Cross-sectional Study

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Clinical profile and dynamic magnetic resonance imaging in Hirayama disease: a single-centered cross-sectional study in Nepal

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Introduction: Hirayama disease (HD) is juvenile monomelic amyotrophy of the distal upper limb first described by Hirayama in 1959 AD. HD is a benign condition with chronic microcirculatory changes. The hallmark of HD is necrosis of the anterior horns of the distal cervical spine.

Materials and Methods: Eighteen patients were assessed for clinical and radiological Hirayama disease. Clinical criteria included insidious onset nonprogressive chronic upper limb weakness and atrophy in teens or early twenties without sensory deficits and coarse tremors. MRI was done in a neutral position followed by neck flexion to evaluate cord atrophy and flattening, abnormal cervical curvature, loss of attachment between the posterior dural sac and subjacent lamina, anterior shifting of the posterior wall of the cervical dural canal, posterior epidural flow voids, and an enhancing epidural component with its dorsal extension.

Results: The mean age was 20.33 years, and the majority, 17 (94.4%), were male. Neutral-position MRI revealed loss of cervical lordosis in 5 (27.8%) patients, cord flattening in all patients with asymmetry in 10 (55.5%), and cord atrophy was observed in 13 (72.2%) patients with localized cervical cord atrophy in only 2 (11.1%) and extension of atrophy to dorsal cord in 11 (61.1%) patients. Intramedullary cord signal change was seen in 7 (38.9%) patients. Loss of attachment of posterior dura and subjacent lamina and anterior displacement of dorsal dura was seen in all patients. A crescent-shaped epidural intense enhancement was noted along the posterior aspect of the distal cervical canal in all patients, with dorsal level extension in 16 (88.89%) patients. The mean thickness of this epidural space was 4.38 ± 2.26 (mean ± 2SD), and the mean extension was 5.5 ± 4.6 vertebral levels (mean ± 2SD).

Conclusion: The high degree of clinical suspicion can guide additional contrast studies in flexion as a set MRI protocol for early detection and avoiding false negative diagnoses of HD.

Keywords: anterior horns, cord atrophy, dynamic MRI, Hirayama, juvenile monomelic amyotrophy, motor neuron

Introduction

Juvenile muscular Atrophy of the distal upper limb, commonly known as HD, is a monomelic amyotrophy affecting young men in their second to third decades. In 1959 AD, Hirayama first described the HD[1]. In contrast to North America and Europe, numerous cases have been reported from Asian countries, particularly Japan, since then.

HIGHLIGHTS

- With high clinical suspicion of Hirayama disease (HD), the MR protocol can be modified by adding contrast study in flexion to increase the early detection in routine sequences.
- HD pathogenesis due to tight Dural sac and anterior displacement of spinal cord.
- MRI in neutral/flexion positions useful for diagnosis of HD
- Loss of cervical curvature and anterior shift of posterior dura seen on flexion MRI.
- Contrast-enhanced studies or fast imaging with steady-state free precession sequences necessary for confirming vascular nature of epidural mass.

HD distinguishes itself among motor neuron diseases as its nature is nonprogressive and pathologic findings at the distal cervical cord that is focal ischaemic necrosis of the anterior horns[2,3]. It is characterized by the insidious onset of unilateral or asymmetric muscle weakness and atrophy in the hand and forearm, demonstrating the hallmark look of oblique amyotrophy, with sparing of the brachioradialis that affects the C7, C8, and T1 myotomes. HD is a self-limiting, benign condition with a natural course of progression of neurological impairments affecting the C7, C8, and T1 myotomes for around 1–5 years, followed by

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spontaneous remission[4]. The hallmark of this pathology is the repeated and/or sustained flexion of the neck causes chronic microcirculatory changes in the territory of the anterior spinal artery. As a result, it led to focal ischaemic necrosis of the anterior horns of the lower cervical cord[2,3]. To diagnose this entity, Various MRI features have been described in the literature. In addition, our study is among the first few reports of Hirayama disease in the Nepalese population. It aims to summarize a single-centre experience of the spectrum of clinical presentation and MRI findings of HD among the studied patient population.

Methods

This cross-sectional study was conducted in a hospital located in Kathmandu, Nepal that specializes in neurological and allied sciences. This study is reported in line with the STROCSS criteria[5]. Eighteen cases with a clinical and radiological diagnosis of HD were studied. Institutional review board ethics permission was obtained.

The inclusion criteria for clinical diagnoses were, (1) persistent weakness and atrophy of the distal upper extremities, (2) a gradual onset in adolescence or early twenties, (3) irregular coarse tremors in the fingers of the affected hand(s), (4) absence of significant sensory impairments, aberrant reflexes, and involvement of the cranial nerve, a pyramidal tract of lower limb, sphincter, or cerebellum. (5) nonprogressive course and remission of disease within a few years of onset, and (6) electromyographic evidence of chronic denervation in clinically or sub-clinically afflicted muscles, with no external sensory loss.

Nerve conduction study and electromyography were done for electrophysiological evaluation. Motor conduction investigations were done on the median, ulnar, and radial nerves (in a few cases) of both upper limbs and one lower limb's peroneal and tibial nerves. Sensory conductions were studied from the median, ulnar, and sural nerves.

The MRI was done on a 1.5T MR unit (Magnetom, Essenza, Siemens). The neutral-position Magnetic resonance Imaging protocol included axial and sagittal T1-weighted (spin echo, repetition time msec/echo time 500–600/15–20), axial and sagittal T2-weighted MRI (fast spin echo, repetition time/echo time 3000–3500/90–140). The flexion MRI technique included axial and sagittal T1 (500–600/15–20) and T2-weighted (4000/85–99) MRI (400–500/15–20, flip angle of 20°–30°, matrix size of 256 × 192) with 30–40° neck flexion. In all cases, post-gadolinium transverse and sagittal T1-weighted images were obtained with a section thickness of 4 mm with a 1-mm gap in all sequences.

In MRI we evaluated (1) cord atrophy, flattening, and symmetry, (2) abnormal cervical curvature, loss of attachment between the posterior dural sac and subjacent lamina, (3) anterior shifting of the posterior wall of the cervical dural canal, (4) flow voids in posterior epidural space, and (5) enhancing epidural component with its dorsal extension. Cord atrophy was defined in axial images as a relative decrease in cord size compared with normal cord above and below the affected levels. Cord flattening was also depicted in axial images as loss of the normal ovoid appearance of the cord in the presence of adequate subarachnoid space around the cord, precluding cord compression. It can be asymmetric (pear-shaped spinal cord), or symmetric cord flattening (a triangular spinal cord). Cervical curvature was classified based on the relationship of the dorsal aspect of the C3 through the C6 vertebral body to a line drawn from the dorsocaudal part of the C2 to the dorsocaudal aspect of the C7. If the dorsal sides of C3 through C6 meet or cross the line from C2 through C7, a curvature is abnormal[6,7]. Posterior dural detachment was noted for loss of attachment between the posterior dural sac and subjacent lamina. On flexion studies, anterior displacement of the dural sac, flow voids in posterior epidural space, and the appearance of enhancing epidural component posterior to the thecal sac, which was inconspicuous in a neutral position, were noted.

Results

The mean age was 20.33 years, with an almost exclusively 17 (94.4%) male distribution. The mean duration from symptom or sign onset to clinical diagnosis was 14.78 months, ranging from 8 to 24 months. Weakness and Atrophy of the distal upper limb were present in all patients. The majority of patients had bilateral upper limb involvement in 9 (50%), with right-hand in 4 (22.2%) and left in 5 (27.8%). Weakness and Atrophy of the hand were associated with tremors in 11 (61.1%) patients. Whereas intrinsic muscles of the hand were involved in all patients, hand extensors were present only in 11 (61.1%) of them (Table 1).

Neutral-position sagittal spine MRI revealed loss of cervical lordosis in 5 (27.8%) patients. (Fig. 1, Table 2). There was asymmetric cord flattening in 10 (55.5%) and atrophic changes of the cord in 13 (72.2%) patients, with localized cervical cord atrophy in only 2 (11.1%) and extension of Atrophy to the dorsal cord in 11 (61.1%) patients. Intramedullary T2 hyperintensity signal change in the cord was seen in 7(38.9) patients. On flexion position imaging, it showed the loss of attachment of the posterior dural sac, subjacent lamina, and anterior displacement of the dorsal dura in all patients (Fig. 1 B). All the patients had a crescent-shaped epidural mass on T1WI (isointense to the cord) and T2W images (hyperintense to the cord) along the posterior aspect of the lower cervical canal. In 16 (88.89%), this space

Table 1

Clinical findings.

Variable	Frequency, *n* (%)
Age (years)	
Range	16–27
Mean	20.33
Sex	
Male	17 (94.4)
Female	1 (5.6)
Clinical	
Duration (months)	24 Aug
Range	14.78
Mean	4 (22.2)
Laterality	5 (27.8)
Right	9 (50)
Left	7 (38.9)
Bilateral	11 (61.1)
Weakness and atrophy only	18 (100)
Weakness and atrophy with tremors	17 (94.4)
Involvement of hand intrinsic muscles	11 (61.1)
Involvement of hand extensors	
Involvement of biceps/triceps	

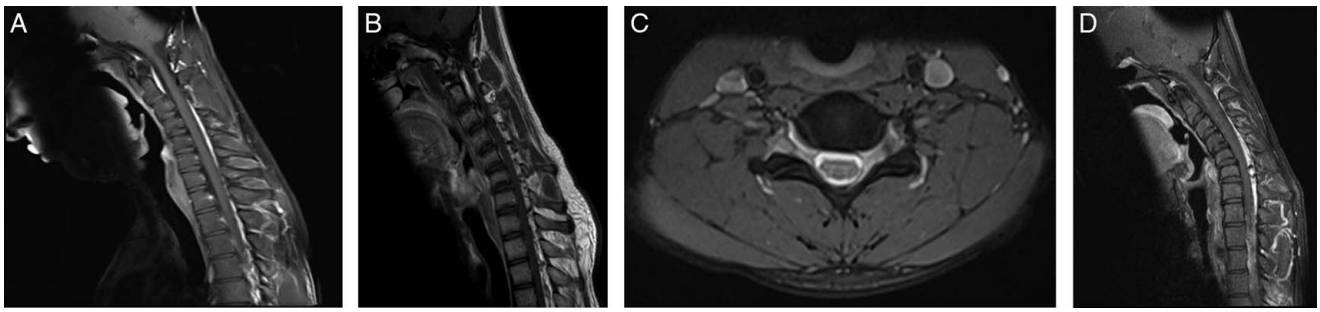

Figure 1. (A) Gadolinium-enhanced T1WI mid-sagittal section demonstrating loss of cervical lordosis. The mid-cervical segment also shows posterior dural detachment with posterior epidural contrast enhancement. (B) Non-contrast T1WI mid-sagittal section in different patients shows serpentine flow voids representing dilated epidural vessels in the posterior epidural space. (C) T2W axial section shows segmental symmetric cord atrophy. (D) Gadolinium-enhanced T1W sagittal section anterior displacement of posterior dura in neck flexion. There is also avid contrast enhancement of the posterior epidural space and mild cord atrophy at the corresponding cervical segment.

extended to the upper dorsal level. The mean thickness of this epidural space was 4.38 ± 2.26 (mean ± 2SD and the mean extension was 5.5 ± 4.6 vertebral levels (mean ± 2SD). Substantial homogeneous enhancement was noted on the contrast-enhanced images in all patients (Fig. 1 C). Cranial extension of this enhancing epidural space was C3 level in 6 (33.33%), C4 in 3 (16.7%), C5 in 4 (22.2%), and C6 in 5 (27.8%). Likewise, the caudal extension was D1 level in 5 (11.1%), D2 in 7 (38.9%), and D3, D4, D5, and D6 levels in 1 (5.6%) patients each.

Discussion

Several hypotheses exist in the literature about the pathogenesis of HD. The disproportionate growth of the vertebral column and the spinal canal contents results in a tight dural sac[8]. Normally, the spinal dura has attachments at the level of the foramen magnum, C2 and C3, and one at the coccyx. It is anchored to the vertebral canal at the nerve root exits. Normal dura is loosely suspended and has several transverse folds, allowing the increased length of the cervical canal to flexion. However, in HD, a short dura cannot compensate for the increased length during neck flexion, which leads to anterior displacement and compression of the spinal cord[8]. Toma and Shiozawa suggested that a rapid juvenile growth spurt accentuates this disproportionate shortening of the dural sac[9]. Chronic repeated flexion, thus compressing the lower cervical cord, ensues microcirculatory ischaemic changes in the territory of the anterior spinal artery at the site of the most kyphotic level, more so at the most susceptible anterior horn, causing atrophy, whereas the white matter is resistant[3].

The involvement of the intrathecal immune/inflammatory process was proposed by Tanaka *et al.*[10], which revealed intrathecal upregulation of IFN-gamma and MIP-1beta in HD patients. On the other hand, Shinomiya and colleagues came up with "the posterior epidural ligament factor" to justify asymmetric cord flattening. They proposed two kinds of ligaments between the posterior dura and the ligamentum flavum, fine ligaments and some larger ligaments that provide resistance against the separation of the posterior dura from the ligamentum flavum. This abnormally unequal ligament distribution may cause cord compression[11].

In addition, localized amyotrophy of the distal arm, like syringomyelia, amyotrophic lateral sclerosis, myelopathy associated with cervical spondylosis, spinal cord tumour, and traumatic myelopathy differentiated from Hirayama disease by imaging modalities[9]. Conventional radiographic studies of the cervical spine are noncontributory and show only loss of cervical lordosis, straight alignment, or scoliosis. Conventional lateral myelograms and computed tomography myelography reveal cord atrophy, asymmetrical cord flattening, and a reduction in the anteroposterior diameter of the dural sac, with the epidural space seen as an area of low density behind the dural sac[1,12]. However, myelography is challenging as retaining the contrast medium in the subarachnoid space of the cervical spine is difficult.

On this note, MRI in neutral and flexion positions is easy to perform and reveals various findings. Focal distal cervical cord atrophy, asymmetric cord flattening, parenchymal changes in the lower cervical cord, abnormal cervical curvature, and loss of attachment between the posterior dural sac and subjacent lamina have been described[13]. The disease can be identified with 80% accuracy by localized lower cervical cord atrophy, asymmetric cord flattening, and loss of attachment. However, the loss of

Table 2
MRI parameters.

MRI parameters	In neutral position, *n* (%)	In flexion position, *n* (%)
Abnormal curvature	5 (27.8)	—
Cord flattening	18 (100)	—
Asymmetric	10 (55.55)	
Symmetric	8 (44.44)	
Cord atrophy	13 (72.2)	—
Localized cervical	2 (11.1)	
Cervico-thoracic	11 (61.1)	
Cord T2 hyperintensity signal	7 (38.9)	—
Posterior dural detachment	—	18 (100)
Posterior epidural space thickness		4.38 ± 2.26 (mean ± 2SD)
Posterior epidural space Extension		5.5 ± 4.6 vertebral levels (mean ± 2SD)
Anterior displacement of the dura (dorsal)	—	18 (100)
Posterior epidural space flow void	—	7 (38.9)
Posterior epidural space contrast enhancement	—	18 (100)

attachment is the most important finding for diagnosing HD in the neutral position[13,14].

Hassan and colleagues and Raval and colleagues depicted that there was a loss of cervical curvature in 91% and 100% of their patients, respectively[15,16]. In addition, Chen and colleagues, in their series, found a statistically significant difference between the healthy and HD patients' groups[12]. However, we have found that only 28% of patients had a loss of cervical lordosis evaluated in a neutral position.

On flexion MRI, the anterior shift of the posterior dura was seen with an increased posterior epidural space[1,17–19]. Zhou and colleagues and Lheman and colleagues reported a prevalence of 71% and 76%, respectively[17–19]. This was found in all of the patients in our series. Interestingly, Lai *et al.*[20] demonstrated a lesser degree of anterior shifting of the posterior dural sac in 46% of healthy subjects, suggesting its presence alone as a normal variation and should not always lead to the diagnosis of HD. A posterior epidural hyperintense, crescentic mass with post-contrast curvilinear flow voids and uniform enhancement can be seen in the posterior epidural space[13]. The disappearance of this mass when the neck is in a neutral position indicates that the posterior internal vertebral venous plexus (IVVP) is congested[8]. This venous plexus congestion is caused by a combination of three mechanisms. An anterior shift of the dural canal establishes a negative pressure in the posterior spinal canal resulting in an increased flow to the IVVP[12]. The anterior displacement of the posterior dura squeezes the anterior IVVP increasing the posterior IPPV load and causing further dilatation[13]. Finally, neck flexion reduces the venous drainage of the jugular veins, which prevents the IVVP[12]. Post-contrast dynamic study to assess the suspected cases of HD was therefore alarmed by Sonwalkar *et al.*[21].

In our study, flow voids within the epidural mass were less frequently visualized on conventional T2W (38.9%). Their vascular nature could be confirmed only after administering contrast (100%), including thoracic extensions in 11 (61.1%) patients. However, recent studies using fast imaging with steady-state free precession have shown to eliminate the requirement for a contrast-enhanced study[22,23]. However, these sequences are not readily available in all centres yet, and dynamic contrast studies in flexion remain the most useful.

One limitation of the research is that the study sample size may not have been large enough to draw statistically significant conclusions about the prevalence of certain imaging findings in Hirayama disease. Additionally, the study design was retrospective, which may have introduced bias or limitations in data collection. The study may also have been limited by the fact that it was conducted at a single centre, which may limit the generalizability of the findings to other populations or geographic locations.

Conclusion

We suggest using neutral and dynamic flexion MRI to diagnose Hirayama disease. The flexion study with contrast, in particular, aids in diagnosing patients with focal wasting even though routine imaging is normal. In this view, with high clinical suspicion of Hirayama disease, the Magnetic resonance Imaging protocol can be modified by adding contrast study in flexion to increase the chances of early detection and reduce the possibility of not diagnosing HD in routine sequences.

Ethical approval

The IRC of the Upendra Devkota Memorial National Institute of Neurological and Allied Sciences granted ethical approval (IRB number: 126/2022).

Consent

Informed consent has been waived from The IRC of the Upendra Devkota Memorial National Institute of Neurological and Allied Sciences

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Author contribution

K.R., S.B., and R.S. contributed to the study concept, data collection, manuscript outlining, writing, and revision. R.S., A.S.M., S.B., and A.P. contributed to the study concept, and critical revision of the manuscript for content. L.J.T. contributed with supervision, and content revision. All named authors accept overall responsibility integrity of the work and have given final approval for its publication.

Conflicts of interest disclosure

None of the authors have any relevant financial and/or non-financial relationships to disclose as defined in the point above.

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