Involuntary Movement Associated with Stroke

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**Background**: Involuntary movement is a rare symptom of stroke. The pathophysiologic mechanism is poorly understood. **Methods**: We retrospectively evaluated the medical records of 1547 stroke patients who have been admitted to the Seoul National University Hospital from March, 1988 to March, 1997. **Results**: We found 18 patients with involuntary movements. Dystonia was observed in 10 patients, ballism or chorea in 8 patients and tremor in 5 patients. Anatomical structures responsible for dystonia were thalamus, lenticular nucleus, caudate nucleus and midbrain. Ballism-chorea was associated with lesions of subthalamic nucleus, thalamus, and lenticular nucleus. Tremor was associated with lesions of thalamus, lenticular nucleus and midbrain. Ballism-chorea was present in the onset of stroke in 6 cases, 2 months after stroke in 1 case, and 21 months after in 1 case. But only 1 case of dystonia was present in the onset of stroke, 2 cases within 7 days, 5 cases in one week to one month, and 2 cases after one month. The involuntary movements subsided in 5 cases of hemiballism-chorea and in 3 cases of dystonia. In most of the improved cases, the symptoms subsided in a month. **Conclusions**: Basal ganglia and thalamus were the main areas involved where lesions associated with involuntary movements were reported. The nature of involuntary movements was variable. However, lesions in subthalamic nucleus resulted only in ballism-chorea. The presence of only ballism chorea, but not any other involuntary movements, due to subthalamic nucleus lesions indicates that an indirect pathway may play a role in the pathogenesis of ballism-chorea. The latency between the onset of stroke and involuntary movements was longer in dystonia than ballism-chorea. The course of ballism-chorea was generally better than dystonia.

**Key Words**: Involuntary movement, Ballism, Chorea, Dystonia, Tremor, Stroke
SUBJECTS AND METHODS

1547 stroke patients were admitted to the department of neurology and all of them were evaluated with CT or MRI at the Seoul National University Hospital (SNUH) from March 1988 to March 1997. We reviewed the patients’ charts, and a questionnaire was devised and distributed to each doctor who saw stroke patients from 1990 to 1997 at SNUH. The questionnaire consisted of questions regarding age, sex, stroke type, the location of lesion, the nature of movement if any, the time of onset of the movement, course, and treatment. Stroke type was classified by the findings from brain imaging correlating with clinical manifestation.

RESULTS

18 patients, consisting of 12 men and 6 women, with involuntary movement were observed after stroke. The mean age at the onset of abnormal movements was 58.6±15.8 years. Out of all the patients reviewed, 1088 were with infarction, and 459 with hemorrhage. The hemorrhage confined to thalamus was seen in 112 cases, putamen in 128 cases, and caudate in 16 cases. The infarction confined to the focal lesion of thalamus was seen in 32 cases and basal ganglia in 47 cases. However, large lesions affecting basal ganglia and thalamus were commonly observed coincidentally or as a part of new infarction in MCA and/or PCA infarction.

THE NATURE OF INVOLUNTARY MOVEMENTS

Dystonia was the most common involuntary movements seen in 10 out of 18 patients. Ballism, chorea, or athetosis was seen in 8 cases. 5 cases of tremor were present and usually associated with other abnormal movements.

LESION

In the patients with ballism-chorea, the lesions were observed in subthalamic nucleus in 2 cases, lenticular nucleus in 2 cases, thalamus in 2 cases, lenticular nucleus extending to thalamus in 1 case, multiple lesions in thalamus, midbrain, and cerebellum in 1 case. In those with dystonia, the lesion was involved in thalamus in 4 cases, lenticular nucleus in 3 cases, caudate nucleus in 1 case, pons and midbrain in 1 case, thalamus and cerebellum in 1 case. Tremor was present in lenticular nucleus in 1 case, thalamus in 2 cases, thalamus, midbrain, and cerebellum in 1 case, pons and midbrain in 1 case (Table, Fig. 1,2,3). Various combinations of abnormal movements were present. In the patients with the lesions of lenticular nucleus, the combination of choreoathetosis and tremor, the combination of dystonia and tremor were present. In those with the lesions of thalamus and thalamus extending to putamen were seen.
mus, the combination of dystonia and tremor; in the lesion of thalamus and cerebellum and midbrain, the combination of ballism and tremor were present. In those with the lesion of pons and midbrain, the combination of dystonia and tremor occurred (Table).

ONSET

6 cases of ballism-chorea was present in the onset of stroke, 1 case at 2 months after stroke, and 1 case at 21 months after stroke. But in dystonia only one case was present in the onset of stroke, and 2 cases were present within 7 days, 5 cases from one week to one month, 2 cases after more than one month after stroke. 1 case of tremor occurred with ictus, 2 cases occurred in 1 month, 2 cases after more than 1 month after stroke (Table).

COURSE

The involuntary movements subsided in 5 cases of ballism-chorea, one case in one day, 3 cases in 15 days and 1 case in 4 months. However, the symptom didn’t subside in 2 cases. Whereas in patients with dystonia, the

Figure 2. The lesions of patients with dystonia.

Figure 3. The lesions of patients with tremor.
symptom disappeared in only 3 cases within a month and persisted in 7 cases during observation period (Table). However, since the follow up period was relatively short in our study, more time may be needed for the long-term prognosis.

**Discussion**

Stroke itself is the common cause of secondary involuntary movement. In 240 cases with abnormal movement with the lesion of basal ganglia, the most common cause was stroke. The region damaged by vascular insult may produce involuntary movement by interrupting the pathway which regulate motor function. Motor control is influenced by several systems; one of which is basal ganglia. Exciting or inhibiting pathways in basal ganglia attribute to the facilitation of motor program. The pathways that regulate motor function in basal ganglia consist of direct and indi-

**Table 1. The lesion and the clinical feature of the patients with involuntary movement after stroke.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>Stroke type</th>
<th>Lesion</th>
<th>Involuntary movement</th>
<th>Onset</th>
<th>Course</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80/F</td>
<td>lt subthalamic hemorrhage</td>
<td>Lt subthalamic Nu</td>
<td>rt arm, leg, head ballism</td>
<td>ictus</td>
<td>1 month (p)</td>
<td>haldol</td>
</tr>
<tr>
<td>2</td>
<td>70/M</td>
<td>rt subthalamic infarct</td>
<td>Rt subthalamic Nu</td>
<td>Lt arm, leg ballism and chorea</td>
<td>ictus</td>
<td>15 days (s)</td>
<td>haldol</td>
</tr>
<tr>
<td>3</td>
<td>62/M</td>
<td>rt thalamic ICH with IVH</td>
<td>rt thalamus</td>
<td>Lt arm ballism</td>
<td>ictus</td>
<td>1day (s)</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>17/F</td>
<td>multi-infarct</td>
<td>rt thalamus, rt midbrain, rt cerebellum</td>
<td>Rt arm tremor, Head titubation, Both legs ballism</td>
<td>ictus</td>
<td>6 months (p)</td>
<td>INH, valium, inderal, madopar</td>
</tr>
<tr>
<td>5</td>
<td>56/M</td>
<td>lt BG infarct</td>
<td>lt lenticular Nu</td>
<td>rt head, trunk chorea</td>
<td>ictus</td>
<td>15 days (s)</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>69/F</td>
<td>rt BG infarct</td>
<td>rt putamen, choreoathetosis</td>
<td>lt arm, leg</td>
<td>2 months</td>
<td>–</td>
<td>artane</td>
</tr>
<tr>
<td>7</td>
<td>56/M</td>
<td>rt thalamic infarct</td>
<td>rt thalamus</td>
<td>lt arm, leg choreoathetosis, rt arm tremor</td>
<td>ictus</td>
<td>?</td>
<td>haldol, inderal, artane, DPH, clonazepam</td>
</tr>
<tr>
<td>8</td>
<td>58/M</td>
<td>rt BG infarct</td>
<td>lt putamen</td>
<td>rt arm choreoathetosis</td>
<td>&gt;21 months</td>
<td>15 days (s)</td>
<td>clonazepam</td>
</tr>
<tr>
<td>9</td>
<td>80/F</td>
<td>rt BG infarct</td>
<td>rt putamen</td>
<td>lt arm dystonia</td>
<td>?(&lt;1month)</td>
<td>?</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>35/M</td>
<td>rt BG infarct</td>
<td>lt lenticular Nu</td>
<td>Rt arm dystonia</td>
<td>1 month</td>
<td>1 month (s)</td>
<td>DPH</td>
</tr>
<tr>
<td>11</td>
<td>61/M</td>
<td>rt BG hemorrhage</td>
<td>rt putamen</td>
<td>rt arm, leg dystonia, rt arm tremor</td>
<td>19 days</td>
<td>1 month (p)</td>
<td>artane</td>
</tr>
<tr>
<td>12</td>
<td>56/F</td>
<td>lt caudate infarct</td>
<td>lt caudate Nu</td>
<td>Rt arm dystonia</td>
<td>2 days</td>
<td>1 month (s)</td>
<td>DPH</td>
</tr>
<tr>
<td>13</td>
<td>60/M</td>
<td>rt thalamic hemorrhage</td>
<td>rt thalamus</td>
<td>lt arm, leg dystonia</td>
<td>2 yrs</td>
<td>6 yrs (p)</td>
<td>artane, madopar</td>
</tr>
<tr>
<td>14</td>
<td>39/M</td>
<td>top of the basilar</td>
<td>both thalamic, both temporo-occipital lobe, both cerebellum</td>
<td>Head, both arms and legs dystonia</td>
<td>1 month</td>
<td>7 months (p)</td>
<td>artane, clonazepam</td>
</tr>
<tr>
<td>15</td>
<td>68/F</td>
<td>rt thalamic hemorrhage</td>
<td>rt thalamus, internal capsule, BG,</td>
<td>lt arm, leg dystonia</td>
<td>9 months</td>
<td>7 months (p)</td>
<td>clonazepam</td>
</tr>
<tr>
<td>16</td>
<td>67/M</td>
<td>rt thalamic infarct</td>
<td>rt thalamus</td>
<td>lt arm dystonia</td>
<td>ictus</td>
<td>41 months (p)</td>
<td>–</td>
</tr>
<tr>
<td>17</td>
<td>53/M</td>
<td>pontine hemorrhage</td>
<td>both pons, lt midbrain involving red Nu</td>
<td>rt arm dystonia</td>
<td>20 days</td>
<td>9 months (p)</td>
<td>clonazepam, inderal</td>
</tr>
<tr>
<td>18</td>
<td>67/M</td>
<td>rt thalamic hemorrhage</td>
<td>rt thalamus</td>
<td>lt arm, leg dystonia</td>
<td>2 days</td>
<td>1 month (s)</td>
<td>–</td>
</tr>
</tbody>
</table>

(p) ; persistent  (s) ; subside  rt ; right   lt ; left   Nu ; nucleus   BG ; basal ganglia   DPH ; phenytoin   INH ; isoniazid
rect pathways. When a particular motor behavior is selected, appropriate thalamic neurons are disinhibited in direct pathway, which facilitate motor program. Whereas the indirect pathway is responsible for suppressing unwanted movements.

THE LESION AND PATHOPHYSIOLOGY

From the case analysis, dystonia was the most frequently occurring movements in patients who have suffered stroke. Basal ganglia and thalamus may be regarded as the main areas where the lesions associated with involuntary movements occur. The nature of involuntary movements were variable, and the combination of abnormal movements could be presented after a focal lesion. However, the lesions of subthalamic nucleus resulted in only ballism-chorea. Subthalamic nucleus is involved only in indirect not in direct pathway; thus, the indirect pathway may play a role in the pathogenesis of ballism-chorea.

A. Ballism-Chorea

In published reports, ballism-chorea is associated with the lesion of subthalamic nucleus, putamen, caudate nucleus, thalamus, and frontal lobe. In our study the patients with ballism or chorea had lesions in subthalamic nucleus, lenticular nucleus, or thalamus. The pathogenesis of Huntington’s chorea helps to understand how the lesions produce ballism-chorea. In Huntington’s disease the striatal projection to the GPe is more severely affected initially, which results in the loss of inhibition of GPe and leads to the inhibition of subthalamic nucleus neurons, and this excessive inactivity of subthalamic nucleus might cause the chorea in Huntington’s disease. The lesions of subthalamic nucleus can also produce hemichorea or hemiballism. The injections of GABA into subthalamic nucleus of monkeys caused contralateral hemiballism-hemichorea. The movements were probably caused by reducing the normal excitatory input from subthalamic nucleus to GPe. The reduced excitatory input reduces the inhibitory output of GPe to thalamus; this disinhibition of thalamus in turn raises excitatory drive in cortex to excessive level and produces contralateral hyperkinetic movements. On the basis of these concepts, chorea or ballism caused by lesions of thalamus may be explained by the assumption that inhibitory input from GPi and SNr may be damaged and led to disinhibition of thalamus. Thus, abnormal excitation of thalamus by some lesions in the indirect pathways such as putamen, GPe, and subthalamic nucleus was appeared to cause chorea or ballism. Patient 8 with diabetes mellitus developed right upper extremity chorea and athetosis and visited emergency room. The level of serum glucose was 600 mg/dL. Hyperglycemia may be the inducing factor of choreoathetosis in addition to an old basal ganglia lesion.

B. Dystonia

The lesions in basal ganglia, thalamus, internal capsule, and parietal lobe were reported to produce dystonia. The patients with dystonia in our study had lesions in thalamus, putamen, lenticular nuclei, caudate nucleus, and midbrain. From the study of the analysis of the 71 cases with dystonia, putamen was found to be the most frequent site of lesions responsible for dystonia. However, thalamic lesions were most common in our study.

Dystonia has been classified according to the distribution of lesions and classified as either focal, multifocal, segmental, or generalized. Generalized dystonia is usually associated with lesions of the both basal ganglia. Hand dystonia is mainly related to lesions of postero-lateral thalamic nuclei. Lesions of caudate nuclei, putamen, and parietal cortex have also been associated with dystonia of hand or arm. Mesodiencephalic region is likely to be the main anatomical basis for symptomatic blepharospasm and perhaps cranial dystonia. But in our study, generalized dystonia was present with the lesions of both thalamus. Hemidystonia was present mainly with the lesions of contralateral thalamus, and hand dystonia with the lesions of putamen, caudate nucleus, and midbrain. In foot dystonia ventral lateral thalamus was involved. Each structure has the somatotopic organization of the whole body; thus, the correlation between a lesion and a
specific symptomatic part requires more discrete imaging or pathology. Many studies were done to find out the pathophysiology of dystonia. However, still some discrepancy exists between the activities of direct and indirect pathway contributing to dystonia. In the direct pathway, a decreased striatal inhibition on GPI, as the result enhanced activity of GPI in the late stage of Huntington’s disease and dystonia associated with putaminal lesion was observed. The opposite activity was postulated on striatal-GPi pathway in levodopa induced dystonia in MPTP treated parkinsonian monkey. Drug induced dystonia is thought to be different from dystonia caused by focal brain damage. The fact that dopamine agonists can also produce dystonia indicates that it has a different pathophysiological mechanism. However, in the indirect pathway, more confusing results in the function of interaction between basal ganglia structures was reported. Enhanced GPe activity was shown in one study but decreased GPe activity was shown in another. There is another speculation in the mechanism of dystonia caused by thalamic lesions. The lesions of ventral intermediate nucleus or ventral caudal nucleus mainly produce distonia. Thus, dystonia is suggested to result from the dysfunction of cerebellar input to thalamus. Such a dysfunction of the cerebellothalamic pathway can explain previous reports of dystonia caused by lesions involving midbrain, or ventral intermediate nucleus, which may interrupt the cerebellothalamic circuit. Patient 17 developed right side hemidystonia after pontine hemorrhage extended to left midbrain including red nucleus. No lesion was found in basal ganglia or thalamus. He had also rt side ataxia. Cerebellothalamic interruption provides the explanation for dystonia in this patient. But in the case of dystonia with thalamic lesions, which wasn’t associated with cerebellar dysfunction, basal ganglio-thalamo-cortical circuit dysfunction might result in dystonia. Ventrolateral thalamus received pallidal inhibitory input and project excitatory output to cortex. Among them, the damage to thalamic outflow was thought to be attributed to dystonia. While damage to basal ganglia has been seen without associated dystonia, the presence of other lesions could mask dystonia by producing hemiparesis, or the damage may have occurred in only a small portion of nuclei.

C. Tremor

Rubral tremor was seen in 2 patients with midbrain lesion. Action tremor in 2 patients with thalamic lesion and 1 patient with putaminal lesion was observed. The so called rubral tremor is a controversial entity, characterized by the presence of a large amplitude tremor at rest with more pronounced tremor when maintaining a fixed posture and further increased tremor in amplitude with intentional voluntary movements. Rubral tremor is probably resulted from the involvement of both nigrostriatal pathway and rubro-olivo-cerebello-rubral loop or both nigrostriatal pathway and dentato-rubro-thalamic tract. It is consisted of resting tremor produced by nigrostriatal dysfunction as in parkinsonian tremor and action tremor which may be caused by rubro-olivo-cerebello-rubral loop or dentato-rubro-thalamic tract. Patient 15 with thalamic lesion had an intention terminal tremor with probable involvement of dentato-rubro-thalamic pathway.

ONSET

Most of chorea-ballism developed in the onset of brain insult or acute stage of stroke, whereas most of dystonia appeared after acute stage. Only one case of dystonia occurred in the onset of stroke; 2 cases within 7 days. Other patients with dystonia occurred in the onset of stroke; 2 cases from 8 days to 1 month, 5 cases after 1 month. "Delayed-onset dystonia" is related to aberrant neuronal sprouting following a lesion. The latency of the onset of movement disorder may reflect the time required for remyelination, denervation supersensitivity, and brain reorganization after deafferentiation. In the study using PET, the patients with hemidystonia after capsular stroke showed the frontal overactivity primarily in contralateral motor areas, whereas the capsular stroke patients without involuntary movement showed overactivity of ipsilateral motor areas. The study indicates that aberrant neuronal sprouting occurs after brain damage.
in patients with hemidystonia. However, in uncomplicated stroke patients, the recruitment of ipsilateral circuit, increased efficacy of existing synapses rather than sprouting and the formation of new synapses play important roles in recovery.16

TREATMENT AND COURSE

Klawans et al found increased levels of cerebrospinal fluid homovanillic acid, a dopamine metabolite, in three of the patients with hemiballism.25 They suggested that increased dopaminergic transmission might play a role in the pathophysiology of this disorder. This suggestion is supported by the observation that dopamine blockers and catecholamine depleting agents often improve hemiballism. Several drugs have been reported to be successful in the treatment of hemiballism. These include reserpine, tetrabenazine, valproic acid, and many neuroleptic drugs like chlorpromazine hydrochloride, haloperidol, and perphenazine hydrochloride.3-25,26,27 In our cases haldol was used in 3 patients during the course of their illness. The medication was proven to be effective in 1 patient but not in the other.2

Hemiballism-hemichorea caused by stroke is commonly reported to improve spontaneously.25 In improved cases, the infarct or hemorrhage is probably due to edema, which makes the neighboring structures relatively ischemic, resulting in involuntary movements. As edema subsides, reperfusion of these areas leads to the disappearance of the movement disorder. In our cases, 5 patients improved spontaneously; however, the symptom persisted in 2 patients. Patient 1 died due to subdural hematoma. Persistent chorea for one month caused subdural hematoma by falling the patient down from bed. Patient 6 showed no improvement for 8 years with medications of clonazepam and artane.

The prognosis of dystonia was generally poor. Only 3 patients out of 10 improved in one month. The remaining 7 patients persisted or progressed in the follow up periods of 1 month to 41 months under artane or clonazepam treatment. The response to medications in the patients with dystonia was reported to be disappointing. Various muscle relaxants, tetrabenazine, and high dosage anticholinergic agents provided a minimal to no improvement in motor performance.11

As to the patients with good prognosis of dystonia or ballism-chorea, the improvement was seen within one month after stroke.

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