

# Acute Rheumatic Fever Presenting with Sydenham's Chorea

CLF *Woo*, KT *Liu*, BWY *Young*

## Abstract

Acute onset of abnormal involuntary movements in children is an unusual clinical encounter in our daily practice. The differential diagnoses could be quite diversified and often pose management difficulties. Sydenham's chorea is still a common cause in developing countries and should be considered in the differential diagnosis. Sydenham's chorea is a major clinical manifestation in acute rheumatic fever. The other major clinical manifestations are migratory polyarthritis, carditis, subcutaneous nodules and erythema marginatum according to Jones Criteria. The incidence of Sydenham's chorea in acute rheumatic fever varies across the decades and populations studied. From 1920 to 1950, more than half of the patients with rheumatic fever had Sydenham's chorea. The incidence decreased to less than five percent in more recent studies. The often-long latent period between Group A beta-haemolytic streptococcal infection and the onset of chorea makes it an uncommon initial presentation in acute rheumatic fever. We report the clinical findings, investigations and the course of clinical development of a nine-year-old girl, who presented with acute onset of abnormal involuntary movements for a history of three days before her admission. Sydenham's chorea and the treatment of rheumatic fever are reviewed.

## Key words

Acute rheumatic fever; Sydenham's chorea

## Introduction

Acute rheumatic fever is a multisystem inflammatory disease which occurs as delayed sequelae to group A streptococcal pharyngitis. The important clinical manifestations are migratory polyarthritis, carditis, chorea, subcutaneous nodules and erythema marginatum occurring in various combinations. Sydenham's chorea, once considered as a self-limiting condition, is now felt to need more aggressive treatment because it can cause great

functional impairment to a patient. A nine-year-old girl presenting with chorea and subsequently diagnosed to have acute rheumatic fever is reported. Sydenham's chorea and the treatment of acute rheumatic fever will be discussed.

## Case Report

The patient was a nine-year-old girl with good past health. She presented with involuntary movements of her body for three days. The involuntary movements involved her limbs, fingers, toes and facial muscles. She had slowing of speech and verbal response. The involuntary movements were severe enough to impair her daily activities such as writing, brushing teeth and holding a bowl. She also had mild arthralgia of her knees for few days. History revealed she had an episode of fever and sore throat one month ago.

Physical examination showed that she was afebrile, alert and oriented. A faint non-specific macular rash was found over her back. She had dysarthria but no dysphonia. There was chorea involving her four limbs with writhing

Department of Paediatrics and Adolescent Medicine, Pamela Youde Nethersole Eastern Hospital, 3 Lok Man Road, Chaiwan, Hong Kong, China

CLF *Woo* (胡立輝) MBBS(HK), MRCP(UK), FHKAM(Paed)  
KT *Liu* (廖鑑添) MBCh(Ire), MRCP(Ire), FHKAM(Paed)  
BWY *Young* (楊允賢) MBBS(HK), FHKAM(Paed), FRCP  
(Edinburg, Glasgow, London)

Correspondence to: Dr CLF *Woo*

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movements of her fingers. Bilateral facial twitching and lips smacking were also observed. The muscle tone, deep tendon reflexes and muscle power were all symmetrical and normal. No cerebellar ataxia was demonstrated. The gait was unsteady. Cardiovascular examination showed normal heart sounds with no heart murmur. Chest was clear. The abdomen was soft with no organomegaly.

Blood test showed normal electrolytes, calcium and complete blood picture. Electroencephalogram showed episodes of slow waves over bilateral temporal and parietal regions with no epileptic focus. CAT scan of the brain was normal.

Her condition deteriorated gradually over the next four days. She also became depressed and lost her appetite as she had difficulty with mastication.

Reassessment on Day 4 of hospitalisation showed that she was alert and oriented. There was a macular rash with erythematous margin and pale centre on the upper and lower limbs, compatible with erythema marginatum. She had no subcutaneous nodule or joint swelling. She could only speak slowly. Due to the chorea movements, she failed the finger-to-nose test and heel-to-shin test. There was also dysdiadochokinesia. She was so unsteady that she could not walk unassisted. The muscle tone was decreased, however her deep tendon reflexes were normal and symmetrical. On cardiovascular examination, her pulse was regular at 82 per minute. Apex was not displaced. Heart sounds were normal but a grade 2/6 ejection systolic murmur could be heard over the left upper sternal border without radiation. The chest was clear. The liver and spleen were not palpable.

Anti-streptolysin O-titre (ASOT) was subsequently shown to be elevated at 600 IU. The erythrocyte sedimentation rate (ESR) was 60 mm/hr. The throat swab showed negative growth for streptococcus. Electrocardiogram showed prolonged PR interval (201 ms). No ST change was observed.

The clinical and laboratory findings were compatible with the diagnosis of acute rheumatic fever, i.e. Sydenham's chorea, erythema marginatum, raised ASOT and ESR and prolonged PR interval on ECG.

The heart murmur became pansystolic on Day 6 of hospitalisation. Echocardiogram demonstrated the presence of rheumatic valvulitis. The anterior mitral valve leaflet was thickened. The left atrium was dilated and there was a mild to moderate degree of mitral incompetence. No pericardial effusion was detected.

Treatment was started on day 5 after admission with oral penicillin V 250 mg QID and aspirin (80 mg/kg/Day). Oral

haloperidol 0.5 mg daily was started for her chorea and was gradually increased to 0.5 mg BD. Clinical improvement was observed two days after the commencement of haloperidol and the patient was fully functioning in her daily activity six days later.

Serial ESRs were taken to monitor the disease activity. It dropped from 60 mm/hr on presentation to 42 mm/hr on Day 9 and 26 mm/hr on day 13 of hospitalisation.

She was discharged on Day 16 with aspirin, haloperidol and ranitidine. 4-weekly benzathine penicillin 1.2 MU IMI was also started after a 10-day course of Penicillin V. Upon discharge, she had no chorea. Her mood was back to her premorbid cheerful state.

During subsequent follow-up, there was no recurrence of chorea and haloperidol was tailed down and given for six weeks in total. She still has on and off erythema marginatum. The ESR was back to normal (9 mm/hr) two months from the onset of illness. Aspirin was then stopped.

## Discussion

There had been a decline in the incidence of rheumatic fever in developed countries between 1950 and 1980.<sup>1</sup> It was believed to be due to improvement in living standard, overall socio-economic development and the wide availability of penicillin. Nevertheless, rheumatic fever is still the major health problem in developing countries, where it and its sequelae account for 25-40% of all cardiac admissions.<sup>2</sup>

The diagnosis of rheumatic fever is based on the Jones criteria<sup>3</sup> (Table 1). Arthritis is the most common manifestation, present in 80% of patients. It is described as painful, migratory and transient. Knees and ankles are more frequently affected. Carditis occurs in 40-75% of patients in the first 3 weeks of the illness. Death may occur in the acute phase.<sup>4</sup> Erythema marginatum and subcutaneous nodules are rare, less than 10% of patients are affected.

Sydenham's chorea is also a rare presentation, affecting less than 5% of patients.<sup>4</sup> The disease was first named by Thomas Sydenham in 1686 as 'St. Vitus Dance' to differentiate it from dancing mania, a practice seen in the religious ceremonies in the older days by those who danced to exorcise prevalent epidemic illness. At that time, he attributed the illness to physical trauma and emotional shock. The association between Sydenham's chorea and arthritis was described by Stroll in 1780.<sup>5</sup> Roger better established the relationship in his articles in 1966 and 1968.<sup>6</sup> This was the prevalent concept in North America until the 1900s. In

**Table 1** Guidelines for the diagnosis of initial attack of rheumatic fever (Jones Criteria)

Major manifestation	Minor manifestation
Carditis	Fever
Migratory polyarthritits	Arthralgia
Sydenham's chorea	Elevated acute phase reactants (ESR, CRP)
Subcutaneous nodules	Prolonged PR interval on ECG
Erythema marginatum	

Diagnosis is established if two major or one major + two minor plus

- Supporting evidence of a recent group A streptococcal infection (positive throat culture or rapid antigen test, elevated or increasing streptococcal antibody test)

1950, the occurrence of an antecedent group A beta-streptococcal infection was confirmed in patients with Sydenham's chorea and rheumatic fever.<sup>7</sup>

The proportion of Sydenham's chorea occurring in patients with rheumatic fever altered across the decades and it also varied among different populations studied. From 1920 to 1950, more than half of the patients with rheumatic fever had Sydenham's chorea. The incidence decreased to less than 5% in more recent studies.<sup>4</sup> Such a decrease in the incidence of Sydenham's chorea might represent the involvement of specific choreogenic streptococcal strains in a particular population or the existence of other nonstreptococcal stimuli that were capable of contributing to the pathogenesis of Sydenham's chorea.

The main feature in Sydenham's chorea is involuntary movements. These can be generalised or unilateral. These movements occur at rest, may start suddenly or gradually, and are exacerbated by stress. They disappear during sleep. Usually the patient has abnormal neurological signs with hypotonia and motor restlessness which can lead to coordination problems, gait disturbances and speech impairment. As a result, the activities of daily living can be severely disrupted.

The differential diagnoses of Sydenham's chorea include atypical seizures, tics disorders, degenerative or neurometabolic causes like Huntington disease, Hallervorden-Spatz disease, Wilson's disease, autoimmune diseases like systemic lupus erythematosus, drugs (phenytoin, aminotriptyline), hormonal-induced causes like oral contraceptive pills, pregnancy/chorea gravidum, endocrine causes like hypoparathyroidism and hyperthyroidism. It can also occur in post-cardiac surgery and post-circulatory arrest.

Patients with Sydenham's chorea can have psychological and psychiatric manifestations such as depression, anxiety, personality changes, emotional lability, obsessive-

compulsive disorder (OCD), tics and attention deficit disorder.<sup>8</sup> These are believed to be secondary to the motor difficulties, although sometimes these symptoms can precede the onset of chorea. Whether the psychiatric symptoms are due to the motor disabilities or as the integral part of the neurological disorder remains obscured. Certainly, in our patient, she had a depressive mood which disappeared when her chorea was controlled with haloperidol.

The majority of patients are between 5-15 years of age, with girls predominating over the age of 11 years, thereby suggesting important hormonal influences. The duration of Sydenham's chorea can last for 4-6 months, however, it can range from as little as one week up to over 2 years.<sup>8</sup> Although most patients recover completely, some may have persistent choreiform movements especially when they are fatigue or under stress. In the setting where penicillin is not available or ineffective, recurrence of Group A beta-haemolytic streptococcal pharyngitis is common, a higher proportion of patients would have relapse. Death is rare as a result of the chorea itself.

Genetic susceptibility probably plays an important role in the pathogenesis of Sydenham's chorea. Individuals developing Sydenham's chorea have an increased frequency of expression of the B-cell alloantigen D8/17.<sup>9</sup> It is thought that M-type specific streptococcal infection in these individuals can result in the production of antineuronal antibodies, which give rise to chorea and psychiatric disturbances.

It is believed that Sydenham's chorea occurs secondary to an autoimmune reaction towards the host's central nervous system, particularly the basal ganglia and its circuits. However, there are few descriptions describing the anatomical pathology in cases of Sydenham's chorea because of the relatively low mortality rate in these patients. Previous work in the 1920s reported neuronal degeneration,

vascular inflammation, and perivascular infiltration within the corpus striatum. Studies during 1940s and 1950s reported diffuse non-specific changes throughout the brain, especially at the frontoparietal cortex, caudate, and putamen. Magnetic Resonance Imagings (MRI) are usually normal, and fluorodeoxyglucose Positron Emission Tomography (PET) scanning may show striatal hypermetabolism.

Neurochemistry study showed a decreased level of gamma aminobutyric acid (GABA) in the basal ganglia circuitry. This can cause a release from inhibition of the external pallidum, activation of thalamocortical neurons, and the projections of the thalamocortical neurons to the motor cortex, facilitating abnormal movements and producing chorea.

Sera from patients with Sydenham's chorea were found to have antibodies, which were immunoreactive to neurons from caudate, thalamus, and subthalamic nucleus. Elevated levels of antineuronal antibodies have also been observed in patients with tics and OCD. These have led to the concept of 'Paediatric Autoimmune Neuropsychiatric Disorder associated with Streptococcal infections' (PANDAS) in recent years.<sup>10</sup>

If the symptoms are severe and cause dysfunction in activities of daily living, treatment should be considered. There are several pharmacological agents which are useful in the treatment of Sydenham's chorea. These include neuroleptics (haloperidol, trifluoperazine, chlorpromazine and pimozide), levodopa, hydroxyzine, phenobarbital, steroids, carbamazepine and valproic acid. Haloperidol acts by blocking the dopamine receptors and it has been found to decrease the severity of choreic movements. Most patients respond to an initial dose of 0.5-1 mg/day with increments of 0.5 mg-1 mg/day every 3 days up to a maximum of 5 mg/day. In our patient, she responded to the haloperidol quite quickly and there were no observable side-effects.

Recently, valproic acid has been advocated to be effective in treating Sydenham's chorea. Its action is by enhancing the activity of GABA, an inhibitory neurotransmitter of the striatonigral and striatopallidal circuit. Response can be observed within 10 days, with a dose of between 15-20 mg/kg/day. Choreic movements may also be treated with carbamazepine, possibly through its cholinergic action in the striatum. It increases the acetylcholine level, inducing equilibrium between the dopaminergic and cholinergic systems.

Immunological therapy with steroids or intravenous immunoglobulin had been tried to treat Sydenham's chorea

but the response was not satisfactory. Further controlled studies are needed to investigate their efficacy.

The outcome of acute attack of rheumatic fever varies from complete recovery to death from heart failure. Recurrence of rheumatic fever tends to occur in the first few years after the acute attack and it is most common in the setting of pre-existing heart disease.

Patients with acute rheumatic fever should have bed rest in the acute phase of carditis. Penicillin for 10 days is the drug of choice to eradicate the streptococcus.<sup>11</sup> Salicylates remain the first-line agent in the treatment of carditis and usually brings about a dramatic improvement. The dose should be 80-100 mg/kg/day in children. Usually a course of 4-6 weeks of treatment is adequate in cases of mild disease.<sup>12</sup> Steroids might be reserved for those with severe carditis. Anti-heart failure treatment including diuretics and digoxin might be required in cases of severe carditis.

Prevention of rheumatic fever is very important. It can be divided into primary and secondary prevention. The goal of primary prevention relies on the correct diagnosis of group A streptococcal infection and effective treatment for eradicating the organisms with appropriate antimicrobial agent. Group A beta-haemolytic streptococcus remains exquisitely sensitive to penicillin, which is still the antibiotic of first choice. Erythromycin or cephalosporin can be considered when the patient is allergic to penicillin (Table 2).

For secondary prevention, prolonged penicillin prophylaxis of previously affected individuals with intramuscular benzathine benzylpenicillin is the most secure method of preventing recurrence. Controversies still exist on the dosage and frequency of administration. The 4-weekly regimen is generally used.<sup>13</sup> If the patient is unable to tolerate intramuscular injection, oral prophylaxis can be used. A daily dose of phenoxymethylpenicillin or sulfadiazine should be employed. In cases of penicillin and sulfonamides allergy, erythromycin may be used instead (Table 3).<sup>13</sup>

There is no consensus on the duration of antibiotic prophylaxis. In developed countries where the incidence of rheumatic fever is low, life-long prophylaxis is probably not necessary. It is reasonable to stop prophylaxis in patients who have reached their early 20s, more than 5 years past their last attack, and are free of rheumatic heart disease. The American Heart Association recommends prophylaxis to be continued at least 10 years after the last episode of rheumatic fever or until the patients are well into adulthood.<sup>13</sup>

**Table 2** Primary prevention of rheumatic fever (treatment of streptococcal tonsillopharyngitis)

Agent	Dosage	Mode	Duration
Benzathine benzylpenicillin	600 000 units for patients $\leq 27$ Kg 1 200 000 units for patients $> 27$ Kg	Intramuscular	Once
or Phenoxymethylpenicillin (Penicillin V)	Children: 250 mg 2-3 times daily Adolescents and adults: 500 mg 2-3 times daily	Oral	10 days
For individual allergic to penicillin			
Erythromycin			
Estolate	20-40 mg/Kg/day 2-4 times daily (max 1 g/day)	Oral	10 days
Ethylsuccinate	40 mg/Kg/day 2-4 times daily (max 1 g/day)	Oral	10 days

**Table 3** Secondary prevention of rheumatic fever (prevention of recurrent attacks)

Agent	Dosage	Route
Benzathine benzylpenicillin	1 200 000 units every 4 weeks*	Intramuscular
or Phenoxymethylpenicillin (Penicillin V)	250 mg twice daily	Oral
or Sulfadiazine	0.5 g once daily $\leq 27$ Kg 1.0 g once daily $> 27$ Kg	Oral
For individual allergic to penicillin and sulfadiazine		
Erythromycin	250 mg twice daily	Oral

\* In high-risk situations, administration every 3 weeks is justified and recommended.

## Conclusion

Sydenham's chorea is a rare presentation of acute rheumatic fever. Treatment with haloperidol may be useful for those having difficulty with their activities of daily living. Long term follow-up and antibiotic prophylaxis are required to prevent recurrence of rheumatic fever.

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