Pregnant and moving involuntarily

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After Ms. A delivers a preterm girl, the obstetrics service notes she has a blunted affect and involuntary movement of the arms and legs. What could be causing her symptoms?

CASE Abnormal movements

Pregnant and unsure of her due date, Ms. A, age 35, presents to the emergency room complaining of hourly uterine contractions for the last 3 days and new onset vaginal bleeding. Ms. A is admitted to the obstetrics (OB) service for preterm labor at 34 and 3/7 weeks as dated by a triage ultrasound.

During initial examination by the OB service, Ms. A's blood pressure is 155/112 mm Hg with a pulse of 126. Her cervix is dilated to 4 centimeters. Her physical exam is notable for rapid, repetitive, involuntary movements in her upper extremities and to a lesser degree in lower extremities. Ms. A is started on IV fluids and hydralazine, 10 mg/d, for elevated blood pressure. Later that day, she delivers a preterm female weighing 2,360 grams in a spontaneous vaginal delivery without any complications.

After delivery, the OB service requests a psychiatric consultation to evaluate Ms. A's "blunted affect," history of heavy alcohol use, and abnormal movements. During examination, Ms. A is alert and oriented to her surroundings. She states that this was her eleventh pregnancy; however, she is unable to recall details of most previous pregnancies. She also cannot remember any significant medical, surgical, or mental health history. Ms. A appears distracted, has difficulty participating in the interview, and gives contradictory histories to different team members. She is well groomed but shows repetitive circular movements of her hands, feet, and jaw that are nearly continuous. In addition, Ms. A has intermittent lip biting and smacking. Her speech is delayed, with increased latency of her responses to basic questions.

Her mood is neutral, her affect is blunted, and she denies any current suicidal or homicidal ideations, delusions, and auditory or visual hallucinations. Although her chart indicates a history of alcohol abuse, she denies this history and current drug or alcohol use. Her Mini-Mental State Exam score is a 22/30, missing points in her ability to copy shapes and write a sentence, complicated by her chorea-like upper body movements. She also demonstrates marked inattentiveness and is unwilling to cooperate with spelling "world." On physical exam, her gait is wide-based but steady.

What is the likely cause of Ms. A's abnormal movements?

a) medication use
b) Huntington's disease
c) substance intoxication
d) chorea gravidarum

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continued

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Clinical Point

Withdrawal dyskinesias can appear as extrapyramidal symptoms, including choreoathetosis similar to what Ms. A experienced

The authors' observations

Determining the cause of Ms. A's abnormal movements, delayed speech, and neutral mood initially proves difficult because she is minimally cooperative with the interview and we find discrepancies between information she provides and her medical records from previous OB admissions. It is unclear whether these inconsistencies are because of her faltering memory—which she admits has worsened in the last year—or unwillingness to provide a complete medical history.

We consider possible substance intoxication given her documented history of substance use. However, an extended drug screen is negative and her laboratory values do not suggest heavy alcohol use.

HISTORY Depression and confusion

The next day, Ms. A is more cooperative with the interview. She says that she began feeling depressed 8 years ago, around the time her brother was killed in a violent crime. She denies previous psychiatric hospitalizations, but says she attempted suicide 4 years ago by stabbing herself in the throat with a fork. After that attempt, she was referred to an outpatient psychiatrist whom she continues to see intermittently. She says that her abnormal movements started 2 years before she first saw her outpatient psychiatrist.

She says she has been prescribed several medications, but remembers only taking quetiapine for depressive symptoms and insomnia. After a discussion with her psychiatrist about the possible effects of quetiapine on the fetus, she discontinued the drug approximately 8 weeks into her pregnancy. Quetiapine decreased her movement symptoms slightly, and she feels her movements have become uncontrollable since discontinuing it.

She reports increased feelings of sadness, worthlessness, guilt, decreased energy, irritability, and difficulty sleeping during her pregnancy. She denies current or past psychotic symptoms or mania. Ms. A says she has noticed problems with her memory as well as increased confusion over recent months. She often gets lost and cannot remember where she lives after leaving her home.

Based on hospital records, we learn that an MRI of the brain without contrast was completed 1 year ago to "evaluate choreiform movements." The scan showed mild atrophy and abnormal signal within the caudate and putamen, as well as volume loss. We consult with the neurology service to evaluate Ms. A's abnormal movements and her previous abnormal brain imaging. The neurologic exam notes that Ms. A has orofacial dyskinesias and near-continuous choreiform movements in her arms and hands. Her gait remains wide-based and she is unable to tandem walk. Because Ms. A shows no new neurologic symptoms, the neurology service does not feel that additional neuroimaging is indicated.

The authors' observations

In consultation with neurology, the leading differential diagnoses include tardive dyskinesia, chorea gravidarum, and Huntington's disease. See the ***Table***[1,2] for the differential diagnosis of chorea.

Ms. A reports taking quetiapine for 3 years, which suggests possible tardive dyskinesia. Although second-generation antipsychotics have a lower incidence of movement disorders than first-generation antipsychotics, the risk still exists. Withdrawal dyskinesias can occur after suddenly stopping or tapering antipsychotics and appear as extrapyramidal symptoms, including choreoathetosis similar to what Ms. A experienced.[3,4] This type of dyskinesia is thought to be secondary to chronic dopamine antagonism leading to increased postsynaptic receptors and dopamine hypersensitivity.[5] Because Ms. A discontinued quetiapine early in her pregnancy, withdrawal dyskinesias are less likely.

Because Ms. A presented with a movement disorder while pregnant, the neurology service considers chorea gravidarum, the term given to chorea occurring dur-

Table

Differential diagnosis for chorea

Genetic	Huntington's disease, benign hereditary chorea, neuroacanthocytosis, dentatorubral-pallidoluysian atrophy, Wilson's disease, spinocerebellar ataxia, Friedreich's ataxia
Rheumatic disorders	Sydenham's chorea, chorea gravidarum
Drug-induced/toxicity	Neuroleptic drugs, steroids, anticonvulsants, antiparkinson agents, stimulants (amphetamines, cocaine), lithium, dopamine agonists
Systemic disorders	Systemic lupus erythematosus, thyrotoxicosis, polycythemia vera, hyperglycemia, AIDS, paraneoplastic syndrome
Vascular/trauma	Cerebral hemorrhage, vasculitis, stroke, antiphospholipid antibody syndrome

AIDS: acquired immune deficiency syndrome

Source: References 1,2

ing pregnancy. This syndrome is thought to be caused by the effects of pregnancy on the basal ganglia.[6] Historically, chorea gravidarum was associated with rheumatic fever (RF); however, with the decline in prevalence of RF, most choreiform movements that appear during pregnancy typically are caused by other diseases, such as systemic lupus erythematosus or Huntington's disease. Approximately one-half of chorea gravidarum cases are idiopathic, with RF and antiphospholipid syndrome accounting for the remainder.[7] Huntington's disease during pregnancy is rare because it tends to present in women beyond childbearing age.

Based on Ms. A's symptoms and previous MRI findings, we ask her if she has a known family history of Huntington's disease. She denies this, but says she has not seen her father since she was very young and is uncertain of his medical history.

TREATMENT Restart medication

Ms. A's laboratory results show a slightly low hemoglobin of 10.5 g/dL and hematocrit of 32.8%. Her mean corpuscular volume is slightly decreased at 77 fL. Her urinalysis is negative, and blood glucose and thyroid-stimulating hormone are within normal limits. Rapid plasma regain, anti-nuclear antibody, and human immunodeficiency virus (HIV) are negative. Based on hospital records, we learn that during the previous admission a year ago a serum ceruloplasmin and serum copper were drawn and were normal.

We contact Ms. A's outpatient psychiatrist for collateral information. The psychiatrist says he first evaluated Ms. A 3 years ago after a friend brought her in because of strange behavior, including talking to herself, making odd facial gestures, and laughing inappropriately. Although Ms. A denies past psychiatric hospitalizations, her psychiatrist states that she was hospitalized for 1 week after the suicide attempt 4 years ago and prescribed lorazepam and sertraline during that admission. He speculates that the suicide attempt may have been related to 5 of her children being taken from her by the Department of Family and Child Services after police raided her home to search for drugs. Custody was awarded to their respective fathers, causing Ms. A to "snap," according to her friend.

Since then, neither Ms. A nor her psychiatrist have reported any further psychotic symptoms. Her psychiatrist confirms that Ms. A's abnormal movements were present before her first appointment with him. He says that he referred Ms. A to a local hospital for a neurology work-up, but she did not schedule an appointment.

When we follow up with Ms. A 2 days after delivery, she continues to deny depressive symptoms, although her affect remains

Clinical Point

Huntington's disease during pregnancy is rare because it tends to present in women beyond childbearing age

Box

Huntington's disease: Genetic abnormalities lead to psychiatric and neurologic symptoms

Huntington's disease is an autosomal dominant disorder characterized by progressive motor, cognitive, and psychiatric disturbances and is the most common genetic cause of chorea. The underlying genetic mutation is a CAG repeat expansion in the Huntington's disease gene. A Huntington's disease diagnosis generally is considered in the presence of the characteristic choreiform movements and slowly progressive cognitive decline.[8] Physical symptoms can present at any age, although they usually begin between age 35 and 44. In early stages of the disease, patients may experience subtle changes in personality, cognition, and physical skills. Although most Huntington's disease patients eventually exhibit similar physical symptoms, the onset, progression, and extent of cognitive and psychiatric symptoms vary among individuals. However, psychiatric symptoms frequently are present during the early stages of the disease, often before motor symptoms begin and can include personality changes, irritability, agitation, apathy, and depression. In addition, up to 23% of patients with Huntington's disease develop psychotic symptoms.[1,9] There is no cure for Huntington's disease, and mean disease duration is 17 to 20 years. The most common cause of death among Huntington's disease patients is pneumonia, followed by suicide.[1]

A Huntington's disease diagnosis is based on clinical symptoms and signs in an individual who has a parent with proven Huntington's disease and is confirmed by DNA tests.[1] Typical neuroanatomic findings include initial neuronal loss in the striatum followed by a diffuse involvement of cortical and subcortical areas.[10] Volume changes in the caudate nucleus and the putamen may be a reliable measure of Huntington's disease and potentially serve as a biomarker.[11]

Clinical Point

Psychiatric symptoms, frequently are present during the early stages of Huntington's disease, often before motor symptoms begin

blunted. She says she is looking forward to going home with the baby, whom she plans to bottle feed. Her choreiform movements appear unchanged. She also continues to experience lip smacking. Although Ms. A recognizes that she has some movements, she minimizes them and says they do not bother her. She continues to demonstrate latency in her verbal responses to questions. Based on the collateral history and positive response with quetiapine, we recommend that Ms. A be restarted on quetiapine, 200 mg/d.

Which psychiatric symptoms are most common in the early states of Huntington's disease?

a) mania
b) cognitive disorders
c) obsessive-compulsive symptoms
d) depression

The authors' observations

Ms. A's choreiform movements started before her psychotic symptoms and subsequent usage of neuroleptic medication, which makes tardive dyskinesia less likely. Laboratory studies rule out systemic lupus erythematosus, HIV, and Wilson's disease as the cause of her abnormal movements.

Ms. A's history is highly suggestive of Huntington's disease. She exhibits classic motor signs, including involuntary choreiform movements in her extremities. She also has psychiatric symptoms that are commonly associated with Huntington's disease, including depression—which preceded her motor symptoms—cognitive decline, apathy, and psychotic symptoms. In addition, her MRI findings of volume changes in the caudate nucleus and the putamen and inability to rule out a family history make Huntington's disease more likely (***Box***).[1,8-11]

Psychiatric symptoms

Psychiatric symptoms frequently are evident in the early stages of Huntington's disease, often before onset of motor symptoms.[1] Depression is the most common sign, and can be difficult to diagnose because weight loss, apathy, and inactivity also oc-

cur in Huntington's disease. Feelings of low self-esteem, guilt, and anxiety can help distinguish depression from symptoms of Huntington's disease. Cognitive decline also may present before the first motor symptoms occur. Cognitive changes typically are related to executive functions and affected individuals may develop impairments in organization and planning. Psychotic symptoms may be present, but are more common in later stages of the disease.[1]

Ms. A reported that quetiapine seemed to lessen her choreiform movements, and dopamine receptor blocking agents (ie, antipsychotics) often are considered for managing chorea and psychosis in Huntington's disease. However, there are few double-blind, placebo-controlled studies evaluating the efficacy of these agents.[12] Small, uncontrolled, nonrandomized trials found quetiapine has some efficacy for both motor and psychiatric symptoms in Huntington's disease.[12-15]

OUTCOME Lost to follow-up

Ms. A is discharged from the hospital 3 days after she delivers her daughter and is given an appointment in 6 weeks at an affiliated movement disorders clinic. Before discharge, she is tested for the Huntington's disease gene mutation with a plan to receive her results during her follow-up visit. During the informed consent process for the genetic testing, Ms. A states that she was tested previously and was quite sure that the test was positive for Huntington's disease, although she could not recall where or when this testing was completed.

Related Resources

- De Marchi N, Mennella R. Huntington's disease and its association with psychopathology. Harv Rev Psychiatry. 2000; 7(5):278-289.
- Revilla FJ, Grutzendler J, Larsh TR. Huntington disease. Medscape. http://emedicine.medscape.com/article/1150165-overview.

Drug Brand Names

Hydralazine • Apresoline
Lithium • Eskalith, Lithobid, others
Lorazepam • Ativan
Quetiapine • Seroquel
Sertraline • Zoloft

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Ms. A also is scheduled to follow up with her obstetrician for a 6-week postpartum checkup and tubal ligation. We encourage Ms. A to make an appointment with her psychiatrist soon after discharge. We also make a referral to the Department of Family and Children Services to provide adequate support and resources to her and her children because of her physical and psychiatric issues.

Ms. A does not show up for her follow-up appointment at the movement disorders clinic. The genetic test is not completed during this admission because of a clerical error, and the serum sample subsequently expires.

The authors' observations

Although Huntington's disease is the most likely cause of Ms. A's presentation, we were unable to confirm the diagnosis with genetic testing. If Ms. A returns to the neurology service and the genetic test is negative for Huntington's disease, other causes of chorea must be investigated.

Clinical Point

Feelings of low self-esteem, guilt, and anxiety can help distinguish depression from Huntington's disease

Bottom Line

Psychiatric symptoms, particularly depression, anxiety, and irritability, are common in Huntington's disease and may appear before neurologic signs. Neuropsychiatric abnormalities are present in almost all patients with Huntington's disease.

continued

Clinical Point

Small trials found that quetiapine has some efficacy for certain symptoms of Huntington's disease

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