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Electrophysiological Characteristics of Hirayama disease

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Abstract
Background: *The purpose of this study was to evaluate the electrophysiological characteristics of Hirayama disease.*
Method: *Electrophysiological characteristics were analyzed retrospectively in 50 patient diagnosed of Hirayama disease by clinical, imaging and electrophysiological studies. Electrophysiological studies include electromyography (EMG) and nerve conduction studies (NCS).*
Results: *Among 50 patients, 49 were male. The mean age (mean ± s.d.) of the patients was 19.98 ± 2.83 years. In NCS, abnormal amplitude of compound muscle action potential (CMAP) < 5 mv were found in Ulnar nerve in 76% of patients and Median nerve in 24% of cases. The mean amplitude for ulnar and median nerve was 3.5 ± 2.64 mv and 9.1 ± 3.97 mv. The Ulnar/Median (U/M) compound muscle action potential (CMAP) amplitude ratio is found to be ≤0.6 in 80% of patients. Distal latencies and F-wave latencies were variably affected. Conduction velocities were normal in all nerves. Sensory conduction study was absolutely normal in all the patients. Neurogenic changes were found in bilateral hand muscles in 96% of patients.*
Conclusions: *Though asymmetric pattern is the predominant clinical presentation, needle EMG found neurogenic changes in most of the patients. In Hirayama disease, thenar muscles of hand are preferentially involved than hypothenar muscles, a reverse Split Hand pattern. Ulnar to median nerve compound muscle action potential (CMAP) ratio are useful methods in arriving at the correct diagnosis of Hirayama disease and should be an essential part of the protocol to differentiate from other motor neuron diseases as Hirayama disease is self limiting and early diagnosis can limit disability in young adults.*
Keywords: *Hirayama disease, Electrophysiological study, reverse split hand.*

Introduction

Hirayama disease (HD) (brachial monomelic amyotrophy), focal amyotrophy of the distal upper limbs, is a rare disease affecting primarily young men in the second to third decades of life.[1,2,3,4] Hirayama disease is a unilateral or grossly asymmetric bilateral disease, often misdiagnosed as motor neuron disease.[5] Hirayama disease differs from classical types of motor neuron diseases (MND) because of its non progressive

course and pathologic findings of chronic microcirculatory changes in the territory of the anterior spinal artery supplying the anterior horns of the lower cervical cord.[3,6,7] Dynamic contrast MRI is gold standard for diagnosis of HD.

Hirayama disease must be differentiated from Amyotrophic lateral sclerosis or cervical spondylotic amyotrophy in patients presenting with upper limb weakness and wasting as prognosis and management are grossly different in these diseases. ALS predominantly affects thenar muscles than hypothenar muscles; known as Split Hand. Studies showed that Hirayama disease also has differential hand muscles involvement.[8,9,10,11]

In this study, we reviewed the electrophysiological pattern of muscle involvement in Hirayama disease.

Methods

We retrospectively reviewed the electrophysiological parameters of 50 patients diagnosed of Hirayama disease who attended to our Neuromuscular Clinic during the period of February 2013 - January 2018. The study was approved by the College Ethics Committee and written informed consent was obtained from all participants.

All patients fulfilling the following criteria were enrolled: 1) Onset of symptoms between their teens and early 20s, 2) Symmetric or asymmetric muscle atrophy in the C7, C8, and T1 myotomal distribution, 3) No sensory loss found in the affected upper limbs and no sensory or motor symptom or sign in lower limbs or any other part of the body, 4) Relative sparing of brachioradialis (oblique atrophy), 5) Tremulousness of fingers seen in outstretched hands, and 6) Initial worsening with cold exposure (cold paresis). Post contrast dynamic MRI of cervical spine done in all patients which shows [3,12,13,14] the following features: localized lower cervical cord atrophy, asymmetric / symmetric cord flattening, loss of attachment between the posterior dural sac and subjacent lamina, anterior shifting of the posterior wall of the cervical dural canal and enhancing epidural component with flow voids.

Electrophysiological studies include electromyography (EMG) and nerve conduction studies (NCS).[9,10]

In Nerve conduction study, motor conduction studies were done in median, ulnar and radial nerves of both upper limbs and peroneal and tibial nerves of lower limbs. In unilateral cases the involved side and asymmetric bilaterally involved cases, the predominantly affected side was studied. The compound motor action potentials (CMAP) of median, ulnar, and radial nerves were used to document symmetry of disease. Less than 20% difference in the CMAP amplitude was taken as the essential criteria to define symmetric involvement of hand and forearm muscles.[15] Sensory nerve conduction was done to rule out axonal forms of polyneuropathy.

All patients will be subjected to EMG of first dorsal interosseous, abductor pollicis brevis (APB), extensor digitorum communis (EDC), brachioradialis and biceps muscles in the upper limbs, and vastus lateralis and tibialis anterior muscles in the lower limbs. Denervation (positive sharp waves and fibrillation) potentials during resting state of muscle were subjectively graded into four grades; i.e., + (occasional) to ++++ (profuse) and the same muscle on the two sides were compared. Similarly, large and wide polyphasic (reinnervation) potentials were studied during mild contraction of each muscle and percentage of such potentials among the total number of MUPs (triphasics plus polyphasics) were calculated. Percentages of such polyphasic potentials were compared between two identical muscles of right and left sides.[15]

For statistical analysis data were entered into a Microsoft excel spreadsheet and then anlysed by SPSS 20.0.1 and Graph Pad Prism version 5. p- value ≤ 0.05 was considered for statistically significant.

Results

Fifty patients who fulfilled the diagnostic criteria were included in this study. In this study, among 50 patients 49 are male (98%) and 1 female (2%), giving a male-to-female ratio of 49:1.

The mean age (mean ± s.d.) of the patients was 19.98 ± 2.83 years with range 14 - 29 years and the median age was 20.0 years. Mean age at disease onset in our study was 17.42 ± 2.31 years. Asymmetric pattern of hand involvement was found to be predominant mode of presentation in our study (62%).

Table 1: Results of motor conduction studies

	Amp (mV)	CV (m/s)
Median nerve	9.1 (3.97)	54.7 (3.9)
Ulnar nerve	3.5 (2.64)	54.0 (4.7)
U/M ratio	0.40 (0.29)	-

Data are presented as mean (standard deviation). U/M ratio, ratio of the ulnar to the median nerve; Amp, negative peak amplitude; CV, conduction velocity.

Table 1 shows the results of motor conduction studies. In NCS, abnormal amplitude of compound muscle action potential (CMAP) < 5 mv were found in Ulnar nerve in 76% of patients and Median nerve in 24% of cases. The mean amplitude for Ulnar and Median nerve was 3.5 ± 2.64 mv and 9.1 ± 3.97 mv.

The mean Median-Ulnar CMAP amplitude difference was 6.3 ± 3.68. The mean Ulnar/Median (U/M) compound muscle action potential (CMAP) amplitude ratio is found to be 0.40 ± 0.29. The Ulnar/Median (U/M) compound muscle action potential (CMAP) amplitude ratio is found to be ≤0.6 in 80% of patients.

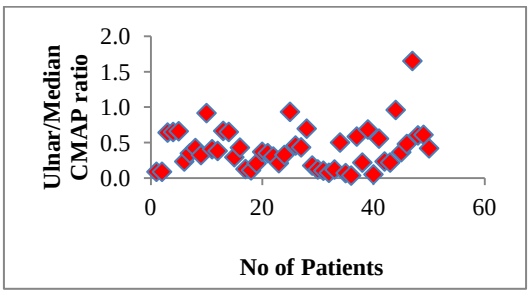

Figure. 1: Distribution of Ulnar/Median CMAP ratio in patients of Hirayama disease

Distal latencies and F-wave latencies were variably affected. Conduction velocities were normal in all nerves. Sensory conduction study was absolutely normal in all the patients.

Abnormal EMG findings were recorded most frequently in the ADM and FDI, followed by the APB, EDC, and triceps muscles. Neurogenic changes in bilateral hand muscles were found in 96% of patients. Though brachioradialis muscle was found clinically spared in all patients, 6 (12%) patients showed neurogenic changes on EMG. The patients with neurogenic involvement in brachioradialis have more severe reduction of Ulnar CMAP, The biceps, deltoid were found normal in all patients.

Out of a total of 50 patients of Hirayama disease, 8 (16%) were found to have apparently bilaterally symmetric electrophysiological involvement.

Discussions

The CMAP of ADM is marginally lower than APB in healthy subjects, so U/M CMAP ratio is 0.82 (range 0.6-1.7).[16] In this study, in patients with Hirayama disease, Ulnar CMAP amplitude in the predominantly affected limb is significantly low than median CMAP. High mean Median – Ulnar CMAP amplitude, low Ulnar/Median (U/M) compound muscle action potential (CMAP) amplitude ratio than normal healthy subjects also suggests preferential affection of thenar muscles in Hirayama disease than hypothenar muscles of hand. The Ulnar/Median (U/M) compound muscle action potential (CMAP) amplitude ratio is found to be ≤0.6 in 80% of our patients.

Various studies also found similar result of significantly lower Ulnar CMAP amplitudes and slightly lower Median CMAP amplitudes for the affected limbs in patients with HD.[[8]-[11]]

Xiang Jin et al[10] proposed that a low Ulnar/ Median CMAP ratio is suggestive of HD, while a high U/M ratio is suggestive of ALS. Thus, a U/M CMAP ratio <0.6 is strongly indicative of a diagnosis of HD but not of ALS. So, reverse "Split Hand" pattern of affection may be highly suggestive of Hirayama disease. The thenar and

hypothenar muscles are affected to a similar extent in patients with cervical spondylotic amyotrophy (CSA). Therefore, the Ulnar/Median CMAP ratio could be considered as a criterion in the differential diagnosis of HD, amyotrophic lateral sclerosis (ALS) and cervical spondylotic amyotrophy (CSA). This differentiation is important as ALS is progressive disease with respiratory involvement. Early diagnosis of Hirayama disease may limit disability with early initiation of cervical collar.

Conclusions

Hirayama disease is though predominantly unilateral in clinical presentation, bilaterally neurogenic changes in EMG is found in most of the patients.

In Hirayama disease, thenar muscles of hand are preferentially involved than hypothenar muscles, a reverse Split Hand pattern.

Ulnar/median nerve compound muscle action potential (CMAP) ratio are useful methods in arriving at the correct diagnosis of Hirayama disease and should be an essential part of the protocol to differentiate from other Motor neuron diseases as Hirayama disease is self limiting and early diagnosis can limit disability in young adults.

Abbreviations

ADM: Abductor digiti minimi; ALS: Amyotrophic lateral sclerosis; APB: Pollicis brevis; CMAP: Compound muscle action potential; CV: Conduction velocities; CSA: Cervical spondylotic amyotrophy; HD: Hirayama disease; U/M: Ulnar/median.

Competing interests: The authors declare that they have no competing interests.

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