

Hirayama Disease - A Fresh Look into an Old Disease

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Abstract: *Hirayama disease is insidious onset gradually progressive, unilateral or asymmetric atrophy of the hand and forearm seen frequently in young males especially from the Asian continent. Pathophysiologically, it is now known that Hirayama disease is not likely to be a motor neuron disease as it was once thought to be, but as a result of 'Cervical flexion induced Myelopathy.' MRI with flexion contrast studies for prompt recognition and early institution of cervical therapy to prevent progression are very important to limit disability in these individuals.*

Keywords: Hirayama Disease

1. Introduction

Hirayama et al in 1959 reported an entity - "juvenile muscular atrophy of the unilateral upper extremity" from Japan [1]. They published 12 cases of this disease which at that time they thought to be a type of progressive and degenerative motor neuron disease. These patients were predominantly young men (teens and early twenties) presenting with an insidious onset of unilateral weakness and muscle wasting involving distal part of the upper limb. These complaints progressed for a variable period and then the progression arrest spontaneously within a few years. This symptom complex came to be known as Hirayama Disease. Later on, descriptions of a similar entity were available from all over the world and more commonly from other Asian countries. Gourie-Devi et al from India in 1984 from Southern part of India identified a similar syndrome and named it as monomelic amyotrophy (MMA) [2]. Biondi et al [3] from France in 1989 called this presentation as juvenile muscular atrophy of the distal upper extremity (JMADUE) while later on in 1997 Pradhan and Gupta from India called it - juvenile asymmetric segmental spinal muscular atrophy (JASSMA) [4]. Other names that have been used in literature to describe this disease include benign juvenile brachial spinal muscular atrophy as well as oblique amyotrophy.

All these conditions however refer to the same clinical phenotype of insidious onset gradually progressive, unilateral or asymmetric atrophy of the hand and forearm with characteristic sparing of brachioradialis (hence earning the name oblique amyotrophy) [5]. Although previously believed to be a form of motor neuron disease (MND), the most popular theory in current practice believes that this disease differs from MNDs due to a non-progressive course and evidence of chronic ischemic changes of anterior horns of the lower cervical cord due to constant compression of the cord and its vascular supply during cervical flexion.

2. Clinical Features

When originally described by Hirayama et al, the classic cardinal clinical features common to most of their patients were : a young male with an insidious onset gradually progressive, unilateral or asymmetrical weakness and wasting in the C7, C8, and T1 myotomes. The disease showed a variable period of progression anywhere between 1- 5years followed by a spontaneous arrest. Most of their original cohort showed 2 associated findings: a) polymini-myoclonus - action induced irregular coarse tremors in the fingers of the affected hands and b) cold paresis – i.e. mild transient worsening of symptoms on exposure to cold. None of the patients described showed any evidence of sensory loss, hyperreflexia, cranial nerve abnormalities, weakness or spasticity in the lower limbs, or bowel/bladder complaints.

Muscle weakness is the most common and predominant symptom. It is accompanied by atrophy of the distal upper limb muscles –including the small muscles of the hand, wrist flexors and extensors, with characteristic sparing of the brachioradialis muscles. Both extensor and flexor muscles of the wrists and fingers are commonly involved, but often the weakness is more in the finger extensors and wrist flexors. For unknown reasons, regardless of the handedness of the patient, the right upper limb is more commonly affected in Hirayama disease. The weakness is classically unilateral but it can be asymmetrically bilateral in some and very rarely, symmetric. Bilaterality at presentation was seen in 3.1% of cases by a National Japan Survey [6] and 10% by Pradhan et al in their case series [7]. Gourie-Devi and Nalini found involvement of the opposite upper limb in up to 20% of forty-four patients that they followed up over nearly ten years [8].

The next most common complaint experienced by these individuals is a transient worsening of the symptoms on exposure to cold. This phenomenon known as cold paresis is believed to be caused by intermittent conduction block of the muscle fiber membrane in the reinnervated muscles in cold temperatures [9]. Other clinical features include tremulousness of the fingers of the outstretched hands in the

involved limb. These are action induced fasciculations known as polymini-myoclonus. However, in the later stages of the disease resting fasciculations can also be seen. Another common complaint is of easy fatiguability and occasional cramps in the involved limb. Although most patients report absence of subjective or objective sensory disturbances, a few patients may complain of slightly reduced sensation in the hand and forearm. Classically deep tendon reflexes are normal in patients with hirayama disease however case reports of hyperreflexia of the lower limbs are present in literature [10, 11].

There are usually no accompanying neurologic symptoms such as cranial nerve involvement or urinary disturbance. The disease follows a progressive course for a variable period, followed by spontaneous arrest within several years. The period of progression usually lasts around 5 years (range 1-8 years) in most patients (around 90%).

3. Pathophysiology

The exact cause of hirayama disease is still under debate. Before imaging studies were available various theories speculated about the origin of Hirayama disease. Some authors believed it be a variant of degenerative motor neuron disease, while others believed that it was either a result of traumatic injury of the cervical spinal cord, or that it could be seen in individuals who have prolonged survival after acute anterior poliomyelitis. However pathologic study of spinal cord was not available till much later (late 80's) when one of Hirayama's original patients died of carcinoma lung at the age of 38 years and his cord was autopsied. Histopathology from the cord showed shrinkage, necrosis, and gliosis in the anterior horns of the spinal cord from C-5 to T-1, particularly marked at C-7 and C-8 levels [12]. The pattern was different from what was seen in the tissue samples of patients with motor neuron disease. Hirayama thus concluded that the changes were probably ischemic in origin [13].

Following this Kikuchi et al. first proposed the tight dural canal hypothesis as the underlying reason for Hirayama Disease [14]. Hirayama also observed that age of onset of the disease was around 2 years after than the growth spurt of juveniles in Japan. Hirayama thus also speculated that disproportional growth between the vertebral column and the contents of the spinal canal, is responsible for the tight dural sac and anterior compression of the cord. The injury was attributed to repeated flexion movements of the neck and the phenomenon was labelled as Cervical Flexion induced Myelopathy. Tashiro et al suggested that the difference in the male and female incidence of the disease resulted due to a more rapid vertical growth of males at puberty compared with females [15].

The spinal dura matter is a loose sheath that is attached to the vertebral canal periosteum in only two places - at the foramen magnum and dorsal surfaces of C2 and C3 with another attachment at the coccyx. The rest of the dura matter is suspended loosely and cushioned by the epidural fat, plexus of veins, and connective tissue in the spinal canal. During neck extension, the dura matter of the cervical spine is lax. However, in neck flexion, the length of the cervical

canal increases and the dura tightens. The loose dura compensates for the increased length during flexion. In Hirayama disease however, the dural canal is no longer lax in extension. This results in a tight dural canal because of the inability of the dural canal to compensate for the increased length of the cervical canal during flexion. This causes anterior shifting of the posterior dural wall with resultant compression of the spinal cord. The chronic compression causes microcirculatory disturbances in the anterior portion of the spinal cord which leads to ischemia and necrosis of the anterior horns with subsequent atrophy. With long standing and severe disease patients can develop extensive cord injury beyond the anterior horns. Such patients may present with brisk deep tendon jerks and other pyramidal signs. The dural displacement decreases gradually with increasing age, which is responsible for the spontaneous arrest of the disease after a few years of progression. Thus in elderly patients whose disease has arrested, imaging studies do not show any forward displacement of the dural sac and cord compression during flexion.

Hirayama disease is nonfamilial in most patients. However, a few reports of familial cases are present in literature. But so far, there are no published reports about the genetics of familial Hirayama disease at present.

4. Diagnosis

On electrophysiology, EMG reveals evidence of active denervation in the form of fibrillations, positive sharp waves, and fasciculations. Also seen is of chronic denervation in form of neurogenic changes in the C7, C8, and T1 myotomes [16]. EMG of deltoid, biceps brachii and brachioradialis (innervated by C5, C6) is usually normal. In radiology, conventional X-Ray studies of the cervical spine may show only loss of cervical lordosis. However, the diagnostic method of choice is a MRI with flexion contrast study. Features on MRI that are consistent with Hirayama disease include:

- Localized cord atrophy of the lower cervical and upper dorsal segments
- Asymmetric or rarely symmetric cord flattening
- Abnormal cervical curvature with loss of cervical lordosis
- Separation of attachment of posterior dural sac from subjacent lamina
- Anterior shift of the posterior wall of the cervical dural canal on flexion
- Crescent shaped Epidural mass with small curvilinear flow voids
- Contrast enhancement of posterior epidural venous plexus during flexion studies

The prominence of the posterior epidural venous plexus is believed to be due to a negative pressure in the posterior spinal canal because of an anterior shift of the dural thereby increasing the flow to the posterior internal vertebral venous plexus. Another reason suggested could be that the anterior displacement of the dural canal compresses the anterior internal vertebral venous plexus and increases the burden of the posterior internal vertebral venous plexus leading to the formation of a posterior mass.

5. Treatment

- A) **Collar therapy:** A hard cervical collar minimizes neck flexion inducing a premature arrest and thereby preventing progressive muscular weakness in the early stages of the disease. Improvement is expected in patients who have shorter duration of illness and have minimal cord atrophy. Tokumaru and Hirayama in 2001 studied role of cervical collar therapy in 38 cases of HD [17]. They found that all 38 cases on treatment showed no further progression of the weakness after instituting cervical collar therapy. Since the progressive stage is arrested spontaneously in a few years, application of a cervical collar for three to four years is the recommended first line therapy.
- B) **Surgery:** Duraplasty, anterior cervical decompression, cervical vertebral fixation and reconstruction of the atrophied muscles with tendon transfers are the available surgical options and have in selected patients have shown encouraging results. Surgery is indicated for patients who do not respond to conservative treatment for more than 5 years after their onset, with continuous progression as this gives these patients a permanent stable fixation reducing flexion induced injury.

6. Conclusion

A disease earlier considered as a type of motor neuron disease is now largely believed to be due to repeated flexion induced injury of the cervical cord. With cervical collar therapy to arrest the progression it also has a benign course and good treatment. Surgical approaches are also coming up in recent times for cervical fixation for advanced cases. Its treatable nature is what makes it an important entity to be recognized so that the correct therapy can be instituted at the earliest. Future considerations need to look into the genetic aspect of Hirayama Disease so that the etiology and risk factors of this condition can be elucidated

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