# Hirayama Disease: A Rare Case Report and Literature Review

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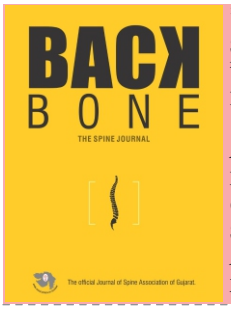
## Abstract

Hirayama disease is a rare neurological condition and is characterized by a sporadic juvenile muscular atrophy of distal upper extremity in young males. The disease is more prevalent in Japan and other Asian countries, though a few cases have been reported in Western countries as well. It manifests as a self-limiting, gradually progressive atrophic weakness of forearm and hand. The anterior displacement of posterior dura during neck flexion leading to cervical cord atrophy has been hypothesized. We discuss a case of a 21-year-old male patient with progressive distal upper extremity weakness, diagnosed with Hirayama disease, and literature review for the same.

**Keywords:** Hirayama Disease, Juvenile muscular atrophy, Monomelic amyotrophy

## Introduction

Hirayama disease was first described by Hirayama and colleagues in 1959. It is characterized by sporadic, insidious-onset, slowly progressive, asymmetric weakness of distal upper extremity, sparing brachioradialis muscle. Hirayama disease is also known as "juvenile muscular atrophy" and "monomelic amyotrophy". It predominantly affects C7-T1 myotomes. The disease occurs commonly in unilateral upper limb, although bilateral upper limbs and occasionally lower limb affection have also been reported. Young males in 2nd and 3rd decades of life are commonly affected. It is a self-limiting disease which ceases to progress after 1-3 years of onset. The exact etiopathogenesis is still unknown. The most widely accepted hypothesis is cervical myelopathy caused due to repeated neck flexion, which leads to anterior shifting of the posterior cervical dura and compression of anterior dura against vertebral body. The key to diagnose Hirayama disease is a high index of suspicion, EMG-NCV studies and dynamic MRI studies. There are no specific guidelines for the treatment of Hirayama disease. Since it is a self-limiting condition, a collar to avoid neck flexion can arrest the progress and lead to clinical improvement. Adjuvant physiotherapy can help prevent stiffness. Surgery is warranted in advanced disease where myelopathy has progressed.

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## Case report

A 21-year-old right-handed male patient presented in out-patient department with gradually progressive weakness in right forearm and right hand for 3 months. He had sustained a right forearm fracture 10 years ago. He was a manual labourer by profession, where his work profile included repeated neck flexion and lifting heavy weights. There was no recent history of trauma. He had no associated neck pain or radiculopathy. There was no gait disturbance. He had not taken any treatment since the onset of symptoms. He had no lower limb or bowel/bladder complaints. On clinical examination, there was wasting of right forearm in the ulnar half (Figure 1). Brachioradialis bulk was normal. There was thenar and hypothenar wasting. The power in each muscle groups is shown in table 1. There was no sensory loss or autonomic dysfunction. The patient had a coarse, irregular tremor in his right hand, more pronounced in the right thumb and index finger. There were no upper motor neuron signs. There was a flexor plantar response and bilateral lower limb jerks were normal. Hoffman's sign was negative. Upper limb reflexes were also normal on both sides. Spurling's maneuver was negative.

EMG-NCV showed features suggestive of motor neuron disease with C7-C8 segments most affected. Dynamic MRI of cervical spine revealed the classic crescent sign (Figure 2) in neck flexion.

There was significant anterior shifting of the posterior cervical dura with neck flexion, measuring 4.2 mm at the apex of

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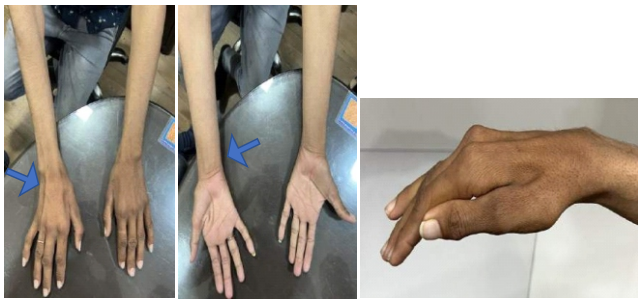

**Figure 1**: (a, b, c): Classical clinical features in the affected limb (thick arrow) showing wasting of forearm muscles except brachioradialis (oblique amyotrophy) as well as wasting of thenar and hypothenar muscles.

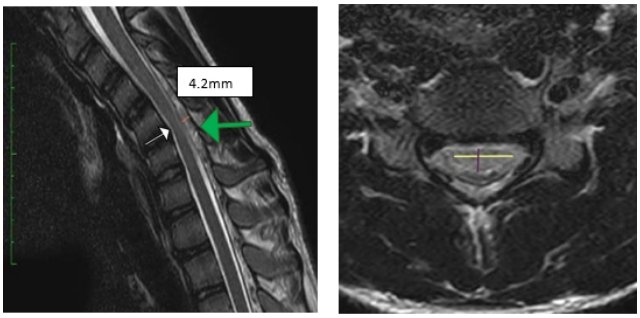


**Figure 2**: MRI of cervical spine in flexion. Sagittal T2-weighted image (a) shows crescent shaped mass (green arrow) in the posterior epidural space, which is due to 4.2mm anterior shifting (orange line) of the posterior cervical dura and compression, flattening, atrophy and myelomalacia of the cervical cord at the apex of kyphosis (white arrow). Axial image (b) at the same level shows severe cord flattening.

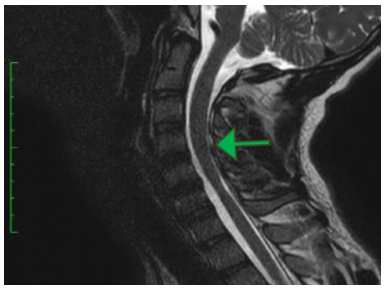

**Figure 3:** T2-weighted sagittal MRI of cervical spine in extension shows complete disappearance (green arrow) of the crescent shaped mass as the neck is moved from flexion to extension position.

cervical kyphosis. The cervical cord showed flattening and atrophy at C5-C6 levels with myelomalacia. The crescent disappeared with neck in neutral and extension positions (Figure 3). The AP and transverse diameters of the cervical cord at the maximum affected level were 4.8 mm and 12.6 mm respectively.

In view of the patient's clinical presentation, EMG-NCV and MRI studies, a diagnosis of Hirayama disease was made. The patient was advised a cervical collar and to avoid activities which required repeated neck flexion. (The patient provided an informed and written consent for his participation in the study, including sharing of his clinical photographs and radiological images with due care to maintain his privacy.)

| Muscle group | Power (Right side) | Power (Left side) |
|---|---|---|
| Shoulder | 5/5 | 5/5 |
| Elbow Flexors | 4/5 | 5/5 |
| Elbow Extensors | 4/5 | 5/5 |
| Wrist Flexors | 3/5 | 5/5 |
| Wrist Extensors | 4/5 | 5/5 |
| Finger Flexors | 3/5 | 5/5 |
| Finger Extensors | 1/5 | 5/5 |
| Finger Abductors | 1/5 | 5/5 |
| Finger Adductors | 1/5 | 5/5 |
| Opposition | 1/5 | 5/5 |

**Table 1:** Muscle charting of bilateral upper limbs

## Discussion

Hirayama disease (HD) was first described by Hirayama and his colleagues in 1959 [1]. They reported 12 cases of a new clinical entity of juvenile muscular atrophy of the distal upper limb. 71 identical cases were then detected in Nagoya University, Japan by Sobue et al [2]. Gourie-Devi and her group named this clinical entity "monomelic amyotrophy" in 1984 [3]. Hirayama disease is more prevalent in Japan, India, and other Asian countries. However, cases have been reported in western countries such as Denmark [4], Netherlands [5], Canada [6] and USA [7] as well. In 2000, Hirayama termed it "Juvenile Muscular Atrophy of Distal Upper Extremity" (JMADUE) [8,9].

HD is characterized by insidious onset, slowly progressive, asymmetrical weakness and wasting of distal muscles of upper extremity, predominantly affecting C7-T1 segmental myotomes and sparing the brachioradialis muscle. As a rule, brachioradialis is not affected (oblique amyotrophy). The onset is usually in 2$^{nd}$ and 3$^{rd}$ decade, and males are more commonly affected [10]. The disease has a self-limiting course, and the disease progression usually stops withing a few years, rendering the disease relatively benign [1, 11]. It may also manifest as irregular tremors (minipolymyoclonus) in the fingers of affected hands, with transient worsening of symptoms on exposure to cold ("cold paresis") [12]. Sensory, reflex, and cranial nerve examination is usually normal. Upper motor neuron signs, lower limb weakness and autonomic

dysfunction are rare. However, with severe cord atrophy, upper motor neuron signs and gait disturbance may be present. In their study, Hassan et al. demonstrated autonomic involvement in 36% and UMN lesion in 18% of their cases [13].

The incidence of HD is very low, and it is very rare in clinical setting. Tashiro et al. [14] laid down the following criteria for its diagnosis: (a) predominant unilateral distal muscle weakness and atrophy in forearm and hand (b) onset between 10-20 years of age (c) insidious onset, slow progression, gradual stabilization of symptoms (d) no lower limb involvement (e) no sensory or autonomic disturbances, no upper motor neuron lesion (f) exclusion of other motor neuron diseases. Although it is predominantly unilateral, cases with bilateral upper limb involvement have also been reported [15].

The exact etiopathogenesis of HD is still unknown. In 1987, a pathological study was done for the first time by Hirayama and his colleagues, in which they demonstrated autopsy findings in a patient suffering from HD, who died due to lung carcinoma [16]. They showed varying degrees of cell shrinkage and necrosis, degeneration of neurons, gliosis, and circulatory insufficiency in anterior horn cells of the cervical cord at affected levels. Atopy and elevated serum IgE levels have been postulated to be precipitating factors for HD [17]. Tanaka et al. showed the upregulation of proinflammatory cytokines and chemokines in CSF of patients with HD, indicating the possibility of intrathecal immunological process in the pathogenesis of HD [18]. The hypothesis proposed by Kikuchi et al. is most widely accepted [19]. The spinal dura mater is loosely attached to the vertebral canal by nerve roots and periosteum at foramen magnum. The posterior cervical dura is short and tight in patients with HD. With neck flexion, the length of the vertebral canal increases, but the tight dura is not able to compensate. This causes anterior shift of the posterior cervical dura and resultant compression of the anterior cervical cord against the posterior part of vertebral body. Repeated neck flexion leads to cumulative ischemic damage to the cervical cord over time, eventually causing myelopathy. Furthermore, the anterior shift of posterior cervical dura causes microcirculatory disturbances in the distribution of anterior spinal artery and anterior portion of the cord [20]. This is further supported by 3D finite element studies of the spinal cord done in neutral position, and 5 and 10 degrees of flexion, which showed that the stresses in the grey matter and white matter, especially in the anterior cord increased significantly in flexion positions, similar to those seen in cervical flexion myelopathy [21].

The diagnosis of HD is made from characteristic clinical features, NCV studies and dynamic MRI of the cervical spine. Conventional X-rays of the cervical spine usually show no abnormalities. MRI of cervical spine in neck flexion is the key to diagnosis of HD, which shows forward displacement of posterior cervical dura and a well-enhanced crescent-shaped mass in the posterior epidural space of lower cervical canal, which may extend into the upper thoracic region. This crescent-shaped mass disappears as the neck moves into a neutral and extension position [19]. The crescent shaped mass is the congested posterior epidural venous plexus, which shows enhancement on contrast MRI scans. The quantification of anterior displacement of posterior dura is important as this phenomenon also occurs in normal individuals [22]. The forward shift is about 1mm in normal individuals as compared to about 6.5-7 mm in individuals with HD [23]. There is also asymmetric flattening and atrophy of the lower cervical cord [20]. MRI in late stages of HD shows "snake-eyes appearance" (SEA), which is a unique symmetrical, small, high intensity, lesion seen in T2-weighted axial images of the affected cervical spine segments. SEA indicates poor prognosis and is associated with upper motor neuron signs, gait disturbances and lower limb involvement [24]. SEA occurs due to irreversible destruction of the gray matter along with severe neural loss in the anterior horn cells [25].

EMG-NCV also shows evidence of chronic denervation in affected muscles. Normal muscles also may show abnormal EMG findings. "Reverse split hand syndrome" is a feature of HD which is characterized by decreased or absent compound muscle action potential (CMAP) in the abductor digiti minimi but preserved CMAP in abductor pollicis brevis. Whereas in ALS, the CMAP shows a classic "split hand syndrome" pattern [26].

The differential diagnosis for HD includes amyotrophic lateral sclerosis (ALS), post-polio syndrome, multifocal motor neuropathy, toxic neuropathy, brachial plexopathy and structural lesions of the cervical cord (e.g., Syringomyelia) These can be differentiated by characteristic clinical features, radiological findings, and electrophysiological features [1]. The ulnar/ median (U/M) nerve CMAP ratio can help differentiate between these disorders. A low U/M CMAP is suggestive of HD, whereas a high U/M CMAP ratio is suggestive of ALS [27]. Anterior tephromalacia of Marie and Foix, now commonly referred to as "Foix-Chavany-Marie" syndrome is also one of the differential diagnoses for HD [28]. Unlike HD, this syndrome is caused due to thrombo-embolic strokes leading to vascular insufficiency in various lobes on the brain.

## Conclusion

HD is a self-limiting condition. The natural course of HD is insidious onset, slow progression for a few years and later,

stabilization. Prevention of neck flexion can help arrest the disease process in early stages. Hence, early diagnosis is the key to prevent severe disease. Decompression and surgical stabilization with neck in extension may be required in cases with rapid progression or with severe myelomalacia.

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**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

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