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Hirayama Disease: A Case Report

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Abstract **Case Report**

Hirayama disease is a rare non-progressive spinal muscular atrophy related to flexion movements of the neck. It is considered a benign motor neuron disorder with a stationary stage after a progressive course. We report a case of an 18-years old male with a history of asymmetric weakness and amyotrophy of the distal right upper extremity, suggestive of Hirayama disease. Magnetic resonance imaging (MRI) of the cervical spine was obtained both in flexion and neutral position. MRI showed loss of cervical lordosis with focal areas of lower cervical cord atrophy with increased T2 signal intensity of the spinal cervical cord in a neutral position and anterior displacement of the detached posterior dura from the underlying flexion position.

Keywords: Hirayama disease, spinal muscular atrophy, cervical cord, dynamic MRI.

INTRODUCTION

Hirayama disease is a rare clinico-radiological diagnosis characterized by distal asymmetric weakness and wasting of upper extremities mainly affecting the C8-T1 or C5-C7 segmental myotomes. It is mostly sporadic and occurs in young adults with a male predominance. It is often presenting with a predominantly unilateral upper extremity weakness and atrophy in the hand and forearm with sparing of the brachioradialis, giving the characteristic appearance of oblique amyotrophy, cold paresis, and no sensory or pyramidal tract involvement. The amyotrophy is unilateral in most patients, asymmetrically bilateral in some and rarely symmetric. A spectrum of diagnostic magnetic resonance imaging (MRI) features has been described in the literature including neutral and flexion positions.

OBSERVATION

We present the case of an 18-year-old male admitted with a history of progressive weakness and amyotrophy of distal upper limb muscles, which was slowly progressive. The patient denied the presence of any sensory disturbance. There was no history of a recent injury, nor was there any family history of neuromuscular disease. Physical examination showed wasting of the intrinsic muscles of the right hand (Figure 1). There was no fasciculation observed. Sensation and tendon reflexes were intact. Because of the clinical suspicion of Hirayama's disease, the neurologist requested an MRI of the cervical spine. Images were acquired on a 1.5 Tesla. The MRI protocol included imaging in the neutral position followed by imaging in hyperflexion (Figure 2). A neutral MRI of the cervical spine showed loss of cervical lordosis, focal atrophy of the lower cervical cord, and associated increased T2 signal intensity of anterior horns was noted at C6/C7 levels. Flexion MRI demonstrated anterior shifting of the posterior dura, with subsequent cervical cord compression. The posterior epidural space was markedly enlarged.

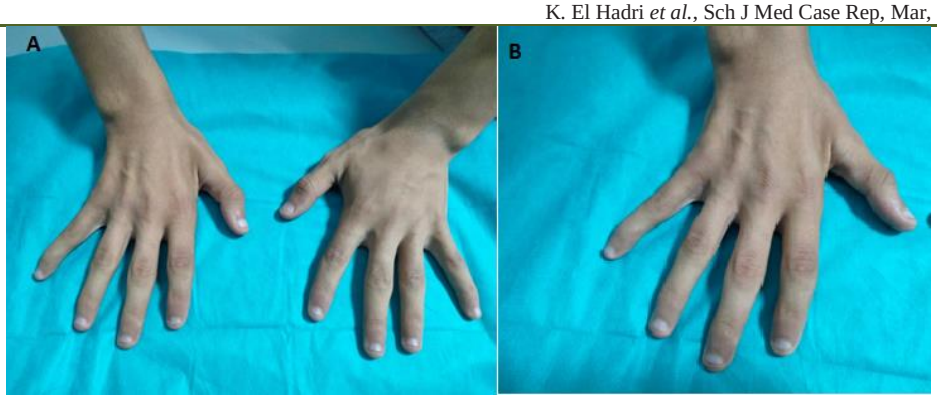

Figure 1 (A and B): Amyotrophy of the dorsal interosseous muscles of the right hand

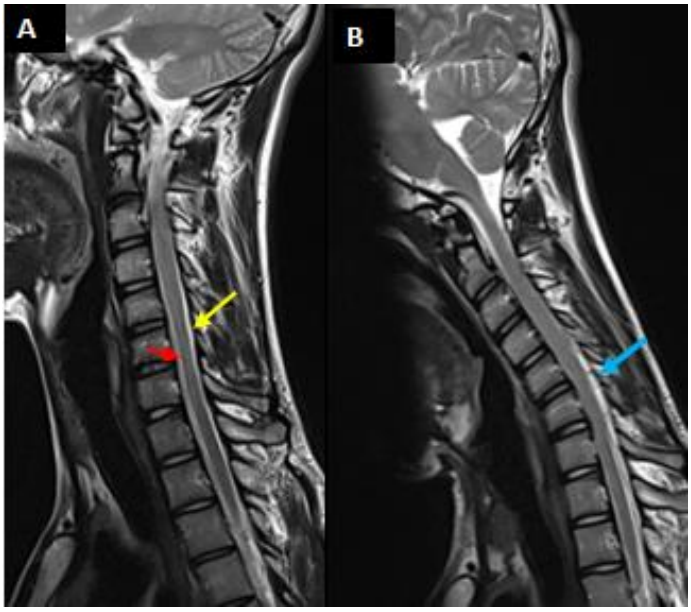

Figure 2: Sagittal T2 weighted MRI of the cervical spine in neutral (A) and neck flexion position (B). Neutralposition (A) of the cervical spine show loss of cervical lordosis, focal atrophy of the lower cervical cord (yellow arrow) and associated increased T2 signal intensity of anterior horns were noted at C6/C7 levels (red arrow). Flexion position (B) demonstrates anterior shifting of the posterior dura, with subsequent cervical cord compression. The posterior epidural space was markedly enlarged (blue arrow).

DISCUSSION

Hirayama disease (HD) also known as "juvenile muscular atrophy of distal upper extremity" (JMADUE), was initially recognized in Japan in 1959 by Hirayama *et al.*, [1].

The disease affects young people and adolescents ranging from 15 to 25 years of age, predominantly men. However, it has also been reported in pediatric and old age groups [2, 3]. Tashiro and colleagues suggested that the difference in the male and female incidence of the disease could be explained by a more rapid increase in height of males at puberty compared with females [4].

To date, the exact etiopathogenesis remains unclear and is strongly debated [5]. The main hypothesis is that HD is myelopathy related to flexion movements of the neck, during which there is a forward displacement of a tight dural sac compressing the cervical cord. The compression would lead to an increased intramedullary pressure causing a microcirculatory disturbance in the anterior horn [5].

Hirayama *et al.*, speculated that disproportionate growth between the vertebral column and its canal contents during a growth spurt could cause a tight dural sac leading to flexion myelopathy [1]. Kira J *et al.*, proposed atopy and elevated serum immunoglobulin E levels as participating factors [6]. Involvement of the intrathecal immune/inflammatory process was proposed by Tanaka *et al.*, [7], which revealed intrathecal upregulation of IFN- gamma and MIP-1beta in HD patients. In 2010, Ciceri *et al.*, proposed that venous congestion in flexion might play an additional role in determining spinal cord ischemic changes. Venous engorgement is thought to be secondary to impaired venous drainage toward the jugular veins during neck flexion and an increased flow to the posterior internal vertebral venous plexus resulting from the negative pressure in the posterior

epidural space because of anterior shifting of the dura [8]. Gamez *et al.,* revealed no relationship between HD pathogenesis and SMN1/SMN2 genes, associated with some motor neuron diseases [9].

Hirayama disease is non-familial in most patients. However, there are a few reports of familial cases. There are no published reports regarding genetic information that may be related to familial Hirayama disease. The explanation for the familial occurrence is indeed interesting and needs further studies [4].

Since HD was first reported, clinicians have continuously updated their understanding of the clinical manifestations of the disease which comprise five primary symptoms [10]:

- Distal weakness and wasting, predominantly on the ulnar side, in one upper extremity or asymmetrically in both upper extremities [10]. Predominant wasting of the ulnar part of the hand leads to the 'reverse split hand sign' that differentiates HD from amyotrophic lateral sclerosis (ALS), this occurs because the anterior horn cells that innervate the ulnar aspect of the upper limb are preferentially affected. Also, preferential medial forearm involvement with the sparing of brachioradialis leads to 'oblique amyotrophy [11].
- Insidious onset between the age of 10 years to early 20s with gradual progression over 3–5 years and followed by quiescence [10, 11].
- Tremors, which are irregular and coarse in the affected fingers, with polyoclonus [11].
- Transient symptomatic worsening in a cold climate. This is attributed to ongoing denervation blocking the conduction of the muscle fiber membrane in reinnervating muscles [12].
- Absence of objective sensory loss [10, 11].

HD also may manifest with some atypical features as given below:

- **Pyramidal Signs:** Hyperreflexia and inverted reflexes can be a feature in some patients due to severe cord involvement [12, 13].
- **Atrophy of the Muscles of the Proximal Upper Extremity:** The lower cervical cord C7–T1 is mainly affected in HD, hence the atrophy usually involves the distal upper limbs. However, in not a few reported cases the symptoms emerge proximally [14, 15].
- **Sensory Involvement:** Sensory tract involvement due to compressive myelopathy can cause sensory deficits in some patients with HD. Tashiro *et al.,* reported that 19.2% of patients had sensory impairment [15].
- **Long Disease Progression:** Most patients progress over 3–5 years and the disease plateaus after that. However, there have been reports of disease progression beyond 10 years [8].

The most important diagnostic tool in evaluating a patient with suspected HD is a dynamic MRI of the cervical spine in two positions: neutral and flexion [16, 17]. The characteristic findings on the neutral position are:

- Asymmetric cord flattening and localized lower cervical cord atrophy due to compression by the tight posterior dural wall, mostly at the C4 to C7 level [15].
- Abnormal cervical curvature (straight or kyphotic cervical spine alignment) [10].
- Loss of attachment between the posterior dural sac and the subjacent lamina (however, this is considered a neck- flexion MRI sign in some studies because it also manifests in normal people when they are in the cervical neutral position) [19].
- Non-compressed intramedullary high signal intensity on T2-weighted imaging (T2WI). Symmetrical bilateral high-signal-intensity lesion on axial T2WI is found in some HD patients; this sign has been termed "snake-eye appearance" [20]. Furthermore, the presence of a snake-eye appearance indicates an irreversible lesion, a poor prognosis and the need for timely surgical intervention [21].

Neck-flexion MRI is considered the most important imaging examination for the diagnosis of HD. Although there are no optimal flexion requirements for cervical-flexion MRI, a cervical flexion angle of 35◦ is recommended to achieve the best appearance and an accurate diagnosis [22]. In HD, lower cervical cord flattening and atrophy are presented similarly to the neutral position [23]. Another hallmark sign is the forward displacement of the spinal cord due to the presence of a shorter dural sac [10]. The disproportionate distance between the vertebrae and their contents due to the juvenile growth spurt and the suspended dura mater anchored only at C2 to C3 and coccyx results in tightness of the dural sac during neck flexion, causing forward displacement of the posterior wall of the cervical dural sac followed by forward displacement of the cervical spinal cord and cord flattening. Consequently, microcirculatory disturbances in the region served by the anterior spinal artery caused by long-term compression bring about ischemia and necrosis of anterior horn cells; as a result, the cord appears thin due to atrophy. In addition, a crescent-shaped high-intensity mass with curvilinear flow-void signals inside it appears in the posterior epidural space during neck flexion. The mass disappears when the neck returns to its normal position, revealing congestion of the venous plexus rather than vascular malformation or tumors [4]. The congestion of the venous plexus is due to the three factors discussed above.

Postgadolinium T1 fat-suppressed images show an enhanced posterior epidural venous plexus with flow voids within it at the affected levels of the spinal cord and asymmetric flattening of the affected hemicord [24].

Diffusion tensor imaging (DTI) can not only evaluate the cord injury but also guide the level at which surgery must be performed [11].

Functional imaging is an important consideration for future research. Functional MRI employing the blood oxygen level-dependent technique was studied in 17 patients with HD who underwent cervical decompression with fusion surgery [25]. Patients were imaged before surgery and then at different intervals post-operatively. The study revealed ipsilateral motor cortex activation when the affected hand was used compared with the unaffected hand. The activation was reduced following surgical fixation [25].

Electrophysiologic studies are critical in supporting the diagnosis and differentiating various HD mimics [10]. The EMG changes are confined to the C7–T1 myotomes [26]. The characteristic EMG findings include fibrillations and positive sharp waves in those with ongoing denervation and large amplitude, long duration, polyphasic, motor unit action potentials with moderate to discrete recruitment in patients with the long-standing disease [27].

CONCLUSION

HD is a rare benign disease that leads to weakness and atrophy of unilateral or bilateral hand muscles, commonly encountered in young males. The pathogenesis of HD is still unknown. Dynamic MRI confirms the diagnosis in a clinically suspected patient. Electrophysiologically, HD is mainly characterized by neurogenic damage without abnormal nerve conduction velocity. Treatment mainly aims to reduce neck flexion; therefore, long-term cervical braces are the mainstay. Surgical treatment is employed in patients who progress with conservative treatment, but the best approach is still debated. Further studies are needed, including genetic studies to unravel the exact HD pathogenesis to develop more effective treatments.

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