Subcortical Infarction in Children

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Background and Purpose This report examines the occurrence of subcortical infarction in 5 children, reviews the English literature, and discusses evaluation of this uncommon childhood illness.

Methods Clinical characteristics and neurological follow-up were examined in children who presented with subcortical infarction within the past 7 years. The English literature over the previous 20 years was reviewed to identify similar patients with radiological documentation of subcortical infarction.

Results Mean age of the patients in this series was 4.8 years (range, 4 months to 12 years); 3 children were female. Three patients presented with the sudden onset of hemiparesis, 1 with dystonia, and 1 with fever and focal seizures. Protein C deficiencies were demonstrated in 2 children; a cardiomyopathy was seen in 1 patient. Mean follow-up was 1.5 years. Two patients were neurologically normal, mild residual symptoms persisted in 2, and 1 patient showed severe dystonia. The estimated incidence of cerebrovascular disease in children is 2.5 per 100,000 per year, with ischemic events occurring one quarter as frequently as hemorrhagic strokes. The occurrence of ischemic lesions confined to the subcortical region is uncommon, and despite several case reports or descriptions of small series of patients, a complete analysis of this illness in childhood is not available. This investigation describes 5 children with subcortical infarction (Scl) and summarizes the clinical presentation, radiographic evaluation, and neurological outcome in reported cases.

Subjects and Methods

A retrospective chart analysis was performed on 5 patients aged 16 years or younger who were diagnosed with Scl between 1985 and 1992. This series represented 6% of all children hospitalized with cerebrovascular disease during this period. Patients with cortical infarctions, neoplasms, or hemorrhages were excluded from the series. Data were recorded from hospital charts and categorized as to age, sex, cause of infarction, clinical presentation, degree of neurological impairment, radiological findings, and outcome. Long-term follow-up was assessed by consecutive outpatient visits, telephone interviews, or written responses.

The medical literature reported in English over the past 20 years was reviewed for children with radiological documentation of Scl. Patients with cortical strokes, neoplasms, or hemorrhages were excluded. Patients were categorized as to age, sex, cause of infarction, clinical presentation, degree of neurological impairment, results of computed tomography (CT), magnetic resonance imaging (MRI) or angiography (MRA), and clinical outcome.

Case Reports

Case 1

The patient was a 12-year-old girl with no prior medical problems who complained of a 10-day history of flulike symptoms including headache, sore throat, and abdominal pain. She developed a right hemiparesis associated with seizure activity on the day of admission. A chest radiograph showed cardiomegaly; coagulation studies, spinal fluid examination, and cranial CT were normal. One week later cardiac catheterization revealed reduced cardiac output with congestive heart failure. Repeat CT examination demonstrated infarction of the left basal ganglia and posterior limb of the internal capsule. The patient showed complete resolution of her right hemiparesis in 2 weeks. Her cardiomyopathy failed to improve, and she underwent cardiac transplantation; organ necropsy revealed idiopathic dilated cardiomyopathy without a source of emboli. She was free of neurological deficits and seizure activity at 6-month follow-up.

Case 2

This previously well 26-month-old boy presented with a history of a 2-minute tonic-clonic seizure associated with fever. Neurological examination on admission was unremarkable. The following day, CT examination revealed a hypodense area involving the anterior limb of the right internal capsule consistent with an ischemic
infarct. Two days later, MRI confirmed the lesion. Coagulation studies and echocardiogram were normal; angiography was refused. The patient was neurologically normal at 6-month follow-up.

Case 3

The patient was a 9-year-old boy in remission from acute lymphocytic leukemia diagnosed and treated with chemotherapy 4 years earlier. The patient suddenly collapsed at school and presented with a left hemiparesis. No history of recent trauma, infection, seizures, or pharmacotherapy was noted. Coagulation studies and echocardiogram were normal. CT performed on the day of admission was unremarkable; MRI performed the following day revealed an infarction involving the right basal ganglia. Two weeks later angiography demonstrated amputation of the thalamostriate and lenticulostriate vessels with slow filling of the right middle cerebral artery. MRI (Fig 1, left panel) and MRA were performed 2 years later; MRI was unchanged, whereas MRA demonstrated marked stenosis of the proximal right middle cerebral artery with reduced blood flow (Fig 1, right panel). A mild left hemiparesis persisted at 3-year follow-up.

Case 4

The patient was a 7-month-old girl who presented with a right hemiparesis greater in the arm. Perinatal history was unremarkable. MRI demonstrated a lacunar infarction involving the posterior limb of the left internal capsule. No additional imaging was done at the time, and laboratory data were unavailable. A severe right hemiparesis persisted at discharge. The patient was first seen at this institution 29 months later when she presented with focal seizures. Examination revealed a mild right hemiparesis, which had improved since the first hospitalization. Laboratory data demonstrated a protein C level of 2.3 μg/L. Additional coagulation studies including prothrombin time, partial thromboplastin time, fibrinogen, protein S, and antithrombin III levels, as well as an echocardiogram and an electrocardiogram, were normal. MRI revealed an ischemic infarction of the posterior limb of the internal capsule; angiography was not performed. Follow-up coagulation studies at 1 month and 6 months remained unchanged. Mild weakness of the right hand persisted at 6 years of age.

Case 5

The patient was a 7-month-old girl who presented with a 3-month history of infantile spasms and left arm dystonia with a hypsarrhythmia pattern on electroencephalography. The child was in the 25th percentile for height and weight with delay in neurodevelopment. MRI revealed bilateral basal ganglia infarcts (Fig 2). CT and angiography were not performed. Laboratory data showed a protein C level of 2.1 μg/L; additional coagulation studies including prothrombin time, partial thromboplastin time, fibrinogen, protein S, and antithrombin III levels and an electrocardiogram were normal. Repeated determination of protein C at 3 months showed a level of 2.0 μg/L. At 24-month follow-up the patient demonstrated a severe dystonia affecting the left arm.
Subcortical Infarction

Risk Factors Associated With Subcortical Infarction in Children

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>29</td>
</tr>
<tr>
<td>Tuberculous meningitis</td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>4</td>
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<tr>
<td>Kawasaki</td>
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<tr>
<td>Cat-scratch disease</td>
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</tr>
<tr>
<td>Unknown</td>
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</tr>
<tr>
<td>Trauma</td>
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</tr>
<tr>
<td>Hematologic</td>
<td>11</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>4</td>
</tr>
<tr>
<td>Sickle-cell anemia</td>
<td>4</td>
</tr>
<tr>
<td>Lipoproteinemia</td>
<td>2</td>
</tr>
<tr>
<td>Antithrombin III deficiency</td>
<td>1</td>
</tr>
<tr>
<td>Vascular</td>
<td>6</td>
</tr>
<tr>
<td>Carotid dissection</td>
<td>3</td>
</tr>
<tr>
<td>Moyamoya</td>
<td>2</td>
</tr>
<tr>
<td>MCA aneurysm</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac</td>
<td>4</td>
</tr>
<tr>
<td>Valvular abnormality</td>
<td>3</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
</tr>
</tbody>
</table>

MCA indicates middle cerebral artery.

Twenty-nine cases were associated with systemic infections, particularly tuberculosis, while 17 had no known risk factors. Trauma was implicated in 12 cases, and a variety of hematologic disorders or vascular or cardiac abnormalities were described in the remaining 21 children.

Discussion

Similar to previous reports, the mean age of our patients was 4.8 years, confirming the occurrence of Scl in younger children. Previous investigators have estimated the incidence of ischemic stroke in children at 0.2 to 0.6 per 100,000 per year. The recent study of Satoh et al showed that 31 of 54 children (57%) sustained ischemic strokes confined to the basal ganglia. Extrapolation of these data to their estimated incidence for all ischemic strokes indicated a rate of approximately 0.1 per 100,000 per year for Scl in children. In our series a precise incidence rate cannot be determined, although the patients represented 6% of all children hospitalized for cerebrovascular disease during the study period.

A protein C deficiency was identified in two patients in our series. This clotting abnormality has been associated with recurrent thrombosis and cortical ischemia in adults but not in children with Scl. Although other laboratory values were unremarkable, a deficiency of this protein, which inhibits the clotting cascade, may have resulted in hypercoagulability and arterial thrombosis. One patient (case 3) completed chemotherapy for acute lymphocytic leukemia 4 years before the onset of symptoms.

Literature Analysis

Analysis of the literature revealed reports of 104 children with radiological confirmation of Scl. Fifty-one patients had complete clinical analysis; these 51 patients formed a comparison group. Mean age for this group was 5.7 years (range, 9 weeks to 17 years) with an equal sex distribution. Forty-six patients (90%) presented with sudden onset of hemiparesis; the remaining patients presented with acute dystonia or focal seizures. Follow-up greater than 5 months was described in 29 patients. Complete resolution of neurological deficits occurred in 12 patients; mild residual deficits were seen in 11 children and severe deficits in 6. Two of 3 patients with dystonia demonstrated severe deficits on follow-up.

Infarctions were diagnosed with CT in 45 patients and with MRI in 1 patient; 5 patients were diagnosed with both examinations. Twenty patients (39%) demonstrated mixed infarctions of the basal ganglia and the internal capsule, 17 (33%) infarcts occurred in the internal capsule, and 14 (28%) localized to the basal ganglia. Bilateral lesions were reported in 2 patients. Three patients had normal CT findings within 24 hours of ictus; MRI, performed within 24 hours, was diagnostic in 2 patients.

Angiography in 22 patients (43%) identified nonspecific vascular narrowing in 10 cases, normal vascular structures in 8, and specific anatomic abnormalities in 4. Carotid dissection was diagnosed in 2 patients, and an asymptomatic middle cerebral artery aneurysm and moyamoya were found in the remaining children.

Risk factors were described in 79 patients (Table).
of Scl. Investigators have implicated venous thrombosis with L-asparaginase therapy or disseminated intravascular coagulation with acute lymphocytic leukemia, but these factors were not present in our patient. While segmental narrowing of the ipsilateral middle cerebral artery seen on angiography and MRA could account for the Scl, a cause for the vascular abnormality was not found.

A cardiomyopathy following a nonspecific viral syndrome was associated with Scl in the first patient. Occlusive vasculitis associated with viral infection has been described in children with Scl (Table), but clinical and necropsy data did not support this possibility. An alternative mechanism may have involved transient occlusion of the middle cerebral artery at the origins of the small perforating arteries. Although cortical injury was not seen on the radiological examination and a source of emboli was not found at necropsy, the occurrence of seizure activity on admission was consistent with this possibility. With occlusion of the middle cerebral artery, cortical perfusion can be maintained through collateral circulation, as shown in several adults with Scl and experimental studies. Direct embolic occlusion of perforating arteries has been reported but was unlikely in this patient.

Seizure activity was observed in three of our patients. In one patient (case 1) the activity may have indicated transient cortical injury from ischemia associated with a cardiomyopathy. In a second patient (case 2) the seizure activity was associated with a febrile illness, while the radiological characteristics of the lesion indicated an old, probably incidental Scl. The third patient (case 4) did not demonstrate evidence of persistent cortical injury. No further seizure activity was seen in these children, and none required anticonvulsant medication. Literature review indicated that 4 of 51 children (8%) presented with seizures, although a thorough description and follow-up were not available. In the absence of additional data, the occurrence of seizure activity in children with Scl was uncommon, transient, and not associated with radiological evidence of cortical injury.

This analysis in five children and reports in adults suggested that MRI was the radiological examination of choice, particularly in the early stage of Scl. The indications for invasive angiography, however, have not been clarified. Zimmerman et al. reported CT-angiographic correlation in 11 patients with Scl. Specific abnormalities were identified in four but were not associated consistently with correctable risk factors. The authors concluded that Scl was secondary to disease processes that involved large intracranial vessels at the origin of the lenticulostriate arteries and suggested that all children should undergo angiographic evaluation. In a recent study the same group described MRA findings in 52 children with varied infarctions and concluded that this examination was a sensitive and specific noninvasive screening test that eliminated angiography. One patient (case 3) in our series underwent MRA, which demonstrated abnormalities similar to previous angiography.

Neurological follow-up revealed good or complete clinical resolution in four patients in our series; the remaining patient with infantile spasms showed a severe dystonia at 3-year follow-up. These findings were similar to previous series that reported that approximately 80% of children with hemiparesis associated with Scl showed good improvement, whereas the sudden onset of dystonia indicated a poor prognosis.

Note added in proof. A recent study described 23 children with Scl, confirmed by CT, following mild head injury. Twenty-two of the children recovered completely within 4 months.

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