

Cerebral Vasculitis in a Case of Sydenham's Chorea

ABSTRACT

A 10-year-old girl with acute-onset hemichorea had multiple areas of abnormal signal seen on magnetic resonance imaging of the brain, associated with middle and anterior cerebral artery vasculitis seen on cerebral angiography. Her serology and clinical course were supportive of the diagnosis of Sydenham's chorea. Other causes of cerebral vasculitis were excluded. Follow-up studies revealed resolution of changes seen on magnetic resonance imaging and partial resolution of angiographic abnormalities. This is the first report of abnormal cerebral angiography in Sydenham's chorea. (*J Child Neurol* 1999;14:815–818).

Case History

A 10-year-old Caucasian girl presented to her pediatrician with uncontrollable writhing movements of the right arm and leg. These commenced suddenly and worsened progressively over 6 days, resulting in difficulty walking. Twitching of the right eye, movements of the peri-oral musculature, and dysarthria then developed. There was no dysphasia or dysphagia.

The movements disappeared completely during sleep and she could voluntarily suppress them briefly. They increased with anxiety or embarrassment. Concomitant with the development of chorea personality change was apparent, with the patient's usual placidity being replaced by emotional lability and agitation.

Two weeks prior to presentation she had pharyngitis associated with cough and rhinorrhea. She had no joint pain, rash, or fever. She had had no other illnesses for more than 1 year. There was no relevant past or family history.

On admission chorea of the right side of the face, right arm, and right leg was present. The patient was generally hypotonic but power, reflexes, and sensation were normal, although she had marked motor impersistence. Coordination on the right side was limited by her chorea. Cardiovascular examination revealed a murmur at the upper left sternal border. Her examination was otherwise normal.

The provisional diagnosis was Sydenham's chorea, and she was started on oral penicillin.

Baseline complete blood count, erythrocyte sedimentation rate, and C-reactive protein level were normal. A throat swab taken on admission was negative, while one taken earlier by her pediatrician grew *Streptococcus oralis* (*Streptococcus viridans*). Initial streptococcal serology revealed an anti-streptolysin O titer (ASOT) of less than 200 IU/L, while a repeat test 5 days later demonstrated a level of 587 (normal, less than 200 IU/L). Assays for anti-DNase B antibodies were repeatedly normal, with an initial level of 120 IU/L, and a level of 40 IU/L on repeat testing (normal, less than 170 IU/L). Negative investigations included serum copper and ceruloplasmin, anti-nuclear antibodies, complement, auto-antibody screening, cerebrospinal fluid microscopy and biochemistry, and urine metabolic screening.

An electrocardiogram and chest radiograph were normal. A cardiologist opinion was sought. A Still's murmur was heard clinically and echocardiography was normal.

On magnetic resonance imaging (MRI) of the brain soon after admission, two areas of high-intensity altered signal (measuring 5 × 5 mm) were seen in the posterior limb of the left internal capsule and the left basal ganglia, on the T₂-weighted sequences (Figure 1). The basal ganglia lesion enhanced with gadolinium contrast. There was no edema or mass effect. No other abnormalities were apparent.

On repeat MRI plus magnetic resonance angiography (MRA) 7 days later, the basal ganglia and internal capsule lesions were less apparent on the T₂- and flair-weighted sequences. Several new small lesions were seen in the left corona radiata extending to the cortex at the level of the parieto-frontal junction (Figure 2). On MRA the intima of the left middle cerebral artery was slightly irregular, although there was no flow void. These lesions were believed to be either ischemic or vasculitic. A cerebral angiogram was performed to clarify this issue. It revealed beading of the distal left middle and proximal left anterior cerebral arteries, consistent with vasculitis (Figure 3).

Serum and cerebrospinal fluid lactate, blood coagulation, and immunoglobulin profiles, and assays for the lupus anticoagulant, anti-neutrophil cytoplasmic antibodies (ANCA), antibodies to proteins C and S, and blood and cerebrospinal fluid serology for *Mycoplasma pneumoniae* were normal.

Marked lability of mood was seen, with uncharacteristic periods of excessive tearfulness and tantrums. Following angiography the patient commenced low-dose aspirin and haloperidol (0.25 mg orally twice per day treatment), with a rapid improvement in her chorea. Within 2 weeks she could write with her right hand. She continued on prophylactic penicillin after discharge.

Two months later the patient's chorea had completely resolved, as had her emotional lability. On repeat cerebral angiography the lesions in the left middle cerebral artery had disappeared, with minimal narrowing of the left anterior cerebral artery persisting, but causing no demonstrable decrease in intracranial blood flow (Figure 4). All other vessels were normal.

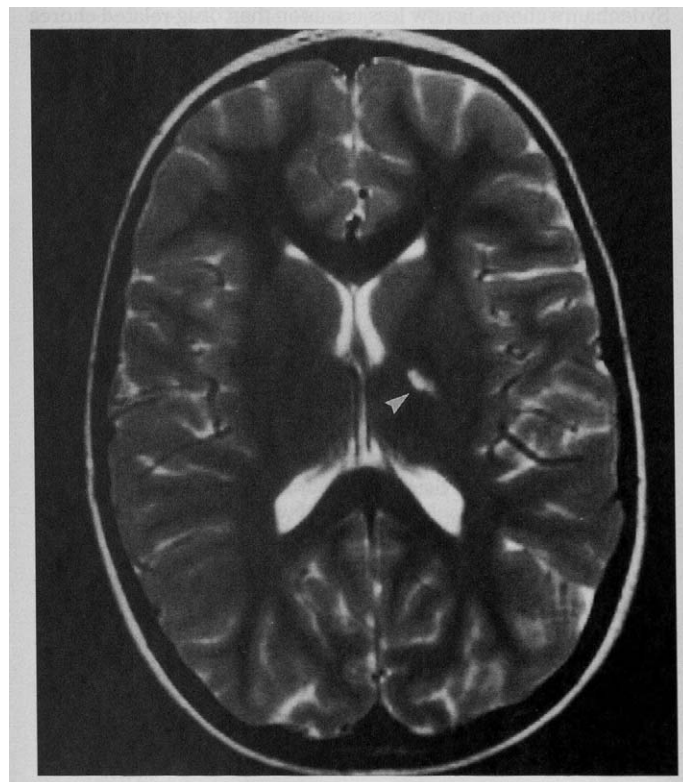


Figure 1. T₂-weighted brain MRI showing a lesion of high signal intensity in the posterior limb of the right internal capsule (arrow).

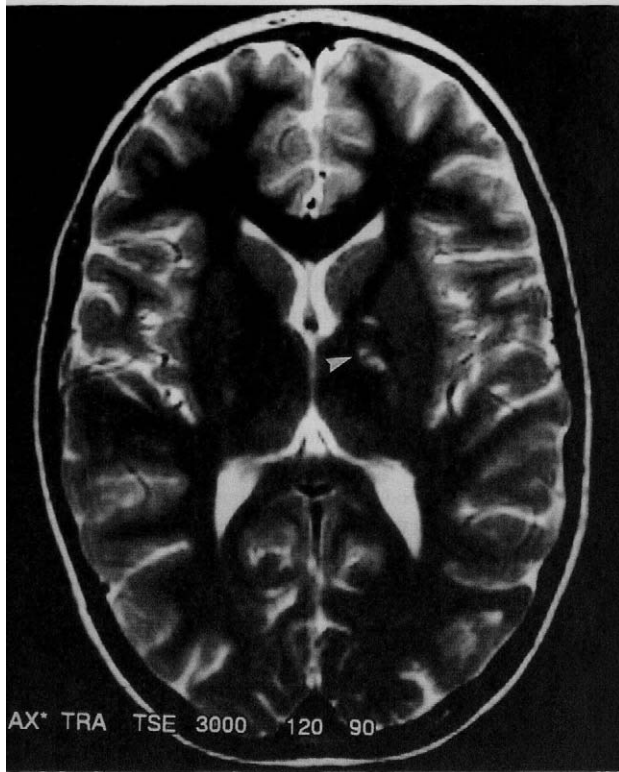


Figure 2. Repeat brain MRI 1 week after initial scan, with additional lesions in the genu of the internal capsule and a new lesion in the globus pallidus (lower lesion below tip of arrowhead).

Discussion

Sydenham's chorea is now less common than drug-related chorea in the Western world.¹ The decline in incidence of rheumatic fever and rheumatic heart disease in recent decades,^{2,3} has been attributed to better standards of healthcare, increased antibiotic use, lower virulence of streptococcal strains, and possibly improved host resistance.⁴

Most cases of Sydenham's chorea are preceded by a streptococcal infection (frequently subclinical) or by other manifestations of rheumatic fever. Approximately 35% of patients with rheumatic fever experience chorea, which is the sole manifestation in as many as 20% of cases.⁵ The combination of chorea and carditis is seen in only 15% of all patients.⁶ When present carditis is frequently subclinical.⁵

Sydenham's chorea is a clinical diagnosis with support derived from laboratory investigations and imaging. The 1992 update of the revised Jones criteria listed isolated chorea as sufficient cause for diagnosis of rheumatic fever, if other causes of chorea have been excluded.⁷ Serologic confirmation of recent streptococcal infection is not required. Because the development of chorea is late, occurring weeks to months after the streptococcal infection, negative serology occurs in 25% of patients and does not exclude the diagnosis. Serologic yield is markedly increased by performing more than one antibody titer.⁸ The antiDNase B could be the most reliable serologic investigation, remaining elevated for longer periods than other markers.⁹

Unilateral movements are not unusual in Sydenham's chorea, and true hemichorea, as seen in this girl, can occur in up to 19%



Figure 3. Initial cerebral angiogram with beading and intimal irregularity evident in the proximal middle cerebral artery (arrowhead).

of cases.¹⁰ The patient's striking motor imperistence was typical. Muscle strength is usually not affected, although severe weakness with associated hypotonia ("chorea mallis") is seen in some patients.

Symptoms are exaggerated by anxiety and fatigue, but subside during sleep. This fact can cause confusion as the disappearance of chorea in sleep can be seen as an indication of hysteria. Psychiatric symptomatology is a common feature of Sydenham's chorea and can cause significant delay in diagnosis. That emotional lability and anxiety occurred in the majority of children with Sydenham's chorea was recognized as early as 1912.¹¹ Children with this disorder have been described as "an emotionally quite sick group, ranging in degree ... from severely neurotic to overtly psychotic."¹² A recent series of 11 children all exhibited obsessive-compulsive symptomatology and emotional lability.¹³ There was no relationship between the severity of chorea and the degree of psychiatric disturbance.

Sydenham's chorea originally was believed to be secondary to basal ganglia disease resulting from embolism of valvular vegetations. In the late 19th century the role of streptococcal infection was recognized, and the presence of inflammatory vasculitis and vessel thrombosis documented on neuropathologic studies.¹⁴⁻¹⁶ In more recent studies nonspecific neuronal swelling and degeneration, arteritis, and petechial hemorrhages have been found inconsistently in the brain without specific localization to the basal ganglia. In chronic cases extensive perivascular lymphocytic infiltration has been described.^{17,18} Identical changes have been found in the brains of patients with rheumatic heart disease without chorea.

The immunopathogenetic mechanism in Sydenham's chorea is thought to be cross-reaction of IgG antibodies between streptococcal M-type specific antigens and antigens in the neuronal cytoplasm of the caudate and subthalamic nuclei.¹⁹ The resultant



Figure 4. Follow-up angiography 2 months later. There has been virtual resolution of the vasculitic changes.

focal blood-brain barrier dysfunction and edema is seen on imaging as areas of altered signal. Computed tomography (CT) can demonstrate areas of low attenuation in the striatum, without mass effect or contrast enhancement.²⁰ MRI shows increased signal intensity on T₂-weighted images with involvement primarily of the putamen but also possibly of the globus pallidus and heads of the caudate nuclei. Changes can be uni- or bilateral.²¹ On volumetric analysis there is a selective increase in basal ganglia volume in patients with Sydenham's chorea, suggesting localized inflammation.²² When MRI is repeated, partial or, more commonly, complete resolution of these changes is often found. In one case, however, serial MRIs showed persistent high-intensity changes associated with the development of cystic changes in the basal ganglia, first seen 22 months after the development of symptoms.²³ Single photon emission computed tomographic (SPECT) scans could be normal or could show increased uptake in the basal ganglia.²⁴

Differential diagnosis for isolated chorea in an adolescent girl includes moyamoya disease, Wilson's disease, systemic lupus erythematosus, and other vasculitides, and side effects of various medications, including the oral contraceptive pill. Known causes of chorea and cerebral vasculitis were excluded prior to our conclusion that this girl had Sydenham's chorea. The absence of a clear history of antecedent pharyngitis was outweighed by her positive serology for recent streptococcal infection. As detailed above, normal cardiologic examination and echocardiography are seen in the majority of cases at initial presentation. Other major criteria for rheumatic fever, such as erythema marginatum, migratory polyarthritides, and raised acute phase reactants are usually absent. While our patient's symptoms developed rather rapidly, acute onset of chorea is by no means unknown. Pure hemichorea is seen in a significant proportion of patients with this disease. Her psychiatric symptomatology also was supportive of our diagnosis.

Findings on cerebral angiography have not been reported previously in Sydenham's chorea. In this case the first suspicion of large-vessel involvement arose on the basis of the findings on MRA. Middle cerebral artery vasculitis, as well as involvement of the anterior cerebral artery, was confirmed on cerebral angiography.

We conclude that large-vessel vasculitis can be a pathologic finding in Sydenham's chorea and suggest that cerebral angiography could be of use in investigation of isolated chorea, not only to exclude moyamoya disease, but to aid in delineation of the underlying pathology. The choice between MRA and cerebral angiography is best made with consideration of the relative risks and potential benefits in individual cases. Further investigation into the pathogenesis of this rare disease could aid in determination of the mechanism of involvement of the major cerebral vessels.

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Postictal Psychosis in a Child

ABSTRACT

Postictal psychoses are brief psychotic episodes that usually occur after poorly controlled partial complex seizure clusters. The psychosis commonly appears following a lucid interval, ranging from a few hours to days after seizure termination. An underlying structural brain abnormality is common and usually involves the temporal lobe. Postictal psychosis, while well known in adults, has not been described previously in children. We describe a 9-year-old boy with right hemiparesis due to a neonatal stroke, who developed a postictal schizophrenia-like psychosis following status epilepticus. Electroencephalography showed left-sided slowing. A brain computed tomographic scan and magnetic resonance imaging revealed left hemisphere hypoplasia. A ^{99m}Tc -ECD single photon emission computed tomographic scan of the brain revealed decreased left-hemisphere perfusion, most pronounced to the medial temporal lobe. The psychosis resolved gradually over 7 days without antipsychotic therapy. To the best of our knowledge, this is the first description of postictal psychosis in a child. (*J Child Neurol* 1999; 14:818-819).

The association between epilepsy and psychiatric disorders, despite being quite common,¹⁻³ is still highly controversial.⁴ A schizophrenia-like psychosis usually evolves after long-standing, poorly controlled complex partial seizures.³⁻⁵ Primary pathologic lesions, either confined to the temporal lobe³⁻⁶ or generalized,⁷ might constitute the underlying mechanism for both the psychosis and the seizures.⁴

The psychosis can be defined as ictal, postictal, or interictal according to the temporal relation to the seizures.⁴ Schizophrenia-like psychosis usually develops in adults whose seizures started in

childhood, persisted during puberty, and were poorly controlled for many years.

We describe a 9-year-old child who developed a psychosis after his second seizure. To the best of our knowledge this is the first report of pediatric postictal psychosis.

Case Report

A 9-year-old boy was admitted for status epilepticus. He was the term, large for gestational age (birthweight, 4200 grams) product of a pregnancy complicated by maternal diabetes mellitus. He underwent blood dilution for polycythemia. Right hemiplegia was diagnosed during the first year of life and was attributed to a neonatal stroke. A brain computed tomographic (CT) scan performed at the age of 2 years showed an enlarged left ventricle and left hemisphere atrophy. He was treated at a child development center for mild motor and speech delay, but he had no seizure history until the age of 9 years, when he was hospitalized for a prolonged left-sided complex partial seizure followed by Todd's paralysis on the right side. The seizure was controlled with phenytoin. An electroencephalogram (EEG) showed slow delta activity in the left hemisphere, most pronounced in the occipital area. A brain CT performed at that time revealed enlargement of the left ventricle, as well as atrophy of the left hemisphere. After the patient's discharge, his parents decreased the phenytoin dosage, resulting in a subtherapeutic drug level. Seizures did not recur until his current hospitalization.

At the age of 9 years, he was admitted for status epilepticus that was controlled only after treatment with intravenous diazepam at 0.1 mg/kg, phenytoin at 20 mg/kg, and midazolam at 0.05 mg/kg. After the cessation of the convulsions the patient remained agitated and confused. He did not recognize his caregivers and was disoriented to time and place. Twenty-four hours later an acute psychotic state was diagnosed. He exhibited psychomotor agitation and disorganized behavior. He developed visual illusions and hallucinations (eg, observed one of the physicians as headless and bleeding, saw butterflies in the air), auditory hallucinations (eg, heard bothering voices of children who were not there), and paranoid ideation (claimed that his schoolmates were coming to harm him). His thought and speech were disorganized and perseverative (eg, started sentences and did not finish them, jumped from one subject to another). He was unable to perform simple calculations (eg, could add only numbers less than 10, could not multiply even small numbers). There was a loss of short- and long-term memory (eg, did not remember what had happened the day or some hours before, did not recognize medical staff he had seen many times during his hospitalization, could not recall events from school), and a short attention span.

His neurologic examination revealed mild right hemiparesis, unchanged from before. Routine serum biochemistry and a complete blood count were normal except for a transient increase in liver enzymes. A lumbar puncture was normal. Repeated EEGs showed left-side slowing, but no epileptic activity. A brain CT and magnetic resonance imaging (MRI) revealed left-hemisphere atrophy with thalamic hypodensity, similar to prior imaging.

A ^{99m}Tc -ECD single photon emission computed tomographic (SPECT) study revealed decreased perfusion to the left hemisphere, including the basal ganglia and the thalamus. The findings were most prominent in the left medial temporal lobe.

The patient was diagnosed as having postictal psychosis. The psychosis lasted for 7 days and resolved gradually without treatment. Valproic acid was started immediately following the status epilepticus. Neither seizures nor psychotic events recurred in the following 6 months.

DISCUSSION

Postictal psychoses are brief psychotic episodes that usually occur after poorly controlled partial complex seizure clusters.^{2-8,9} Most authors agree that they are related to temporal lobe epilepsy^{3,5,6} and usually appear after secondarily generalized seizures^{3,8,9} or during antiepileptic drug tapering.⁵ Their incidence is as high as 6.25% among epileptic patients undergoing video-EEG monitoring.² Often patients experience a psychic aura (ie, fear) before the seizure.^{3,5}