소아에서의 히라야마병 2예

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Two Cases of Hirayama Disease in a Pediatric Clinic

We report two pediatric cases with Hirayama disease—a 16-year-old boy with a left wrist drop and a 14-year-old-boy with weakness and muscle atrophy of right hand. Motor nerve conduction study revealed decreased motor nerve action potential amplitudes in the ulnar nerve and radial nerve of the affected hands. The former patient showed normal magnetic resonance imaging (MRI) of the cervical spine, but the latter showed mild, asymmetric thinning of the anterior spinal cord at levels C5 to C7. Following active rehabilitation and avoidance of neck flexion, no further progression of neurological findings was noticed. These clinical findings were typical of Hirayama disease. We show that timely and accurate diagnosis for Hirayama disease is possible with awareness of disease history, careful physical examination, and the use of neurophysiological studies and MRI studies.

Key Words: Hirayama disease, Juvenile muscular atrophy, Monomelic amyotrophy

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Introduction

Hirayama disease is an entity of "juvenile muscular atrophy of the unilateral upper extremity," and is a rare form of benign, self-limiting cervical myelopathy first described by Hirayama et al, in 1959¹⁾. The clinical diagnostic criteria as originally described by Hirayama include (a) weakness and wasting predominantly in C7, C8 and T1 myotomes in one upper limb or asymmetrically in both upper limbs, (b) Insidious onset in teens and early twenties, (c) initial fast progression for 1-3 years followed by arrest of disease or relatively benign course, (d) irregular coarse tremors in the fingers of the affected hand(s), (e) mild transient worsening of symptoms on exposure to cold, (f) electromyography evidence of chronic denervation in the clinically affected muscles, and (g) absence of substantial sensory loss/reflex abnormalities, cranial nerve, pyramidal tract in lower limb, sphincter, or cerebellar deficits²⁾.

Hirayama disease occurs mainly in Asian people, especially in Japan and India, in their teens and early twenties with a male predominance^{3,4)}. It differs from other classic types of motor neuron diseases due to its non-progressive course and pathologic findings²⁾. Hirayama disease is caused by forward displacement of the posterior cervical dural sac caused on neck flexion. Patients suffering from Hirayama disease are often accompanied by cold paresis and irregular tremor as well as insidious onset of muscular weakness and atrophy of the hands and

The poster of this report was presented at the symposium of the Korean Child Neurology Society. (2015.5.)

Submitted: 21 August, 2017
Revised: 13 September, 2017
Accepted: 14 September, 2017

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forearms including C7, C8 and T1 myotomal distribution (thenar, hypothenar, interossei muscles, wrist flexors and extensors), with relative sparing of brachioradialis muscle⁵).

Clinical features of Hirayama disease include symmetric or asymmetric progressive onset of muscular weakness and atrophy. Bilateral symmetric involvement occurs in about 10% of cases⁶. Some reports have shown that Hirayama disease can affect the proximal portion as an initial presentation or a secondary progression⁷. Symptoms are related to neck flexion and often exacerbated by cold weather³. Clinical courses are stabilized within five years in approximately 90% of cases⁴.

Avoidance of neck flexion is an effective therapeutic measure for Hirayama disease. Thus, early recognition of the disease and timely intervention have been shown to be effective in stopping disease progression. However, the disease is often left undiagnosed due to its rare occurrence. Here, we report two cases of Hirayama disease presenting as unilateral wrist drop in one case and unilateral upper extremity weakness in another.

Case reports

Case 1

A right handed 16-year-old boy visited our pediatric neurology clinic due to left wrist drop. One year before the visit, he started to feel tremor in his left 2nd-5th fingers. The tremor was progressive and at the time of visit, he could clench his fingers but had difficulties in opening his left hands and dorsiflexing his left wrist. The weakness was reported to be

worsened by playing computer games. There was no other history of trauma or infectious disease. On neurological examination, motor power of the left metacarpophalangeal, proximal, and distal inter-phalangeal joint extensor muscle was grade IV plus, which was weaker than that of the right side; also, atrophy of first dorsal interossei and abductor digit minimi was noticed. Other motor and sensory examinations were normal. Laboratory test results were normal for plasma electrolytes, chemistry, and MLPA (Multiplex Ligation-dependent Probe Amplification) analysis of PMP22 gene. Cervical spine magnetic resonance imaging was normal (Fig. 1A). A Motor nerve conduction study revealed decreased motor nerve action potential amplitudes in the left ulnar nerve and radial nerve (Fig. 2). Based on the diagnosis of Hirayama disease, the patient was educated to avoid neck flexion and subjected to active rehabilitation. At 6-months follow-up, we observed no further progression of the initial neurological findings.

Case 2

A previously healthy 14-year-old boy presented with insidious onset of weakness in the right hand. The patient experienced increasing difficulty to write correctly during the past 5 months. He felt no pain and sensory abnormalities. He was right-handed, and there was neither history of trauma nor family history of neuromuscular disease. During his physical examination, muscular wasting was evident in the thenar and midpalmar muscles of his right hand (Fig. 3) and weakness in the right flexor digitorum superficialis, opponens pollicis, first lumbrical, flexor carpi ulnaris, flexor digitorum profundus III & IV, flexor digiti minimi, adductor pollicis, 1st dorsal interosseous and 1st palmar interosseous, grade III of muscle power was noticed. There was no aggravation factor. No sensory disturbance was evident, and deep tendon responses were normal in all extremities. Laboratory tests showed normal results for plasma electrolytes and serum glucose. Magnetic resonance imaging of the neck revealed mild, asymmetric thinning of the spinal cord in the anterior horn at the level of C5 to C7 (Fig. 1B). A Motor nerve conduction study revealed decreased amplitude of compound muscle action potentials in right ulnar and radial nerves. The diagnosis of Hirayama disease was made on the basis of these findings, and the patient underwent rehabilitation treatments without medication. The rehabilitation treatments consisted of neutral neck positioning without cervical neck collar, and exercise for strengthening and coordination of fingers & wrists. Six months later, his writing ability was shown to be improved.

Fig. 1. Sagittal T2-weighted C-spine Magnetic resonance imaging (MRI) in Patient 1 (A) and Patient 2 (B). (A) Neutral position image showing no evidence of spinal cord signal change, abnormal enhancement, or disc herniation. (B) Neutral position image showing asymmetric mild thinning of spinal cord from C5 to C7 (arrows).

Fig. 2. (Patient 1) A Motor nerve conduction study revealed decreased motor nerve action potential amplitudes in the left ulnar nerve and radial nerve.

Fig. 3. (Patient 2) Muscular atrophy in a 16-year-old boy with Hirayama disease. Muscular atrophy is evident in the thenar and midpalmar muscles of the right hand (arrowhead).

Discussion

We report two patients who showed typical features of Hirayama disease. They were male in their mid-teens and visited our clinic with unilateral muscular weakness (one with wrist drop and another with writing difficulty) and atrophy. Based on their age and clinical symptoms, we suspected Hirayama disease. One patient complained that the symptoms worsened when he played computer games, which might be associated with neck flexion. Neither of them showed symptom exacerbation by cold

weather.

In 1982, the first autopsy case was obtained by Hirayama and his colleagues, representing anterior-posterior flattening of the lower cervical cord associated with ischemic and atrophic changes of the anterior horn cell⁽⁸⁾. The exact pathogenesis of the disease is still uncertain. Generally, it is known to be associated with a tight dural canal during neck flexion⁽⁹⁾. The relatively short and tight dura mater seen in patients with Hirayama disease cannot be compensated for the increased length of the vertebral canal during neck flexion. The tightened dural canal can cause spinal cord compression by forward displacement of the posterior dural sac⁽⁹⁾. The high incidence rates in Asian men and reports of familial cases suggest that genetic susceptibility may play an important role in the pathogenesis of Hirayama disease.

In patients with Hirayama disease, neither sensory nor pyramidal tract is involved⁽⁸⁾. Sensory nerve conduction study is generally within normal range, but motor nerve conduction study shows significantly reduced ulnar compound muscle action potential (CMAP) amplitude than the median one⁽¹⁰⁾. In MRI studies, dynamic imaging on neck flexion shows anterior shifting of posterior dura at the lower cervical spinal canal and neutral position (non-flexion) imaging shows unremarkable findings or asymmetric cord atrophy^(5,11). Focal cord atrophy in neutral neck position on MRI has been reported to have occur-

rence rate as high as 50–100%¹²). Thus, flexion cervical MRI may play a major role for making a diagnosis if MRI of neutral position appears normal and if other motor neuron diseases have been excluded^{5,13}). To achieve real dynamic spinal imaging, specialized equipment such as multi-positional MRI scanners is required. However, if these devices are not available, optimizing neutral and flexion cervical spine MRI scan can be performed by using standard MRI equipment¹⁴). In our cases, upon suspicion of Hirayama disease, we carried out laboratory tests, sensory/motor nerve conduction study, and cervical spine MRI to confirm. Laboratory tests and sensory nerve conduction studies were within normal range. In motor nerve conduction studies, decreased motor nerve action potential amplitudes in the ulnar nerve and radial nerve of the affected hand were observed. In imaging study, one patient had normal MRI of the cervical spine, but the other patient showed mild asymmetric thinning of the anterior spinal cord from C5 to C7. With their clinical presentations and study findings, we made the diagnosis of Hirayama disease. Although the first case showed no typical features of Hirayama disease in the neutral position neck MRI, we were able to make a differential diagnosis between Hirayama disease and other disease that can induce localized amyotrophy of the distal arm such as syringomyelia, motor neuron disease, cervical spondylotic myelopathy, spinal cord tumor, and traumatic myelopathy through routine neck MRI¹³). If a patient with focal hand wasting has normal findings in routine neck MRI, it may be useful to verify if neck flexion MR shows typical features of Hirayama disease¹³).

For patients with Hirayama disease, the most effective treatment is avoiding neck flexion by using neck collars, which significantly halts the disease progression¹⁵). In our case, the two Hirayama disease patients underwent active rehabilitation with avoidance of neck flexion. Following proper interventions, no further progression of neurological findings has been noticed. Thus, early diagnosis of the disease is critical for patients with Hirayama disease to implement early treatment.

In Korea, six cases have been reported from 2004 to 2016, but there was no nationwide survey. They were all male between ages from 15 to 29, and some of them showed atypical clinical features^{7,16-19}). Four of the six patients showed involvement of proximal upper extremities, while the other two showed involvement of distal upper extremities. Five of them showed unilateral involvement, and one showed bilateral involvement. One patient was 29-year-old who was diagnosed with Hirayama disease 9 years ago with no further progression of muscle weakness afterward. However, 8 years later, he visited a hospital with relapsed unilateral weakness of proximal upper limb. His

neutral position neck MRI findings showed no abnormal cervical vertebrae, and anterior shifting of the spinal cord during cervical vertebrae flexion was not observed⁷). This is consistent with the report which showed that abnormal MRI results are lessened or even disappear naturally¹²). Other five patients showed anterior displacement of posterior dural sac and/or segmental cord atrophy in neck flexion MRI. Five out of six cases have improved without any deterioration, and one relapse case was suggested to be vigilant against possible recurrence.

요약

히라야마병은 감각 및 중추신경계의 증상 없이 상지의 근위축과 근력약화가 진행되는 경추척수증으로 매우 드문 질환이다. 이에 저자들은 일측 손목 하수와 일측 근력약화, 근위축을 보인 소아에서의 히라야마병 2예를 보고하는 바이다. 첫번째 환자는 16세 남자로 좌측 손목 하수와 함께 동측의 2-5번째 손가락의 떨림이 진행되는 것으로 내원하였고, 신체진찰상 중수수지, 지질간관절의 근력약화, 배측골간근, 소지외전근의 근위축이 확인되었다. 두번째 환자는 14세 남자로 우측 손의 근력약화와 글씨를 바르게 쓰기 어려운 것이 진행하여 내원하였고, 신체진찰상 천지굴근, 모지대립근, 충양근, 척추수근굴근, 심지굴근, 소지굴근, 무지내전근, 배측골간근, 수장측골간근의 근력약화와 무지구근, 중간구근의 근위축이 확인되었다. 두 환자는 특별한 과거력은 없었고, 전해질 및 혈당 검사는 정상이었다. 운동신경전도검사에서 척골신경과 요골신경의 운동신경활동전위진폭이 감소하였고, 척추자기공명영상검사에서 전자는 정상이었으나 후자는 C5-C7의 앞쪽 척수가 약간 비대칭적으로 얇아진 소견이 확인되었다. 두 환자 모두 경추굽힘을 피하도록 하면서 재활치료를 받으면서 증상의 추가적인 진행은 없었다. 히라야마병은 유병률이 높지 않아 쉽게 간과되거나 오진될 수 있으나 조기에 진단하여 반복적인 경추굽힘으로 인해 병이 진행하지 않도록 예방할 수 있는 병이다. 그러므로 소아에서 감각이상 없이 원위부 근력 약화나 근위축을 보일 때 히라야마병의 가능성을 고려하는 것이 중요하겠다.

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