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Case Report

Case Report of a Singular Presentation of Sydenham's Chorea in Acute Rheumatic Fever

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Abstract

The following case report illustrates the significance of patient history and always having a broad differential diagnosis. A four-year-old boy presented in our clinic with the solitary symptom of intermittent shoulder spasms. The patient's mother described frequent episodes of twitching lasting twenty to thirty seconds and occurring ten times per day, which concerned her for a possible tic disorder. During his examination, the patient had a single episode of the reported dystonia, which was felt to be choreoathetoid in nature. We were suspicious of an atypical presentation of acute rheumatic fever (ARF), and subsequent laboratory findings revealed a mildly elevated Anti-streptolys in O Antibody (ASO) titer. Focused history-taking uncovered that the patient had a febrile illness and a self-limiting rash one month prior to his presentation for which he did not seek care. After consultation with a pediatric infectious disease specialist, Group A Beta-Hemolytic *Streptococcus* (GABHS) prophylaxis was started, and he was referred to cardiology. His cardiologist performed an echocardiogram which demonstrated mild mitral regurgitation that was felt to be highly unusual for a child his age. He was diagnosed by his cardiologist with mitral valvulitis, and it was recommended that he continue Bicillin intramuscular injections for *Streptococcal prophylaxis*. The ultimate outcome of this case was the diagnosis of ARF in a patient whose only presentation was Sydenham's chorea. The main take-away from this case was the importance of always considering ARF in a patient who presents with only chorea as his or her primary symptom.

ABBREVIATIONS

ARF: Acute Rheumatic Fever; SC: Sydenham's Chorea; GABHS: Group A Beta-Hemolytic *Streptococcus*; GAS: Group A *Streptococcus*; ASO: Anti-streptolysin O

INTRODUCTION

Acute rheumatic fever (ARF) is a non-suppurative autoimmune inflammatory process resulting from a Group A *Streptococcus* (GAS) pharyngeal infection. The incidence of ARF and rheumatic heart disease are highest in countries with increased rates of poverty. ARF rates have declined markedly in the past 50 years within the United States and Western Europe. However, in developing countries, GAS infections are estimated to affect over 33 million people [1] and are the leading cause of cardiovascular death during the first five decades of life [2,3]. Most cases of ARF occur in children 5 to 15 years of age, but can occur at any age [4].

ARF presents with various manifestations that may include arthralgia, carditis, chorea, subcutaneous nodules, and erythema marginatum. The "Jones Criteria", last updated in 2015, were first published in 1944, and are currently the basis of clinical guidelines for diagnosing ARF. The diagnosis is made with evidence of a preceding GAS infection (positive throat culture for group A beta-hemolytic *Streptococci*, positive rapid *Streptococcal* antigen test, or an elevated or rising anti-*Streptococcal* antibody titer) and the presence of two major or one major and two minor criteria. Refer to Table 1.

In this article, I present a unique case of ARF, in which the solitary physical exam finding was Sydenham's chorea one month following an acute febrile illness.

CASE PRESENTATION

A four-year-old boy was evaluated in our clinic for intermittent shoulder spasms. The patient's mother described his

Table 1: The Jones Criteria.	
Major manifestations (and percent of patients with each):	
1.	Carditis and valvulitisthat is clinical or subclinical – 50 to 70%
2.	Arthritis (usually migratory polyarthritis predominantly involving the large joints) – 35 to 66%
3.	Central nervous system involvement (e.g. Sydenham chorea) – 10 to 30%
4.	Subcutaneous nodules – 0 to 10%
5.	Erythema marginatum – <6%
Minor manifestations:	
1.	Arthralgia
2.	Fever
3.	Elevated acute phase reactants (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP])
4.	Prolonged PR interval on electrocardiogram

symptoms as episodes of right shoulder twitching that began two weeks prior to his doctor's visit. The episodes lasted for twenty to thirty seconds, occurred about ten times per day, and always spontaneously resolved. The patient appeared to have no control over his movements and occasionally complained of some pain during the episodes. The patient's mother denied that he had any other symptoms including fever, chills, night sweats, cough, rhinorrhea, arthralgia, vomiting, or sore throat. She denied any recent upper respiratory infections or sore throat. Social history was unremarkable. The patient was a healthy boy and lived with his mother, father, and younger brother. There was a family history of obsessive compulsive disorder and attention deficit hyperactivity disorder, but no history of diabetes, coronary artery disease, or seizures.

On physical examination, the patient was alert and engaged, in no apparent distress, and did not appear toxic. His body temperature was 36.5°C, pulses were symmetrical, blood pressure was 93/59 mmHg, and heart rate 105 beats/min. He had a regular heart rate and rhythm, and no systolic or diastolic murmurs were appreciated. Cranial nerves II through XII were grossly intact. The remainder of his exam was unremarkable. During the examination, the patient had a single episode which consisted of him dropping the right shoulder and forcefully rolling the shoulder forward. It was spontaneous, brief, rhythmic, forceful, and slow. A complete blood count and basic metabolic panel were obtained and were within normal limits, but an anti-streptolysin O antibody titer was drawn which was later reported to be mildly elevated.

We referred the patient to neurology, but upon receiving the results of his ASO titer, we instructed the patient and his mother to return to clinic for follow-up to screen for symptoms of ARF. After some focused questioning, the patient's mother reported that he had exhibited a recent decrease in energy, and she recalled that a month prior to his dystonic symptoms, he had a red bumpy rash that spontaneously resolved, and thus, prompted no further medical attention. In light of his new onset choreoathetoid movements and an elevated ASO titer, his case was discussed with an infectious disease specialist, and GABHS prophylaxis was started. He was referred to a cardiologist for further evaluation to rule out any evidence of rheumatic heart disease. In the meantime, we obtained an electrocardiogram which revealed no cardiomegaly or ST segment elevations, but did show a mildly prolonged PR interval for the patient's age (170 milliseconds).

The patient was evaluated by a cardiologist three weeks later. The frequency of episodes of his irregular right shoulder movements decreased considerably following his first treatment with Bicillin. His cardiologist obtained anti-DNAse B, anti-streptokinase, and anti-hyaluronidase titers, a CRP, and an ESR. Results of these tests revealed elevated streptococcal titers, but normal inflammatory markers. His physical exam was notable for a Grade 1 musical still's murmur, but no evidence of a mitral regurgitation murmur. A repeat 12-lead electrocardiogram was read as normal. The cardiologist performed an echocardiogram that demonstrated mild hemodynamically insignificant mitral regurgitation which he felt was highly unusual for a child of that age. The patient was subsequently diagnosed with mitral valvulitis and recommended to continue Bicillin intramuscular injections every 28 days as per the standard treatment for Streptococcal prophylaxis to avoid a recurrence of rheumatic fever. A follow-up echocardiogram performed one month later revealed a resolution of the previously seen mitral regurgitation. His cardiologist concluded that the patient had suffered from acute rheumatic fever one month prior to his first presentation in our clinic.

DISCUSSION

In the case above, the patient presented with what was felt by his mother to be a motor tic disorder, but due to the choreoathetoid nature of his dystonic motions, we considered an atypical presentation of acute rheumatic fever (ARF). The patient's mother witnessed only the unusual movements of his right shoulder, which began spontaneously about one month following a self-limiting rash. She did not consider that his symptoms may have been related to a previous infection. Nonetheless, Sydenham's Chorea (SC) is one of the major clinical manifestations of ARF and may be the only manifestation of ARF presenting as late as six months after the initiating *Streptococcal pharyngitis* [5,6]. SC is the most common form of acquired chorea in childhood and is a movement disorder characterized by involuntary brief, random and irregular movements of the limbs and face often accompanied by emotional liability and hypotonia. It is not surprising that our patient's mother was initially concerned with Tourette's syndrome because mild cases

of SC without other manifestations of rheumatic fever are often mistakenly ascribed by parents and teachers to behavioral or emotional disorders, motor tics, restlessness, or clumsiness [7].

The pathophysiology of SC in ARF is believed to stem from the process of molecular mimicry occurring specifically within the basal ganglia. The basal ganglia is one of the primary cortical targets of post-streptococcal immune responses as evidenced by clinical findings and data from magnetic resonance imaging suggesting that the basal ganglia is attacked by antibodies which contribute to the pathology in Sydenham's chorea [8,9].

By the mechanism of molecular mimicry, antibodies directed against part of the group A *Streptococcus* bacterium cross-react with host antigens. In ARF, antibodies produced by the infected host target N-acetyl-beta-D-glucosamine (GlcNAc), which is the immuno dominant epitope of the group A carbohydrate (GAC). Antibodies specific for the GAC can recognize a variety of host tissues and demonstrate cross-reactivity with a variety of mammalian proteins [10-12]. In SC, membrane antibodies specific for GlcNAc cross-react with mammalian gangliosides [13], which are a diverse family of glycolipids that show specific developmental and differential expression within the brain and contribute to multiple functions mediated at the cell surface including signal transduction [14,15]. The ganglioside targeted in SC is lysoganglioside GM1, a CNS ganglioside shown to influence neuronal signal transduction [14,16]. It is unclear how antibodies mediate neurologic dysfunction in SC; however, clinical data suggests that antibodies in SC promote signal transduction that may lead to the release of excitatory neurotransmitters.

CONCLUSION

Despite the initial differential diagnosis, some clinical suspicion and a more thorough history proved invaluable in determining the ultimate diagnosis for our patient and getting him the most appropriate therapy. The main lesson learned in this case is that it is important to always consider acute rheumatic fever in a patient who presents with only chorea as his or her primary symptom. When chorea is identified, it is important to further question the patient's remote history to uncover a previous febrile illness, sore throat, or a rash consistent with scarlet fever. Once a thorough history has been obtained, *Streptococcal serologies* can be helpful in confirming a previous diagnosis of Group A *Streptococcus* infection.

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