However, it is always important to ask patients about depressed mood and anhedonia. Patients’ responses to these questions help not only to distinguish depression from manifestations of movement disorders, but also to differentiate depression from other neuropsychiatric syndromes that present with similar features (e.g., abulia, aprosodia).

Movement disorders that cause degeneration of the frontal lobes can result in disinhibition, emotional liability, and poor executive function. Although Mr. A’s combativeness could have been related to his underlying pneumonia and hypoxia, it is also possible that frontal dysfunction could have contributed, especially given his poor performance on the Draw-A-Clock test. Formal neuropsychological testing can be useful to help clarify the role of regional brain dysfunction in behavioral symptoms.

What Treatment Is Available for Psychotic and Affective Symptoms Associated With Movement Disorders?

Because many antipsychotic medications act as dopamine- receptor antagonists, their use in patients with movement disorders can exacerbate motor symptoms. Risperidone (as we saw with Mr. A) and typical antipsychotics are frequent culprits in this regard. Clozapine is an atypical antipsychotic associated with virtually no extrapyramidal symptoms, and its efficacy in patients with movement disorders with mood and psychotic features has been well documented. However, due to the risk of agranulocytosis and the necessity of frequent blood draws, the use of clozapine creates logistical difficulties for patients and clinicians. Quetiapine is widely considered the next best choice for controlling psychotic symptoms in patients with movement disorders and appears less likely to exacerbate motor symptoms than do other antipsychotics.

Selective serotonin reuptake inhibitors (SSRIs) appear to improve depression and anxiety symptoms in patients with movement disorders, although to date they have not been as well studied as tricyclic antidepressants (TCAs). A clear advantage of SSRIs over TCAs is their improved side effect profile: the use of TCAs in the elderly and the medically ill is limited by adverse effects (including anticholinergic delirium, cardiac arrhythmias, hypotension, and urinary retention). Although not yet supported by well-controlled studies, the use of electroconvulsive therapy (ECT) appears to be effective in treating depression among patients with movement disorders. Patients with Parkinson’s disease have also seen the added benefit of improvements in motor function with ECT, although this effect is often transient. However, patients with movement disorders may also be more vulnerable to ECT-related mental status changes, including memory loss and delirium. Thus, although several effective treatments for affective and psychotic symptoms in patients with movement disorders exist, given the unique vulnerabilities of this patient population, careful scrutiny must be given to the potential adverse effects of these interventions.

REFERENCES

ANNOTATED BIBLIOGRAPHY

--This overview describes the epidemiology, clinical presentations, differential diagnosis, and management of patients with progressive supranuclear palsy (PSP). The authors focus on factors leading to the clinical misdiagnosis of PSP, a pattern that is being recognized with greater frequency.

--Presentations of cognitive, behavioral, and affective symptoms in Parkinson’s disease are reviewed, with emphasis on diagnosis and treatment (including neurosurgical options).

--The authors describe why atypical antipsychotics are less prone to exacerbate motor symptoms in patients with movement disorders. They review the literature on the use of clozapine, risperidone, olanzapine, and quetiapine in patients with Parkinson’s disease and associated disorders.