



Case Report

A Vietnamese Case of Hirayama Disease and Narrative Review of Literature

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Abstract

Hirayama disease is a rare form of myelopathy caused by dynamic compression of the spinal cord in flexion position of the neck. It is a benign and non-progressive condition affecting male adolescents and characterized by wasting of intrinsic muscle of the hands and forearms. This benign focal cervical poliopathy is caused by forward displacement of the posterior dura resulting in cord compression during neck flexion. We present the first reported Hirayama disease patient in Vietnam who was conservatively treated with hard collar and physiotherapy and had successful preliminary outcome. The true prevalence should be higher due to hidden pathological findings on neutral cervical MRI scan.

Keywords: Hirayama disease; Juvenile brachial spinal muscular atrophy; Juvenile asymmetric segmental spinal muscular atrophy; Juvenile muscular atrophy of the distal upper extremity; Monomelic amyotrophy; Oblique amyotrophy

Introduction

Hirayama disease (HD) or juvenile muscular atrophy of unilateral upper extremity was initially reported in 1959 by Hirayama et al. [11] this disorder was more frequently discovered in Asian countries and initially thought to spare Caucasian populations. However, there were increasing number of cases discovered in other non-Asian countries over time [8]. HD predominantly affects young male population (male/female ratio of 10/1). [10, 30] Most HD patients complain about asymmetric muscular atrophy in the hands and forearms, with relative preservation of the brachioradialis muscle. Most authors believed that the etiology of this disease is dynamic cord compression during flexion of the neck due to anterior displacement of the dura matter, resulting in the necrosis of neuron cells in the anterior horns of the grey matter. [9, 13, 11, 30] The true incidence of HD is speculated to be higher than reported in the literature as conventional cervical MRI scan in neutral position may overlook the pathology [3].

Case Presentation

A 17-year-old male patient went to our department with chief complaint of weakness and clumsiness of his right hand. This condition started 10 months prior to admission with slow progression. About 3 months ago, he noticed muscle wasting as well as decrease of grip strength and dexterity of his right hand, to the extent that he had difficulty with daily activity such as using chopsticks, buttoning and writing. He also complained of tremors of his fingers, more severe when being focused. There was no relevant past medical history and none of his family members experienced the same condition. No known allergies have been noticed by the patient.

Examination

Physical examination revealed normal vital signs and the body mass index was 19.8kg/m². Patient had no ulcers, scars or hypertrophied nerve were detected on examination of both elbows. Cranial nerve examination was within normal limits. On motor system examination, atrophy of intrinsic muscles (including thenar, hypothenar and interosseous muscles) of the right hand was noted (Figure 1 and 2). There was a relative preservation of brachioradialis muscles on both sides, with marked muscular

wasting of the ulnar part of the right forearm (Figure 3). Muscle power was normal in all the muscle groups in both upper limbs and lower limbs including intrinsic muscles of both hands. The Froment's sign, specific to ulnar nerve palsy was negative bilaterally. Deep tendon reflexes were normal and no pyramidal tract signs were detected. Sensory system examination showed normal pain, temperature as well as proprioceptive components. Polyminimyoclonus could be found in the right hand.



Figure 1: Dorsal aspect of both hands of patient. Note the marked atrophy of the interosseous muscles of the right hand when compared with the contralateral side.



Figure 2: Volar aspect of both hands. Note the atrophy of thenar and hypothenar muscles of the right hand when compared with the contralateral side.

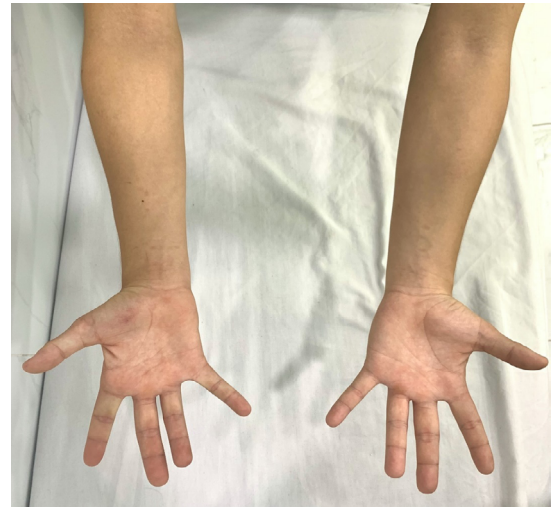


Figure 3: Forearms of patient. Note the atrophy of ulnar-side muscle of right forearm when compared with the contralateral side.

Investigations

Conventional cervical MRI in neutral position revealed no obvious compression of the spinal cord. However, the cord was suspiciously thin at C5, 6 and 7 vertebral levels with relative hyperintensity of the cord within the same area on T2 weighted sagittal scan (Figure 4). The hyperintensity mainly occurred in the right half of the cord on axial MRI, which corresponded to the clinical symptoms. Patient underwent a second cervical MRI scan in flexion position of the neck, and the latter depicted forward shifting of the spinal cord and collapse of the posterior dura, aggravated by venous engorgement resulting in compression of cervical cord at C5, 6 and 7 vertebral levels (corresponding to the aforementioned atrophied portion of cord) (Figure 4 and 5). Nerve conduction studies showed normal sensory nerve action potentials, reduced amplitude of right ulnar compound action potentials due to atrophy of muscles. Needle electromyography (EMG) revealed a neuropathic pattern like large-amplitude Motor Unit Action Potentials. Fasciculation, fibrillations and reduced recruitment was seen in both first dorsal inter-rosei, abductor pollicis brevis and adductor digiti minimi. Deltoid and Biceps needle EMG was normal.



Figure 4: T2 Sagittal MRI of cervical spine in neutral position (left image) and in flexion (right image). The atrophied cord with hyper intensity and without obvious compression could be seen in neutral position of the neck. In contrast, when the neck is flexed, the posterior dura displaces anteriorly and compresses the cord against the vertebral bodies in the front. Note the flow-void of venous engorgement within the epidural space when the neck is flexed.

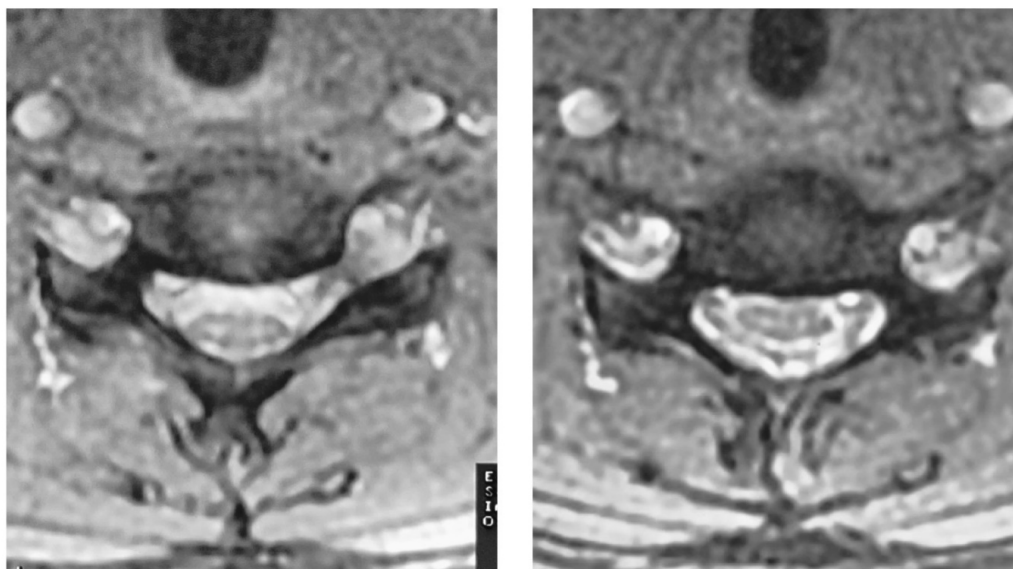


Figure 5: T2 axial MRI of cervical spine in neutral position (left image) and in flexion (right image) at C5-6 discal space. Note the cord atrophy with hyperintensity predominantly on the right side. In contrast, when the neck is flexed, both the cord and posterior dura displace to the front and the cord is flattened due to compression. The epidural space, absent on neutral MRI, becomes visible with marked thickness on flexion MRI.

Treatment

After discussing with patient and his family in regards to the etiology, benign evolution and possible solutions as well as outcome of his condition, conservative treatment with hard collar was given. Physical exercises including hand, wrist and neck extensor muscles enhancement was indicated to our patient in order to restore the muscle volume of the affected areas as well as stabilize the cervical spine.

Outcome and follow-up

On follow-up visit after 3 months, the patient had a positive feedback in regards to decreasing tremor and better handgrip strength. However, there was no change in hand muscle volume. Despite the tropical weather in our country, his reported compliance with collar was good and both him and his family considered surgical treatment as the last resort.

Discussion

Hirayama disease is known by many other names including benign juvenile brachial spinal muscular atrophy, juvenile asymmetric segmental spinal muscular atrophy, and juvenile muscular atrophy of the distal upper extremity, monomelic amyotrophy, and oblique amyotrophy. This condition was first described by Hirayama et al in 1959, with a series of 12 cases with new clinical presentation of progressive and degenerative motor neuron disease. [11] After this discovery, a number of similar cases have been reported in Japan and other Asian countries. [1, 4, 9, 11, 22, 31] A smaller number of HD patients were reported from Europe and North America, suggesting possible ethnical or regional contributing factors to the etiology of HD. [8, 17, 25] In the 1960s and early 1970s, confirmed diagnosis relied on clinical features and electrophysiological evaluation. The true pathology remained unclear until 1982, the first autopsy case was done by Hirayama and colleagues. The pathological result was anterior-posterior flattening of the lower cervical cord associated with ischemic and atrophic changes of the anterior horn cells, suggesting the vascular origin of the disease. [13] In the late 1980s, imaging studies with the application of MRI and CT scan (in neutral and flexion position of the neck) revealed the forward displacement of the posterior dura, causing anterior-posterior flattening and atrophy of the lower cervical cords. This finding corresponded to the “tight dural canal theory in flexion”, proposed by Iwasaki et al in 1987. [16] According to the latter, the superior anchors of the posterior dura to the lamina were insufficient in HD patients and therefore, during neck flexion, the dura mater would collapse and displace anteriorly which in turn compressed the cord. In line with that theory, Toshio speculated that the “loss of dorsal dural attachment from the pedicle due to immunological abnormalities of the dura and posterior ligaments” resulted in the dehiscence

of the dura mater from the neural arch during neck flexion and gave space to the venous engorgement and the latter aggravated the cord compression. [6] The repetitive subclinical trauma and micro-ischemia of the anterior horn of the cord due to multiple displacement of the cord and the dura during neck motion become permanent and correspond to the clinical features of HD. The natural fulcrum of the entire cervical spine locates at C5-6 discal space [29] and this is where the cord is compressed the most during neck flexion in HD patients. [12, 23, 24] This could somehow explain why the clinical symptoms occurred within the cord area from C7 to T1 myotomes and the upper levels are usually spared. Hirayama postulated the “stagnation of the posterior epidural venous plexus” as contribution factor of cord compression [20] and venous engorgement also disturbed the microcirculation and aggravated the local ischemia within the cord [14].

HD affects predominantly male population, with male/female ratio approximately 10/1. [30] HD often has an insidious onset at puberty with slow progression in the next 2 to 5 years before reaching the plateau phase. [30] Most patients have stabilizing condition in their late 20s. [30] The starting time of HD corresponded to the growth spurs of juvenile males in Japan, and this reinforced the theory of “growth imbalance between the vertebral column and dural canal”. [30] One hallmark of HD is that in the majority of cases, the condition including weakness and muscle atrophy is unilateral or at least asymmetric. To be specific, the HD affects predominantly the right-hand side muscles, regardless of the hand dominance. Bilateral HD was considered as severe form with poor prognosis [7].

The most affected muscle groups are the intrinsic muscles of the hand including thenar, hypothenar and interosseous muscles. The forearm muscles are also target of HD except the brachioradialis in most cases and that pattern gives the name “oblique amyotrophy” to HD. [31] Weakness of the wrist and finger movements is often reported by the patient, owing to the involvement of the C7-T1 cord portion. However, it is not pure weakness due to neurological deficit but rather the incapability of synchronizing the action of different small muscles during delicate motion of the hand, which is frequent in cervical myelopathy. Therefore, patients usually have difficulties in controlling their fingers to perform precise tasks and lose their dexterity. More proximal muscle groups (from elbow to shoulder) of the upper limbs are mostly unaffected. Sensory exams often reveal no abnormality as the cord lesion located mainly in the anterior horn of the grey matter. Pulses are normal with good capillary refill. No long tract signs are present, except in severe and rare forms of HD [30].

The gold standard of diagnosis of HD is dynamic MRI scan with the neck in flexion position. [3, 21, 23, 24] The typical imaging findings is anterior shifting of the cervical cord and the posterior dura matter with venous engorgement. In healthy

individuals, there is also a displacement of the cord and the dura during cervical movement, however this physiological translation is mild and has minimal effect on the cross-sectional area of the dural sac.[19] In HD patients, due to the laxity of attachment of the dura to surrounding structures, that displacement becomes pathological when the cord is severely compressed between the vertebral bodies in the front and the dura in the back. The chronic compression of the cord may lead to permanent cord damage in the form of atrophy and hyperintensity detected on T2 MRI scans. [24] One suspicious sign suggesting HD on neutral sagittal T2 MRI scan is cervical cord atrophy without obvious compression or other pathological reasons, especially when the lesion location is around C5, 6 and 7 levels and the condition occurs in young male teenagers. [27] Most authors recommend routine dynamic MRI to unveil hidden pathologies like HD. [3, 23] The “snake eye” sign on T2 sagittal MRI is considered as indication of poor prognosis [21].

Electromyogram (EMG) and nerve conduction study (NCS) are helpful in diagnostic protocol of HD, especially when they can help to differentiate HD from other mimic conditions. EMG and NCS show significant findings in the C7, C8 and T1 innervated muscles. NCS has intermittently demonstrated decreased compound muscle action potential (CMAP) amplitude, most noticeable in the median nerve. The low ulnar/medial compound motor action potential within C7-T1 myotomes is very helpful in differentiating it from other mimics. [26] EMG findings indicate chronic denervation seen as a high amplitude of action potential with prolonged duration, without active denervation (absence of positive sharp waves or fibrillation potentials), and no resting fasciculations in the C7, C8, and T1 innervated muscles. “Reverse split hand syndrome,” which shows decreased/absent CMAP amplitude in the abductor digiti minimi while preserved in the abductor pollicis brevis, is observed in Hirayama disease helps to differentiate it from amyotrophic lateral sclerosis, which shows “reverse hand syndrome”. [5] The progression of the lesion is associated with progressive decrement followed by loss of the F wave [2].

For treatment, conservative approach with physiotherapy and hard collar should be the first choice, even in cases with long onset duration. HD is a self-limiting condition with insidious onset, followed by a progressive phase in the first 2 to 5 years, then a plateau phase when the patient’s condition stabilizes. Hence, hard collar using is encouraged in at least 2 years during growth spurts in order to protect the cord from being more damaged during cervical flexion. Surgical intervention is reserved only for more advanced, severe or refractory cases. Huashan et al [28] have proposed a clinical classification for treatment guiding purpose. He divided HD patients in three types:

Type 1: Atrophy of hand and forearm muscles or asymmetric bilateral atrophy in upper limbs. Type 1 is further divided into 2 subtypes based on clinical evolution: 1a (stable) and 1b (progressive).

Type 2: Atrophy with present of pyramidal tract sign.

Type 3: A typical with atrophy of proximal upper limb muscle or symmetric upper limbs or presence of sensory dysfunction.

Conservative treatment usually suffices for type 1 and 3 patients, whereas surgery is often indicated for type 2 cases. Based on surgical approach, there are 2 types of operations applicable for HD patients. The first type of surgery is anterior cervical discectomy and fusion. [18] The main principle of this approach is similar to hard collar use: no cervical flexion is equivalent to no dynamic compression and no further neurological deterioration. The downside of this approach is sacrificing the motion of the lower cervical spine. The second type of surgery is posterior approach with laminoplasty and duroplasty with tenting suture. [15] According to the latter technique, the “tight dural canal theory” and the laxity of posterior attachment of the dura are considered as pathological origin and therefore, enlarging the dural sac and reattaching it firmly to the lamina could sustainably protect the cord without immobilizing the cervical spine. The disadvantages of the posterior approach include technical demanding operation, CSF leakage and risk of meningitis. A meta-analysis study in 2021 found no difference between the two aforementioned modalities and the chosen technique should be based of surgeon’s preference and experience [26].

Our patient represents a typical case of HD, from clinical to imaging presentations. He is classified as type 1 according to Huashan classification with the best prognosis. [28] Given his young age and mild to moderate symptoms, our first choice is conservative treatment. The result of non-operative method highly depends on the compliance of patient, as wearing hard collar all day could be challenging in tropical countries like Vietnam. Hitherto, the condition of our patient seems to stabilize and therefore conservative treatment with hard collar appears to be a reasonable choice.

Learning points

- HD is a rare condition affecting young male individuals with hand muscle wasting and weakness as characteristic clinical symptoms.
- The clinical pattern is asymmetric in most cases, with right-hand side predominantly affected.
- Diagnosis based on clinical presentation, epidemiologic factors and dynamic MRI findings.
- HD is considered as benign with self-limiting tendency, usually suitable for conservative treatment.

- In some rare forms with aggressive evolution and severe neurological deterioration, surgical intervention is required to protect the cord from further damage.

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