Chorea among Older Adults

Bhaskar Ghosh, MD, DNB, DM, MNAMS, Movement Disorders Program, Department of Clinical Neurosciences, University of Calgary, Calgary, AB.

Oksana Suchowersky, MD, FRCPC, FCCMG, Movement Disorders Program, Department of Clinical Neurosciences, Department of Medical Genetics, Faculty of Medicine, University of Calgary, Calgary, AB.

Chorea is a hyperkinetic movement disorder characterized by nonsustained, rapid, and random contractions that may affect all body parts. Chorea is hypothesized to be due to an imbalance between the direct and indirect pathways in the basal ganglia circuitry. Important causes of chorea among older adults include medications, stroke, and toxic-metabolic, infective, immune-mediated, and genetic causes. The history and clinical examination guide appropriate investigations and help determine an accurate diagnosis. In secondary causes, removal of the precipitating cause is the mainstay of treatment. If the chorea is persistent or progressive, drug therapy may be instituted. Genetic counselling is important in hereditary chorea.

Key words: movement disorders, chorea, older adults, diagnosis, treatment

Introduction

Movement disorders can be subdivided into two types: hypokinetic, such as parkinsonism, and hyperkinetic, characterized by an excessive amount of motor activity. The hyperkinetic disorders are further characterized as rhythmic or nonrhythmic. The prototypic rhythmic hyperkinetic movement disorder is tremor, while irregular (or nonrhythmic) hyperkinetic movement disorders include chorea, ballismus, athetosis, dystonia, tics, and myoclonus.

Of the arrhythmic hyperkinetic movement disorders, chorea is one of the most common. The term chorea comes from the Greek word khoreia, which means “dancing.” It is characterized by continuous, unsustained, rapid, and random contractions. Chorea may affect the distal limbs, face, and trunk. When the movements are slow and more sinuous, the term athetosis is used. Very proximal flinging movements are referred to as ballismus.

The History of Chorea

The root of chorea can be traced to the Middle Ages, when, coincident with the Black Plague, “dancing mania,” as chorea was then known, erupted in central Europe. Victims formed circles and persisted to dance together in wild delirium for hours on end. During a second plague outbreak in 1414, St. Guy or St. Vitus and, in later epochs, St. Willibrord, were called upon to intercede. The mystic and reformer Paracelsus introduced the concept of chorea as a naturally occurring medical condition, chorea naturalis, in contradistinction to consciously or unconsciously based emotional origins. Sydenham followed with more medical details, but the relationship between streptococcal endocarditis and resultant chorea were appreciated in the 19th century, largely due to Charcot and his French colleagues. In 1872, George Huntington published a report of adult-onset hereditary chorea, and, in 1896, the pathological changes of caudate atrophy and neuronal degeneration in Hunting-
Chorea among Older Adults

Toxins and Substance Abuse
Acute chorea is associated with exposure to toxins and abuse of substances, including alcohol, amphetamines, heroin, glue, thallium, and mercury.7

Vascular Causes
In the older adult population, vascular conditions are an important cause of acute chorea. Although hyperkinetic movement disorders are uncommon after acute stroke (occurring in only 1% of the stroke population), chorea is the most common, with the usual manifestation of hemichorea contralateral to the affected hemisphere.13 The subthalamic nucleus is thought to be the most commonly involved site due to either hemorrhage or ischemia. This typically results in hemiballismus at the acute stage. Gradually, the hemiballismus is replaced by chorea, with resolution in 3–6 months. Some individuals with vascular chorea have lesions outside the subthalamus, including other parts of the striatum, thalamus, and even cortex.14 Uncommon causes of vascular chorea among older adults include postpump chorea15 and cerebral arteriovenous malformations.16,17

Cerebral Trauma
Rarely, chorea can occur after cerebral trauma. Acute-onset generalized chorea has been reported with bilateral chronic subdural hematomas.18

Metabolic Disorders
When chorea presents acutely, metabolic disorders should be considered. Nonketotic hyperglycemia, hypoglycemia, hypernatremia, hyponatremia, hypomagnesemia, hypocalcemia, hepatic failure, and renal failure have been implicated in the development of chorea.7 Recent interest has been focused on chorea associated with nonketotic hyperglycemia. This is associated with high-signal intensity lesions on T1-weighted brain magnetic resonance images (due to microhemorrhages in the pallidum) and is recognized as a unique syndrome that predominantly affects older women of Asian ethnic background. In most cases, chorea or hemichorea improves with the disappearance of the lesions seen on magnetic resonance images when hyperglycemia is controlled.19

Central Nervous System Infection
Chorea can occur in the settings of acute toxoplasmosis, syphilis, neurosyphilis, Creutzfeldt-Jakob disease, neuroimmunodeficiency, and paraneoplastic syndromes.
manifestation of bacterial meningitis, encephalitis, tuberculous meningitis, tuberculoma, and aseptic meningitis. Movement disorders are also encountered in 2–3% of all persons with acquired immunodeficiency syndrome (AIDS). Hemichorea and hemiballismus are relatively common among individuals with AIDS due to toxoplasmosis abscess; however, direct invasion of the human immunodeficiency virus (HIV) and injury to the basal ganglia may also result in chorea. In the latter situation, the onset of chorea is gradual and may be chronic. Less commonly, Lyme’s disease has been reported to cause chorea as has Creutzfeldt-Jakob disease. Rarely, chorea may be a presenting symptom of neurosyphilis.

Immune-Mediated Causes
Although systemic lupus erythematosus (SLE) has traditionally been considered a disease occurring primarily among premenopausal women, recent reports have led to the recognition of this disease occurring among older adults. Up to 20% of individuals with SLE may present in later life. Central nervous system involvement in SLE is common, occurring in 50–70% of cases; however, chorea has been reported in <2% of these individuals. Chorea is seen in about 1.3% of individuals with antiphospholipid syndrome (APLS). Although generalized or hemichorea develops at an average age of 21 years with a predominance in young women, APLS has been reported among older adults. Less commonly, chorea can be associated with other autoimmune diseases, including Behçet’s disease, polyarteritis nodosa, isolated angiitis of the central nervous system, and primary Sjögren’s syndrome. Chorea has been reported with Hashimoto’s encephalopathy with a high antithyroid antibody titre. Paraneoplastic syndromes associated with anti-Hu and anti-CRMP5 antibodies in persons with small cell lung carcinoma can rarely present with chorea.

Sydenham’s chorea is common in children and young adults following an episode of rheumatic fever. Recurrence of chorea has been reported among older adults. This delayed manifestation was not associated with antibasal ganglia antibodies (associated with 100% of acute cases and 69% of persistent cases of Sydenham’s chorea).

Recurrence of chorea in these situations may also be triggered by hormone replacement therapy.
Chorea among Older Adults

Genetic Causes
The most important cause of hereditary chorea is Huntington’s disease (HD), which occurs worldwide with a prevalence of 10 cases per 100,000 and is inherited as an autosomal dominant trait with complete penetrance. It has been shown to be due to a mutation in the Huntington gene on the short arm of chromosome 4. Specifically, an expanded and unstable region of three repeating nucleotides (CAG) is seen in the first coding region of the gene. Normally, the CAG repeating sequence varies from 11 to 34 (median 19); the HD mutation occurs when the repeats expand above 36. Age of onset is inversely correlated with the size of the repeat; individuals with 37–40 repeats usually have an older age of onset. Symptoms typically include motor, cognitive, and psychiatric abnormalities. The disorder starts insidiously with restlessness, which is noted by relatives. Individuals may exhibit depression or subtle cognitive changes such as difficulty with multitasking and making judgments. Gradually, over 10–20 years, the condition progresses to involve generalized chorea and dementia. When the number of repeats is in the 36–38 range, onset may be quite late in life. Chorea may remain mild and cognitive changes minimal. Thus, any individual diagnosed with senile chorea should be considered as having HD, with appropriate genetic testing.

Huntington’s disease has been seen in families living in Cumbria in the northwest of England. Affected individuals typically present at the fourth to sixth decades with chorea, dystonia, bradykinesia, or a mixture of the three. Dystonia is extremely common. Serum ferritin is found to be low in this condition, and advanced cases show a T2 hyperintensity in the basal ganglia on magnetic resonance imaging.

Dentatorubropallidoluysian atrophy (DRPLA) is due to an expansion of the CAG triplet repeats in the open reading frame of a gene named atrophin located on chromosome 12. Larger expansions are found among individuals with earlier onset. Normally, the repeat length is <26; among individuals with DRPLA, the number of repeats is ≥49. Anticipation occurs in successive generations—who inherit the disease from their father. The disease has a variable presentation that may include progressive ataxia, choreoathetosis, dystonia, seizures, myoclonus, psychiatric disturbances, and dementia. The autosomal dominant spinocerebellar ataxias type 2, 3, and 17 may be associated with chorea.

Older adults who present with chorea that is of gradual onset should have DNA testing for these genetics disorders. This testing is available through Molecular Diagnostic Laboratories in North America.

Miscellaneous Causes
Rarely, chorea is associated with hypothyroidism, polycythemia rubra vera, and nutritional deficiency (vitamin B12). In polycythemia rubra vera, hemichorea has been reported.

If all causes have been excluded, a diagnosis of idiopathic senile chorea may be considered, although this entity remains controversial. Recently, it has been recognized that older adults have an increased incidence of involuntary lingual-facial-bucal movements. These can be seen in the

<table>
<thead>
<tr>
<th>Table 3: Recommended Investigations for Individuals with Chorea*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count, electrolytes, glucose, calcium, magnesium, vitamin B12</td>
</tr>
<tr>
<td>Renal function tests, thyroid function tests</td>
</tr>
<tr>
<td>Antinuclear antibody, antiphospholipid antibody, erythrocyte sedimentation rate, antistreptolysin O titre (in cases with suspected streptococcal infection)</td>
</tr>
<tr>
<td>Venereal Disease Research Laboratory test</td>
</tr>
<tr>
<td>Antibody for human immunodeficiency virus</td>
</tr>
<tr>
<td>Lyme disease—in cases with recent travel history to endemic areas</td>
</tr>
<tr>
<td>Toxoplasmosis titres in immunosuppressed patients</td>
</tr>
<tr>
<td>Smear for acanthocytosis</td>
</tr>
<tr>
<td>Cerebrospinal fluid in cases with suspected intracranial infection</td>
</tr>
<tr>
<td>Computed tomography scan of brain in cases of suspected intracranial hemorrhage, cerebral calcifications</td>
</tr>
<tr>
<td>Magnetic resonance imaging—to rule out intracranial structural lesion, especially in the setting of acute choreiform movements in older patients</td>
</tr>
<tr>
<td>Electroencephalography when needed to differentiate between paroxysmal movement disorders and seizures</td>
</tr>
<tr>
<td>Genetic testing (in Huntington’s disease, spinocerebellar ataxia 1–8 and 17, dentatorubropallidoluysian atrophy)</td>
</tr>
<tr>
<td>Positron emission tomography/single-photon emission computed tomography where indicated to study changes in basal ganglia metabolism and perfusion in degenerative and autoimmune choreas</td>
</tr>
</tbody>
</table>

*A careful history-taking and physical examination guide individual workups.

Source: Adapted from Bhidayasiri R and Truong DD, 2004.
and levetiracetam.

There is one case report of chorea involving a history of drug intake and clinical symptoms. Important questions are associated systemic or neurological dyskinesia or can be idiopathic.

Diagnosis involves a careful history-taking and an assessment of whether the chorea is of acute or chronic duration, whether it is progressive, and whether there are associated systemic or neurological symptoms. Important questions involve a history of drug intake and exposure to toxins and whether a family history is present. Progressive chorea of gradual onset suggests a hereditary cause. In acute-onset chorea, toxic-metabolic, autoimmune, and vascular causes should be considered. Further investigation depends upon the history and clinical examination (see Table 3).

**Diagnosis of the Etiology**

Diagnosis involves a careful history-taking and an assessment of whether the chorea is of acute or chronic duration, whether it is progressive, and whether there are associated systemic or neurological symptoms. Important questions involve a history of drug intake and exposure to toxins and whether a family history is present. Progressive chorea of gradual onset suggests a hereditary cause. In acute-onset chorea, toxic-metabolic, autoimmune, and vascular causes should be considered. Further investigation depends upon the history and clinical examination (see Table 3).

**Principles of Treatment**

The initial treatment of chorea depends upon the underlying cause. Removal of the causative factors—such as the correction of metabolic abnormalities, withdrawal of offending drugs and toxins, and control of infections—alleviates chorea in most of these cases. Resolution of choreic movements associated with HIV encephalitis with antiretroviral therapy has been reported. Chorea of Hashimoto’s encephalopathy responds to steroid treatment.

For the hereditary choreas, genetic counselling is very important. As HD is a dominantly inherited genetic disorder, the diagnosis has a tremendous impact on the family. The siblings and the children of an individual with HD are not only caregivers but are at risk of developing the disease. Comprehensive care of HD requires management of these at-risk individuals as well as care for affected individuals in a multidisciplinary setting.

If chorea is severe enough to result in disability or impact on activities of daily living, one has to consider symptomatic treatment (Table 4). Tetrabenazine, a dopamine-depleting agent, is useful as a symptomatic treatment for moderate chorea of any etiology. Atypical antipsychotics such as risperidone and olanzapine may be used as symptomatic treatments of more severe chorea. All these medications have the potential to cause parkinsonism, increased rigidity, and postural instability. Older adults are more susceptible to these side effects compared with younger patients. Thus, use of the lowest dose possible and careful regular monitoring of the patient are important. Although typical neuroleptics such as haloperidol and chlorpromazine are quite effective in reducing chorea, they are better avoided among older adults as there is a higher risk that these drugs will produce significant side effects.

Amantadine has been shown to alleviate chorea in Huntington’s disease; this effect is presumed to be mediated by amantadine’s antiglutamate action. There are case reports of chorea responding to newer drugs: persistent vascular chorea has been treated successfully with topiramate and levetiracetam. There is one case report of chorea in HD responding to high-dose quetiapine (600 mg/d).

**Conclusion**

Chorea seen in the older adult population can have a variety of etiologies. Appropriate investigations lead to an accurate diagnosis in almost all cases. Management begins with treatment of the underlying cause. Medications such as tetrabenazine and atypical neuroleptics are useful in more severe cases.

No competing financial interests declared.

**References**


---

**Table 4: Medications for the Management of Chorea**

<table>
<thead>
<tr>
<th>Neuroleptic medications: atypical agents</th>
<th>Clozapine</th>
<th>Olanzapine</th>
<th>Quetiapine (high dose)</th>
<th>Risperidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine-depleting agents</td>
<td>Tetrabenazine</td>
<td>Reserpine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABAergic agent: amantadine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Topiramate</td>
<td>Levetiracetam</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GABAergic = transmitting or secreting gamma-aminobutyric acid (GABA).

Source: Adapted from Fahn S, 2000.

---

**Key Points**

<table>
<thead>
<tr>
<th>Chorea is the most common of the arrhythmic hyperkinetic movement disorders, which also include ballismus, athetosis, dystonia, tics, and myoclonus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drugs are one of the most common causes of chorea; onset of chorea after prolonged use of dopamine-blocking agents is likely the commonest cause of choreiform movements among older adults.</td>
</tr>
<tr>
<td>Diagnosing chorea involves taking a careful history, assessing whether the chorea is of acute or chronic duration, whether it is progressive, and whether there are associated systemic or neurological symptoms.</td>
</tr>
<tr>
<td>Removal of the causative factors, such as correction of metabolic abnormalities, withdrawal of offending drugs and toxins, and control of infections, alleviates chorea in most cases.</td>
</tr>
<tr>
<td>Medications such as tetrabenazine and atypical neuroleptics are useful in treating symptoms of chorea in more severe cases.</td>
</tr>
</tbody>
</table>
Chorea among Older Adults

den krankheiten so die Vernunft berauben.1591.


