Involuntary movement induced by cerebral ischemia: pathogenesis and surgical outcome

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Object. Involuntary movement is an uncommon manifestation of a transient ischemic attack. It may be induced by cerebral hemodynamic insufficiency, which is associated with several cerebral ischemic diseases. The authors present three cases of limb shaking due to moyamoya disease (MMD) or radiation-induced middle cerebral artery stenosis, and three additional cases of choreic movement due to MMD. Neuroimaging studies and surgical outcomes in these patients were retrospectively analyzed to investigate the pathological mechanism underlying the symptoms and to provide guidance for the management of involuntary movement disorders in cases of ischemic cerebral disease.

Methods. The patient population included two children and four adults with ages at presentation ranging between 7 and 50 years. The initial presenting symptoms were involuntary movements in all six cases. A magnetic resonance imaging finding common in all cases was a small infarct in the frontal corona radiata, which did not extend to the cortex or basal ganglia. A perfusion defect in the frontoparietal cortical and subcortical regions was demonstrated by single-photon emission computed tomography in all patients. Improved hemodynamic circulation in the frontoparietal cortical and subcortical regions occurred in parallel with clinical improvement following indirect or direct bypass surgery.

Conclusions. Ischemic dysfunction of the frontoparietal and subcortical motor pathways rather than that of the basal ganglia was suspected to be the cause of the observed contralateral involuntary movements. Direct and indirect bypass surgery can be used effectively to treat involuntary movements in patients with cerebral ischemic diseases such as MMD and in those with stenosis of an intracranial major artery.

KEY WORDS • moyamoya disease • involuntary movement • cerebral hemodynamics • bypass procedure

MOYAMOYA disease is a documented chronic hemodynamic ischemic disease of the central nervous system, which usually presents as recurrent episodes of TIAs. Involuntary movements such as chorea or limb shaking are unusual manifestations of TIA caused by an underlying cerebral ischemic disease.7,17,21,24–27 Although a few case reports contain descriptions of chorea or limb shaking in patients with MMD, collated data concerning the pathological mechanisms, surgical treatment, and outcome of MMD-associated involuntary movements are limited.10,17,21,26 Such involuntary movements may be caused by a complex alteration in the balance between the basal ganglia and the cerebral cortices via direct or indirect pathways.1,3,8,22 Ischemic dysfunctions of the basal ganglia, thalamus, brainstem, cortex, and subcortical white matter have been suggested as causes of many subtypes of simple or complex involuntary movement disorders.5,4,8,11,13,18,20,25,27 In our opinion, an involuntary movement disorder associated with an ischemic cerebral disease provides a valuable means for understanding the pathological mechanisms of involuntary movements, especially in terms of the regional cerebral hypofunction that is induced by a regional cerebral hemodynamic insufficiency, as demonstrated by cerebral angiography and cerebral perfusion studies. This report provides limited insight into the pathological mechanisms of involuntary movement disorders, and may be helpful for the management of involuntary movements in patients with ischemic cerebral disease. Moreover, in our study we describe three adult cases of MMD-related involuntary movement disorders, which are extremely rare in the literature.

Clinical Material and Methods

We retrospectively reviewed five cases of MMD (Cases 1–4; 6) and one case of radiation-induced MCA stenosis (Case 5), in which the patients’ initial and predominant presenting symptoms were involuntary movements with sudden onset. One (Case 3) of the five patients had probable MMD.9 Another patient (Case 5) had undergone conventional radiation therapy after a right frontal craniotomy for the resection of craniopharyngioma 8 years before the clinical presentation with involuntary movements.

Cerebral angiography, MR imaging, and Tc-hexamethylypropyleneamine oxime SPECT of the brain were performed both preoperatively and postoperatively in all pa-
Summary of clinical features in six patients with involuntary movements caused by cerebral ischemic disease*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Triggering Factor</th>
<th>Presentation</th>
<th>Diagnosis</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7, F</td>
<td>emotional tension &amp; hyperventilation</td>
<td>chorea</td>
<td>MMD</td>
<td>EDAS</td>
</tr>
<tr>
<td>2</td>
<td>13, F</td>
<td>emotional tension &amp; hyperventilation</td>
<td>chorea</td>
<td>MMD</td>
<td>EDAS &amp; EGS</td>
</tr>
<tr>
<td>3</td>
<td>21, F</td>
<td>none</td>
<td>chorea</td>
<td>probable MMD</td>
<td>STA–MCA</td>
</tr>
<tr>
<td>4</td>
<td>44, M</td>
<td>exercise &amp; smoking</td>
<td>limb shaking</td>
<td>MMD</td>
<td>EDAS</td>
</tr>
<tr>
<td>5</td>
<td>50, M</td>
<td>exercise</td>
<td>limb shaking</td>
<td>MCA stenosis</td>
<td>STA–MCA</td>
</tr>
<tr>
<td>6</td>
<td>28, F</td>
<td>emotional tension &amp; exercise</td>
<td>limb shaking</td>
<td>MMD</td>
<td>STA–MCA</td>
</tr>
</tbody>
</table>

* STA–MCA = STA–MCA anastomosis.

Summary of clinical features in six patients with involuntary movements caused by cerebral ischemic disease

Clinical Symptoms and Signs

Recurrent involuntary movements appeared unilaterally or bilaterally: four limbs demonstrated choreic movement in Case 1; there was a right-sided unilateral choreic movement in Cases 2 and 3; and left-sided unilateral limb shaking in Cases 4, 5, and 6. In Case 1, the choreic movements were more severe on the left side and were often accompanied by dystonic posturing of the left neck, nasal sniffing, phonic tics, and tongue protrusion. In Case 3, the involuntary movements were characterized by repetitive wiggling movements of the patient’s right fingers and toes, and were continuous day and night. Involuntary movements sometimes affected the right upper limb and the perioral area in the patient in Case 3. Transient ischemic attacks with hemiparesis (Cases 2 and 4) and somatosensory changes (Case 6) often accompanied the involuntary movements and occurred on the same side as the involuntary movements.

Electroencephalography was performed in four patients (Cases 1, 2, 4, and 6); in all cases the studies were performed in an awake patient. The results of waking electroencephalography monitoring in the three patients (Cases 1, 4 and 6) were normal; there was no epileptiform discharge and photic stimulation and hyperventilation revealed no abnormalities. The waking electroencephalography study performed in the patient in Case 2 indicated nonspecific diffuse cerebral dysfunction and demonstrated a spike discharge from the right frontal area during hyperventilation. Involuntary movements of all patients were evaluated by neurologists, who concluded that the involuntary movements were not partial seizures.

Neuroimaging Findings

An infarct in the frontal subcortical white matter, which varied in size and did not extend to the cortex or basal ganglia, was a common MR finding in all patients (Figs. 1 and 2). In no case was there evidence of an infarct in the basal ganglia or thalamus. A perfusion defect in the frontoparietal cortical and subcortical regions was demonstrated on SPECT images obtained in all patients (Fig. 3). A SPECT study performed using acetazolamide enhancement revealed a cerebral hemodynamic insufficiency involving the basal ganglia in only two cases.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Infarct on MRI</th>
<th>Perfusion Defect on Baseline SPECT</th>
<th>Impaired Reserve on AZM-Enhanced SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>bilat frontal WM</td>
<td>bilat hemispheres</td>
<td>study not done</td>
</tr>
<tr>
<td>2</td>
<td>rt frontal WM &amp; lt frontoparietal WM</td>
<td>bilat pst border zones (lt &gt; rt)</td>
<td>bilat pst border zones</td>
</tr>
<tr>
<td>3</td>
<td>lt frontal WM</td>
<td>lt frontal</td>
<td>lt frontal</td>
</tr>
<tr>
<td>4</td>
<td>rt frontal WM</td>
<td>rt frontoparietal</td>
<td>rt frontoparietal</td>
</tr>
<tr>
<td>5</td>
<td>rt frontal WM</td>
<td>rt frontotemporoparietal</td>
<td>rt frontotemporoparietal</td>
</tr>
<tr>
<td>6</td>
<td>rt frontal WM</td>
<td>rt frontoparietal</td>
<td>rt frontoparietal, BG</td>
</tr>
</tbody>
</table>

* AZM = acetazolamide; BG = basal ganglia; pst = posterior; WM = white matter.
Surgical Treatment

Indirect or direct bypass surgery was performed to improve the cerebral hemodynamic insufficiency. The surgery involved EDAS, EGS, and STA–MCA end-to-side anastomosis. Pediatric patients underwent bilateral surgery to treat both hemispheres and adult patients underwent unilateral surgery on the side opposite the abnormal limb movement. The differences in treatment were based on the different types of disease progression found in children and adults—children usually display more rapid disease progression. Encephaloduroarteriosynangiosis was performed in the manner described by Matsushima and Inaba. Bilateral surgery was performed in two stages, with the symptomatic and hemodynamically affected hemisphere treated initially. The interval between right- and left-sided surgery was 3 weeks in Case 1 and 4 months in Case 2.

Patient Outcomes

A patent bypass and excellent collateral circulation development was confirmed on postoperative cerebral angiograms obtained after STA–MCA anastomosis in Cases 3, 5, and 6 (Fig. 1). Postoperative follow-up cerebral angiography revealed an improved blood supply to the ACA and MCA territories through well-developed internal collateral vessels from the STA and reduced numbers of basal collateral vessels after EDAS in Cases 1, 2, and 4 (Fig. 2).

Postoperative SPECT images demonstrated elevated regional cerebral perfusion and improved vascular reserves in the frontoparietal area, which preoperatively had impaired perfusion and vascular reserves (Fig. 3).

In all cases involuntary movements gradually improved and completely disappeared within 3 months postoperatively. In Case 2, the patient’s right-sided TIAs transiently increased in frequency after the operation and then disappeared on postoperative Day 10. In this patient new left-sided choreic movements developed postoperatively, but completely disappeared 3 months after the patient underwent right-sided EDAS.

No relapse of neurological dysfunction occurred in any case during the follow-up period, which ranged from 18 months to 8.5 years in Cases 1 through 5. In the most recent cases, the follow-up period was longer, ranging from 3 to 8.5 years.

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The patient experienced two attacks of abnormal movements of a lesser degree postoperatively, but no relapse of neurological symptoms occurred subsequently.

**Discussion**

Moyamoya disease is a cerebrovascular disease featuring a slowly progressive stenosis or occlusion that starts at the distal ICA and the proximal ACA and MCA. Any failure to compensate for blood flow insufficiency by the collateral circulation is expressed as ischemic episodes of acute motor and sensory deficits, speech disturbances, headaches, or seizure in patients with MMD. Involuntary movement is an uncommon ischemic symptom of MMD and has only been reported as isolated cases. Moyamoya disease-related involuntary movements usually wax and wane and are triggered by excitement, emotional strain, or hyperventilation. Although some controversy exists regarding vascular or epileptiform origins for limb-shaking movement disorders, limb-shaking TIAs are clinically different from episodes of focal epilepsy. Epileptic spells usually include rhythmic tonic and/or clonic jerking of the extremities, head or eye turning, speech or visual disturbances, and loss of consciousness. These characteristics are not observed in limb-shaking spells. In our patients, limb-shaking TIAs were brief, nonrhythmic bursts of activity that involved the upper and lower extremities as described in the literature. The choreic movements are also different from movements observed during epileptic episodes and their presence, in our patients (Cases 1–3), was confirmed by experienced neurologists. Dysfunction in the basal ganglia and its related structures caused by reversible, transient ischemia under stressful conditions is considered to induce involuntary movements in patients with MMD. Although the basal ganglia is intimately concerned with movement control, other structures such as motor cortex circuits are also critical in the pathogenesis of involuntary movements. Any lesion, superficial or deep, that interrupts the cortical-striatal-pallidal-thalamic-cortical circuits may be a potential cause of an involuntary movement disorder; this issue has been addressed by some authors. Involuntary movement due to a lesion in the basal ganglia has frequent-
ly been described in the literature; however, an involuntary movement associated with corticosubcortical lesions that spare the basal ganglia has been reported less commonly. In our cases, a frontal subcortical infarct on MR images and impaired perfusion of the frontal lobe on SPECT images were common neuroimaging findings, and this may be an important clue to understanding the pathological mechanism of involuntary movements in our patients. Consider-

**Fig. 3.** Single-photon emission computerized tomography scans. Case 3. A: Preoperative basal scan revealing marked hypoperfusion in the left frontal cortical and subcortical regions around the infarcted area. B: Preoperative acetazolamide-enhanced scan revealing reduced perfusion in the left frontal cortical and subcortical regions. Postoperative basal (C) and acetazolamide-enhanced (D) scans obtained 2 years postoperatively, demonstrating elevated cerebral perfusion in the left frontal lobe. Case 4. Preoperative basal (E) and acetazolamide-enhanced (F) scans revealing reduced perfusion in the right frontal cortical and subcortical regions. Postoperative basal (G) and acetazolamide-enhanced (H) scans obtained 6 months after surgery, demonstrating elevated cerebral perfusion in the right frontal lobe. Case 5. Preoperative basal (I) and acetazolamide-enhanced (J) scans revealing hypoperfusion in the right frontal cortical and subcortical regions. Postoperative basal (K) and acetazolamide-enhanced (L) scans obtained 2 years postoperatively, demonstrating an improved perfusion pattern. Case 6. Preoperative basal (M) and acetazolamide-enhanced (N) scans revealing hypoperfusion in the right frontal cortical and subcortical regions. Postoperative basal (O) and acetazolamide-enhanced (P) scans obtained 2 weeks after surgery, demonstrating an improved perfusion pattern.
ing the focal frontal subcortical infarct, the most severely impaired perfusion area is likely to be the frontal subcortical area; moreover, hyperperfusion was confirmed in the frontal cortical and subcortical areas around the infarcted lesion by our cerebral perfusion studies. In addition, the involuntary movement disappeared along with an improvement in perfusion in frontal areas after a revascularizing operation. The basal ganglia receives cortical afferents from associative cortical areas such as the prefrontal, temporal, posterior parietal, and preoccipital cortices. In four cases, no definite evidence of hemodynamic insufficiency was observed in the basal ganglia. These findings indicate that the observed involuntary movements were probably caused by an abnormality at the connections between the basal ganglia and the cerebral cortices in the contralateral motor pathway, without direct involvement of the basal ganglia. We think that the subcortical lesion inhibits cortical input to the basal ganglia or thalamus, or interferes with neural circuits between cortical regions and the basal ganglia or thalamus. Involuntary movements develop as a result of these interruptions of interactions between functionally related basal ganglia-thalamus-cortex circuits by focal subcortical dysfunction. Our observation supports the concept of a functional network between cortical areas and the basal ganglia or thalamus.

Although the optimal treatment of involuntary movements is still under debate, because of its unclear pathogenesis the establishment of an adequate collateral blood circulation to ischemic brain tissue should be considered for the management of involuntary movements.

Conclusions

We suspect that ischemic dysfunction of the frontal cortical and subcortical motor pathways, rather than that of the basal ganglia, was the cause of contralateral involuntary movements in our patients. Direct and indirect bypass surgery offers an effective means of treating involuntary movements in patients with cerebral ischemic diseases such as MMD and stenosis of an intracranial major artery.

References