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Juvenile Muscular Atrophy of Unilateral Upper Extremity (Hirayama Disease)

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Abstract We have clinically examined 9 patients with juvenile muscular atrophy of unilateral upper extremity (Hirayama disease), which is characterized by exclusive juvenile male occurrence, insidious onset, unilateral muscular atrophy of the hand and forearm, lack of definite sensory disturbances and non or very slow progressive course. Although the clinical features of our patients were basically consistent with those in previous reports, their ages at onset were slightly higher and cold paresis and fasciculation occurred less frequently in our cases. Five patients were examined by cervical magnetic resonance imaging (MRI) at the anteflexed position in addition to the routine neutral position. As a result, 4 were found to show both the spinal cord thinning and anterior shifting of the dural sac at levels of C5-C7 ; especially in 2 patients, the findings were obtained only at the anteflexed position (not at the neutral one). The present results clearly provide the evidence that MRI at the anteflexed position was efficient for detection of Hirayama disease and strongly support the hypothesis that the disease is caused by chronic circulatory insufficiency due to compression of the spinal cord resulting from repeated anterior shifting of the dural sac.

Key words : Hirayama disease, cervical MRI, flexion myelopathy

Introduction

In 1959, Hirayama and his associates[1] first described juvenile muscular atrophy of unilateral upper extremity (Hirayama disease) as a distinct clinical entity. Hirayama disease is characterized by 1)exclusive occurrence in juvenile males, 2) insidious onset, 3) unilateral muscular atrophy of the hand and forearm, so-called oblique atrophy, 4) cold paresis and tremor-like involuntary movement of the fingers, 5) progression for months to a few years followed by a stationary course, 6) absence of sensory and long tract signs and 7) absence of family history. The origin of this disease remains unknown, though various theories have been proposed[2,3,4] including degenerative, ischemic, viral, and other infectious or aseptic inflammatory etiologies. Recently, as a result of radiological examinations including CT myelography and magnetic resonance imaging (MRI)[5,6,7], several investigators have reported the radiological presence of dynamic compression of the spinal cord in Hirayama disease . The cause of this clinical manifestation, however, has yet to be determined. In this study, we reevaluated the clinical features of the patients with Hirayama disease who visited our clinic from 1990 to 1997, and discuss the pathomechanism on the basis of the present and previously accumulated MRI results.

Materials and Methods

A total of 9 patients including 8 males and one female was examined. Their average of ages at disease onset was 19.2 years (ranging from 13 to 44) , while the average of ages at study was 23.3 years. As to past history, 2 patients had external wounds, 3 had sports careers, and 2 were involved in physical labor. No patient had a family history of any neuromuscular disease.

MRI studies were performed on a superconductive unit operating at 1.5 tesla (Siemens Magnetom). T1-weighted images were obtained in sagittal and axial sections using a spin-echo (SE) sequence (TR 400-600/TE 15) ; gradient-echo (GE) images were obtained in sagittal and axial sections using a fast, low-angle shot (FLASH) sequence (TR 400-500/TE 10-18/flip angle 15 degrees).

Results

Neurological findings

All patients were right-handed. Unilateral involvement was seen in 8 patients, and bilateral involvement in only one. In the affected side, grasping power ranged from 0 to 28.5kg (average, 11.9kg). Oblique atrophy was found in all patients. Figure 1 shows muscular atrophy in a patient who had bilateral involvement. Atrophy in the hands and distal forearms is striking, though present only in the ulnar side of the proximal forearms. The brachioradial muscle is usually spared, giving an aspect of "oblique" atrophy. Cold paresis was observed in 6 patients, finger tremor, in 7 ; fasciculation, in 4 ; and sensory disturbance, in 1. Tendon reflexes in the brachioradialis were decreased in 3 patients. Increased tendon reflexes were found in the biceps in 1 patient and in the legs in 1, with positive Babinski sign in 1.

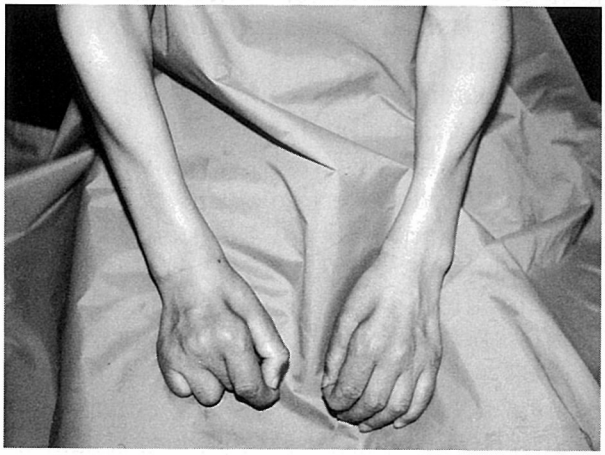

Fig.1 Typical severe muscular atrophy of both hands and the forearms ("oblique atrophy")

Laboratory studies

In all the patients, the results of routine urinalysis, RBC and WBC counts, creatinine kinase levels, and electrolyte levels were normal. In cerebrospinal fluid (CSF), cell count and protein concentration were normal in all patients, although Queckenstedt test was positive in one patient. Concerning electrophysiological findings, one patient had reduced amplitude of the ulnar and median compound muscle action potential (CMAP), mildly slow conduction in the ulnar nerve, and F wave abnormality were found in 1 patient.. Neurogenic changes in electromyography (EMG) were observed in 5 patients. Cervical spine X-ray findings were normal in 5 patients. One patient showed a straight neck and mild local angulation at the level of C4-C5, and the remaining one with bony spur at C4-C6 level. Table 1 shows the summary of cervical MRI findings. In the neutral neck position, spinal cord atrophy was seen at the level of C5-C6 or C7 vertebral bodies in 4 patients, more marked on the side of muscular atrophy. Five patients were examined by cervical magnetic resonance imaging (MRI) at the anteflexed position in addition to the routine neutral position. As a result, 4 were found to have both spinal cord thinning and anterior shifting of the dural sac at levels of C5-C7 ; especially in 2 patients, the findings were obtained only at the anteflexed position (not at the neutral one).

Case report

A 16-year-old Japanese male was admitted to our hospital because of weakness of the left hand. There was no neuromuscular disease in the patient's family and no significant event in his personal history. He noted the insidious onset of difficulty in fine movement of the left hand on cold days at age 14. Symptoms

Table 1. Summary of MRI findings

Patient No.	Muscle atrophy	Cervical cord thinning* ⟨neutral position⟩	⟨neck anteflexion⟩	Anterior shifting of the dural sac
1	L	−	−	−
2	R	C5-C6 (R=L)	C5-C6 (R=L)	C5-C6
3	R < L	−	n.e.	n.e.
4	R	n.e.	n.e.	n.e.
5	R	−	C5-C6 (R=L)	C5-C6
6	L	−	C5-C7 (R=L)	C5-C7
7	L	C5-C7 (R<L)	n.e.	n.e.
8	R	C5-C6 (R>L)	n.e.	n.e.
9	R	C6-C7 (R>L)	C6-C7 (R>L)	C5-C7

* =level of vertebral body ; R=right ; L=left ; −=absent ; n.e.=not examined

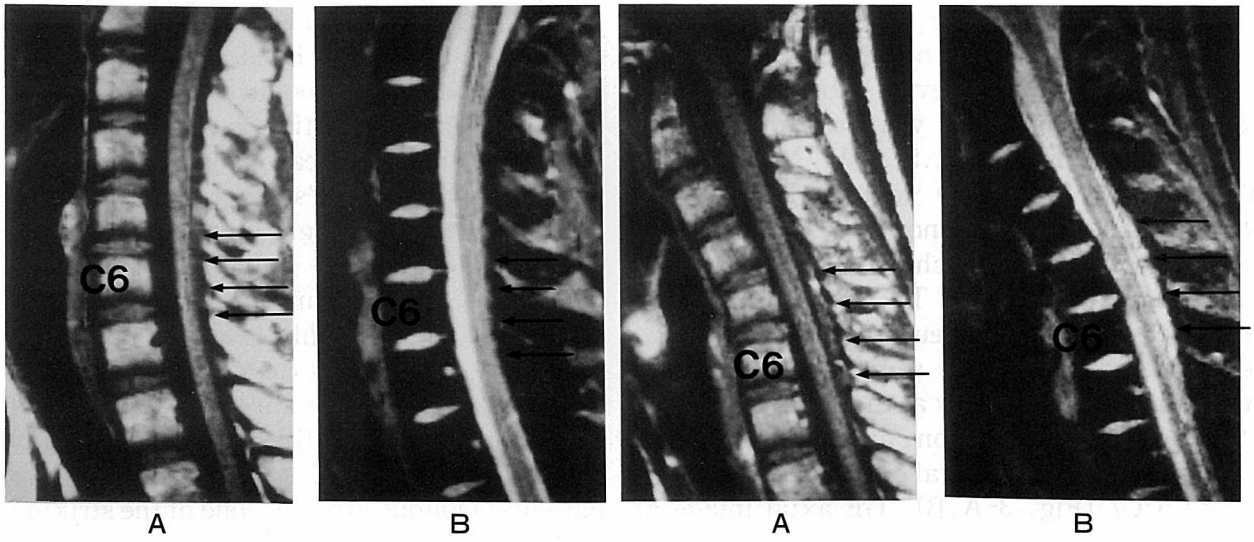

Fig.2 (A) T1-weighted sagittal spin-echo (SE) image. (B) Gradient-echo (GE) sagittal image. In the neutral neck position, localized cord atrophy at the C5-7 level is seen (arrows).

Fig. 3 (A) T1-weighted sagittal SE image. (B) GE sagittal image. In the anteflexed position, the narrowing and anterior shifting of the dural sac are seen at C5-C7(arrows).

progressed slowly for 2 years, but stablized thereafter. Examionation at age 16 showed marked atrophy and weakness of the left hand, as well as in the distal half and the ulnar side of the proximal half of the right forearm, apparently including the thenar, hypothenar, and interosseus muscles of the hand, the flexor carpi ulnaris and radialis, extensor carpi, and extensor digitorum muscles of the forearm. However, the brachioradial muscle was spared. Occasional fasciculations were observed in the atrophied muscles. A tremor -like, involuntary movement of the fingers of the left hand was observed at rest, and became more distinct when the fingers were extended. Tendon reflexes were normal. Babinski sign was absent. There was no sign of involvement of either the cranial nerves, cerebellum, sensory system, or the extrapyramidal system. Routine blood tests, urinalysis, EKG, spine and chest X-ray, and CSF examinations were all normal. Nerve

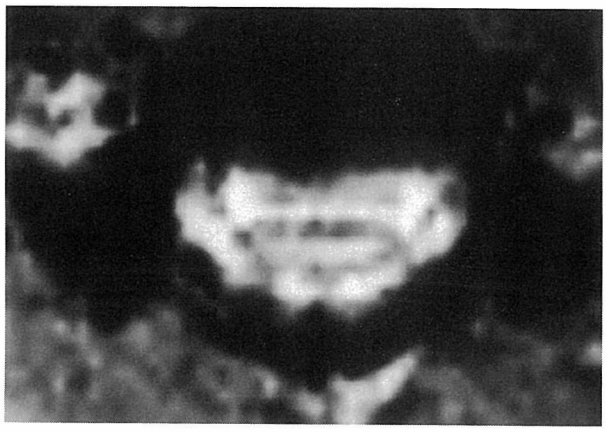

Fig. 4 GE axial image at C6 level. Flattening of the cord is seen.

conduction studies showed reduced amplitude and mildly slow conduction in the left ulnar motor nerve and mild prolongation of the F wave latency. During needle EMG of the left abductor pollicis brevis, fibrillations and positive sharp waves were seen. MRI was performed using a 1.5 tesla MRI system (Siemens Magnetom) with a T1-weighted spin-echo (SE) sequence (TR 450 / TE 15) and a gradient-echo (GE) sequence (FLASH, TR 470/ TE 18/flip angle 15 degrees). In the neutral neck position, T1-weighted and GE sagittal MRI showed localized cord atrophy at the C5-7 level (Fig. 2-A,B). At anteflexion, narrowing and anterior shifting of the dural sac were clearly seen at C5-C7 (Fig. 3-A,B). GE axial image at C5-7 level revealed a flattening of the cord (Fig. 4).

Discussion

The clinical summary of 63 cases of Hirayama disease reported by Hirayama in 1993[8] was slightly different from that of our 9 patients (Table 2). Compared to the previously reported cases, the age at onset was slightly later in our patients. The reason is that a 44-year-old female was included among our subjects. In this case, however, the age at onset was not early, although other clinical findings, including the characteristic MRI findings described later were consistent with the features of Hirayama disease. In the patients with Hirayama disease summarized previously, the affection was comparatively marked in the right hand, though such a tendency was not seen in our cases. The reason that the affection is confined to one upper limb in this disease is unknown. In 46 patients of Hirayama's cases, the weakness was confined to the right upper limb, and 41 of these patients were right-handed. On the other hand, in 14 patients whose affected limb was on the left side, only 4 were left-handed. Therefore, there was no clear relationship between the side of the muscular atrophy and handedness in these patients. Cold paresis and fasciculation were less frequent in our patients. Oblique atrophy, one of the striking

Table 2. Clinical summary of reported cases by Hirayama and our patients

	Reported cases*	Our patients
Age at onset (years)	16.1±2.1 (range 11-22)	19.2±9.5 (range 13-44)
Sex (male : female)	60 : 3	8 : 1
Affected side (R : L)	46 : 14	5 : 4
Laterality •unilateral	73%	8/9 (89%)
•bilateral	25%	1/9 (11%)
Obique atrophy	100%	9/9 (100%)
Cold paresis	97%	6/9 (67%)
Finger tremor	80%	7/9 (78%)
Fasciculation	60%	4/9 (44%)
Progressive phase duration	2-3 (1-8) years	1-5 years

* : 63 cases of Hirayama disease reported by Hirayama in 1993.

features in this disease, was found in all patients in both series.

The etiology and pathogenesis of this disease are not fully elucidated. One widely accepted pathomechanism is a flexion myelopathy[9]. During neck anteflexion, the posterior wall of the dural sac shifts anteriorly around the 6th cervical vertebra, causing an antero-posterior compression of the cord segment from C5 to T1, most marked at C7 and C8, resulting in circulatory insufficiency and neuronal damage. It is well known that the anterior horn cells are most sensitive to arterial or venous ischemia and, perhaps, the lower cervical cord is most susceptible to vascular compromise such as torsion effects associated with rotatory motion and a narrow spinal canal[10].

MRI studies on the pathogenesis of Hirayama disease have been few. MRI findings led Mukai et al[11]. to suggest that this disease was caused by chronic circulatory insufficiency due to compression of the spinal cord resulting from repeated anterior shifting of the dural sac. Proposed theories supporting the anterior shift of the posterior wall of the dural sac are "overstretch mechanism[5, 6]" and "tight dural canal in flexion[7]". These two theories are based on the differential growth in the length between the cervical vertebral column and either the spinal cord or the dura. Developmental disorders of this type seem to manifest at the juvenile age when the skeleton is developing and, thereafter, seem to stabilized. The pathomechanism in some of our 9 patients, whose MRI studies in neck anteflexion showed an anterior shifting of the dura, might be explained by these theories. Kitagawa et al[12]. performed the myelography in 12 patients with Hirayama disease. Seven patients showed an anterior shifting of the lower cervical dural canal in anteflexion as did some of our patients, however, the other 5 patients did not show such findings. Thus, there may be other etiological factors in this disease. Recently, Robberecht et al[13]. suggested that Hirayama disease might be associated with mutations of the superoxide dismutase 1 (SOD1) gene, which have been found in familial amyotrophic lateral sclerosis (ALS).

Based on radiological findings, a neck brace which prevents persisting neck flexion is the most commonly used treatment in this disorder. Hirayama[8] reported that in patients with a brace, disease progression stopped earlier than in patients without a brace and, moreover, one-third of the patients who used a neck brace from the early stage showed an improvement in muscle strength. Since progression of the symptoms of our patients had almost ceased when they visited our clinic, no particular medical treatment was performed.

Although the diagnosis of Hirayama disease is based on neurologic and neurophysiologic data, MRI studies also provide siginificant data for the diagnosis, as well as useful information contributing to an understanding of the pathomechanism of this disease. Hirayama disease occurs most often in young people, restricting their life plans for the future such as choice of occupation because of their disabled upper limb. Therefore, the early diagnosis and treatment of this disease are very important. The clinical features of this disease should be more widely known not only among neurologists, but also among other persons engaged in medicine.

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