Clinical Reasoning:

A 6-year-old boy with uncontrollable right-sided movements

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Kevin.Gurcharran@mssm.edu**SECTION 1**

A 6-year-old boy with no significant medical history presents for uncontrollable abnormal movements of the right side for 3 days. Four days prior to presentation, he complained to his mother that “something was wrong” with his right hand. Three days prior to presentation, his mother noticed he would drop things like books and pencils and be unable to pick them up, had difficulty feeding himself, and when he would try to run he would hop. He complained of difficulty writing and his handwriting was

uncharacteristically messy. His mother began to notice odd movements of his right upper extremity, such as rolling his wrist and rotating his shoulder. One day prior to presentation, he was complaining of generalized right-sided weakness and his mother noted he had difficulty lifting his right arm.

Questions for consideration:

1. What is the differential diagnosis?
2. What would you look for on review of systems? On physical examination?

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SECTION 2

The differential of a child with chorea is large and includes collagen vascular diseases, Wilson disease, Sydenham chorea (SC), paroxysmal dyskinesia, hyperthyroidism, drug intoxication, Tourette syndrome, and encephalitis, among others (table). Although its existence is unproven, pediatric autoimmune neuropsychiatric disease associated with streptococcal infection (PANDAS) should be kept in mind as it shares characteristics with SC.

Table	Features of selected differential diagnoses of chorea	
	Age at onset	Features
Wilson disease	5–40 y	Liver disease is most common initial presentation. Neurologic symptoms can include chorea, parkinsonian symptoms, and incoordination. Kayser-Fleischer rings may be present. Common findings: abnormal liver function tests, low serum ceruloplasmin.
Tourette syndrome	Before age 18	Multiple motor and vocal tics nearly every day for a whole year. Cannot be asymptomatic for >3 consecutive months.
Sydenham chorea	3–15 y	Typically insidious chorea. Emotional lability and OCD may occur. May see other signs of RF at presentation.
PANDAS	Similar to SC	Abrupt onset OCD and tic disorder (vocal, motor, or TS). Must have evidence of recent strep infection. None of the non-neuropsychiatric symptoms of RF are present.
Paroxysmal kinesogenic dyskinesia	Early adolescence	Paroxysmal dystonic, choreic, or ballistic movements. Can have >100 attacks a day, which last seconds to minutes. Triggered by startle, or sudden movement. Associated with aura of muscle tightening or tingling.
Paroxysmal nonkinesogenic dyskinesia	Same as PKD	Movements similar to PKD. Only several attacks per day or per year, which last seconds to hours. No motor triggers, but provoked by caffeine, stress, alcohol, hunger.

Abbreviations: OCD = obsessive-compulsive disorder; PANDAS = pediatric autoimmune neuropsychiatric disease associated with streptococcal infection; PKD = paroxysmal kinesogenic dyskinesia; RF = rheumatic fever; SC = Sydenham chorea; TS = Tourette syndrome.

The patient denied any fever, chills, nausea, headache, sore throat, recent infections, throat clearing, history of seizures, recent trauma, rashes, dizziness, numbness, tingling, or joint pains. He was unable to suppress the movements, although they disappeared during sleep. His mother denied any changes in mood, appetite, or sleep. No obsessive thoughts or compulsive behaviors were noticed. No recent travel or sick contacts were reported. He was not on any medications or supplements. His last illness was a sore throat 14 months ago.

Neither past medical history nor family history was significant. There was no history of developmental delay. He is right handed.

On examination, he appeared well-developed and was alert and oriented to person, place, and time with reading and math skills above his grade level. Vital signs were within normal limits. No Kayser-Fleischer rings were present. Cardiac examination was significant for a III/VI blowing systolic ejection murmur loudest at the apex; his mother was not aware of a heart murmur before then. Motor examination was significant for nonstereotyped choreiform movements of the right arm and foot; subtle choreiform movements on the left; pronation on right arm extension overhead; milkmaid's grasp on the right; piano movements in the fingers and toes, worse on the right; and poor reproduction of Archimedes spiral (figure). Sensation was intact. Coordination and gait were normal, although choreiform movements sometimes interfered with smooth movements.

Questions for consideration:

1. What is your leading diagnosis?
2. What tests would you order?

Figure Patient reproduction of Archimedes spiral at presentation (A), at 2-week follow-up (B), and at 6-week follow-up (C)

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SECTION 3

Given his chorea and new murmur, SC was the working diagnosis. Tests ordered included head CT, EKG, complete blood count, erythrocyte sedimentation rate, metabolic panel, antistreptolysin O (ASLO), anti-DNAse B strep antibodies, thyroid tests, rapid plasma reagin, blood culture, and serum levels of ionized calcium, ceruloplasmin, copper, folate, parathyroid hormone, and vitamin B12. Given no changes in cognition or personality, no alteration of consciousness, and no abnormal sensations, EEG was not warranted. All tests were negative except for the ASLO and anti-DNAse B. In rheumatic fever (RF), the most common EKG finding is first-degree heart block; however, saddle ST elevation and T wave inversion can be seen.¹ EKG is not sensitive for early valvular lesions and a normal EKG does not preclude the presence of carditis. Echocardiography is more sensitive for cardiac lesions seen in RF and can identify silent carditis in patients with a normal EKG.¹ Therefore, if SC is suspected, echocardiography is vital.

A cardiology consult was obtained. Repeat EKG was normal. Echocardiography revealed mitral regurgitation and left ventricle diastolic dysfunction. With the clinical picture of carditis and chorea and the antistreptococcal studies, the diagnosis of RF was given and the chorea was confirmed as SC. He was discharged with IM penicillin as monthly antibiotic prophylaxis.

DISCUSSION SC is the neuropsychiatric manifestation of the poststreptococcal autoimmune disease, RF. SC is the most common acquired chorea.² It typically manifests during ages 5–15 and is twice as common in girls as in boys.³ Due to the recognition and appropriate treatment of streptococcal pharyngitis, the incidence of both SC and RF has decreased. However, RF is still significantly present in developing nations and still occasionally occurs in the United States.⁴

SC typically occurs 1–6 months after group A streptococcus (GAS) pharyngitis. While the exact pathophysiology is still under investigation, it is proposed that antibodies formed against GAS cross-react with neurons of the basal ganglia, ultimately leading to dopamine dysregulation and chorea.⁵ PANDAS is proposed to have this mechanism as well.

Clinical manifestations of SC are divided into neurologic and psychiatric. Neurologic manifestations include chorea, muscle weakness, and other motor symptoms. Chorea is described as abrupt, involuntary, irregular dance-like movements that flow from one body part to the next randomly. They are nonstereotyped and usually improve during sleep.

The face and extremities are typically affected; however, any muscle can be involved. Usually the chorea is generalized, although hemichorea is not uncommon.⁶ Other motor manifestations include grimacing, dysarthria, difficulty with writing, and hypotonia.⁷ Rarely, these patients become bedridden because of generalized hypotonia, referred to as chorea paralytica.² Psychiatric symptoms include mood lability and obsessive-compulsive disorder (OCD) and usually start 2 to 4 weeks before the movement symptoms.⁷

SC usually self-resolves within 6 months, but can last for as little as a week or as long as 3 years.⁴ Recurrent chorea is a possible long-term effect. Although SC has a relatively benign course, it is important to identify because it is often a presenting sign of RF.⁶ Sometimes carditis silently co-occurs and if not present at the time of presentation, there is a significant chance that carditis will develop later.^{2,6}

Imaging, EEG, and CSF studies, while not helpful in the diagnosis of SC, can help rule out other etiologies. Diagnosis of SC is clinical. Signs include motor impersistence, the inability to sustain muscle contraction, which can be demonstrated with tongue protrusion or testing grip strength (milkmaid's grasp); pronator sign, the pronation of one or both hands when held overhead; choreic hand, holding of the arms outstretched causing hyperextension of the fingers with dorsiflexion of the wrist; and diffuse hypotonia.³ The Jones criteria for RF (major: migratory arthritis, carditis, SC, erythema marginatum, subcutaneous nodules; minor: arthralgia, fever, elevated acute phase reactants, heart block on EKG) should be kept in mind and a thorough cardiac examination should be performed. No laboratory study is diagnostic of SC; however, ASLO and anti-DNAse can aid in the diagnosis. ASLO titers peak around 5 weeks then decline and may not be useful since the presentation of SC is often later. Anti-DNAse peaks around 8 weeks and remains elevated longer, making it more useful.⁸

Treatment is divided into treatment of the underlying infection, prophylaxis, and symptomatic treatment. The efficacy of antibiotic treatment of streptococcal pharyngitis is questionable and usually SC presents well after pharyngitis, but if present a 10-day course of oral penicillin is recommended. While SC is not particularly dangerous, the carditis associated with RF is. Therefore, once RF is diagnosed, prophylactic penicillin is started and maintained depending on the severity of carditis at the time of presentation. Without carditis, prophylaxis is continued for 5 years or until age 18, whichever is longer. With carditis, prophylaxis is continued for 10

years or until age 25, whichever is longer. With severe valvular disease, prophylaxis is lifelong.⁹

Symptomatic treatment of chorea is not necessary unless it is debilitating. In this case, drugs that antagonize dopamine or increase γ -aminobutyric acid (GABA) help to regulate dysfunctional neurons. Dopamine receptor antagonists like haloperidol have been effective. Antiepileptic drugs like valproate, which increase GABA, have been effective. The use of both classes of these drugs is off-label and they have side effects that require monitoring. Recently, tetrabenazine has been approved for the use of hyperkinetic disorders; it also is a dopamine receptor antagonist but does not carry the risk of tardive dyskinesia.

Treatment of the autoimmune component of SC may be helpful and includes corticosteroids, IV immunoglobulins (IVIg), and plasma exchange therapy. Small studies have shown corticosteroids improve chorea and reduce relapses.² IVIg is thought to inactivate autoantibodies, while plasma exchange removes the autoantibodies. A double-blind study compared plasma exchange and IVIg with prednisone and showed no significant difference between groups.² Given the lack of research, significant side effects, and high costs of IVIg and plasma exchange, the use of these 3 drugs should be reserved for patients with significant symptoms that are refractory to the other treatments. Finally, the psychiatric symptoms usually resolve with use of the treatments mentioned but selective serotonin reuptake inhibitors can help obsessive-compulsive disorder symptoms.

Despite the decreased incidence of SC, it is still present and can be the initial sign of RF. The long-term effects of RF are life-threatening, but can be

prevented. Therefore maintaining suspicion of SC in the evaluation of chorea is vital and can be lifesaving.

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