Abstract — Hirayama disease (HD), also termed monomelic amyotrophy or non-progressive juvenile spinal muscular atrophy, is a rare and benign focal amyotrophy of the distal upper limb. It is characterized by insidious unilateral muscular atrophy and weakness of the forearm and hand, without sensory or long tract signs. While the diagnosis is often made clinically, diagnostic imaging studies such as dynamic MR imaging can be confirmatory. Functional MR imaging may also provide an additional biomarker which may provide additional insight to its pathophysiology. To date, there are no published DTI parameters of the spinal cord in patients afflicted with HD. In this report, we presented the utility of routine, dynamic and functional MR imaging in a 20-year-old man with HD. Our preliminary findings suggested that DTI, as a complementary diagnostic tool, can be used in the evaluation of HD, and potentially for exploring the underlying its pathophysiology.

Keywords — Diffusion tensor imaging, flexion, neutral, Hirayama disease, monomelic amyotrophy.

I. INTRODUCTION

Hirayama Disease (HD) is an insidious, benign lower motor neuron disease.1 HD affects young individuals mostly at the ages of 15-25 years with male preponderance (male to female ratio = 20:1).1 Muscle weakness and atrophy in the distal upper extremity causes functional and social handicaps. HD has multiple names including monomelic atrophy. Sobotka disease, juvenile non-progressive amyotrophy and juvenile asymmetric segmental spinal muscular atrophy. Patients with HD usually manifest with a unilateral arm atrophy involving the C7, C8 and T1 myotomes but rarely both upper extremity involvement in either an asymmetric or symmetric fashion.2 Sensory deficits are usually absent. HD classically presents with an initial progressive phase of weakness that usually stabilizes after a few years. Most reported cases are from Japan, India, and other Asian countries, but cases have also been reported in North America, Europe, and the Middle East.1

Diagnostic tools employed in assisting clinical diagnosis and exploring its underlying pathogenesis include electroneuropysilologic studies, such as nerve conduction studies, electromyography, and evoked potentials; neuroimaging studies, such as magnetic resonance imaging (MRI) with dynamic positioning with neck flexion. To our knowledge, there is no published study demonstrating the use of MRI diffusion tensor imaging (DTI) in evaluating patients with HD in neutral and flexion positions. In this case report, we demonstrated the potential use of DTI as a complementary diagnostic tool in the evaluation of HD.

II. CASE REPORT

A 20-year-old man recently immigrated from Hong Kong to USA presented with an insidious onset of, but relatively static, muscle weakness and atrophy of his left hand for 8 years [Figure 1]. There was no history of trauma or family history of neurologic or neuromuscular disease.

On examination, he was well developed and nourished. He had weakness in his left intrinsic hand muscles (4/5, Medical Research Council) and significant muscle atrophy of his left forearm, especially the intrinsic hand muscles. The circumferences of his left upper extremity were 26 cm on the left and 29 cm on the right at 20 cm above the elbow; and 22 cm on the left and 26.5 cm on the right at 5 cm below the elbow [Figure 1]. No other abnormal neurologic findings were noted including in cranial nerves, coordination, sensations, motor functions of his other limbs, tendon reflexes, and gait.

III. METHODS

Electroneurophysiologic studies:

Conventional nerve conduction study (NCS) and needle electromyography (EMG) was performed in his left upper extremity. Significantly reduced amplitude of compound muscle action potentials was seen in the muscles supplied by left ulnar and median nerves. F-wave was absent in the left
ulnar nerve. EMG showed both active and chronic neurogenic changes with fibrillation potentials, positive sharp waves, fasciculation potentials, enlarged motor action potential units with unstable configuration, and reduced recruitment pattern seen in C7 and C8 greater than T1 myotomes.

**Imaging**

If you are using Word, use either the Microsoft Equation Editor or the MathType add-on (http://www.mathtype.com) for equations in your paper (Insert | Object | Create New | Microsoft Equation or MathType Equation). “Float over text” should not be selected.

**Diffusion tensor imaging (DTI) Post-processing**

DTI analysis was performed using MedINRIA software, INRIA Sophia Antipolis, Cedex - France. Regions of interest were manually drawn on the axial B0 Diffusion images at the mid vertebral body and disc levels with the exception of the C5-6 disc level due to image distortion artifact [Figure 2b]. FA values were tabulated and graphically represented.

**IV. RESULTS**

**MRI Findings**

Axial images showed left hemicord volume loss from C4-C5 through C6-C7 with minimal corresponding T2 prolongation [Figure 2]. In neutral positioning, a thin T2 hyperintense collection is seen in the dorsal epidural space extending from C3 through the upper thoracic spinal canal [Figure 3]. In flexion, the collection markedly increases in size, resulting in effacement of the thecal sac, obliteration of the anterior CSF space, and compression of the spinal cord. Axial and sagittal T2 weighted images in flexion show similar findings, with marked anterior displacement of the spinal cord compared to the neutral axial images [Figure 4].

**DTI Findings**

Axial T2 and B0 images were utilized to localize the regions of abnormal cord signal and asymmetric volume loss (Figure 2a). Regions of interest (ROI) were manually drawn on the B0 images. Four quadrant ROI analysis was manually performed to isolate the anterior, posterior, left and right segments of the spinal cord during the flexed and neutral position (Figure 2b). FA values were calculated at multiple spinal cord levels with the exception of the C5-6 disc level where artifact prevented proper FA calculation. DTI analysis demonstrated reduced FA values within the left anterior and posterior hemicord during neutral and flexed position (Figure 5).

**V. DISCUSSION**

Our patient manifested a classical HD appearance evidenced by his clinical presentation, electrodiagnostic evaluation, and MRI findings. Findings of conventional MRI with dynamic positioning in neck flexion showed an enlargement of the posterior epidural space and anterior displacement of the spinal cord, which are in agreement with previous reports. Further findings from DTI showed asymmetric quantitative decrease in fractional anisotropy in the left hemicord, which provide additional evidence of underlying physiologic changes of HD (Figure 5).

The etiology for the development of HD is not completely understood but postulated of a pathophysiologic related to intermittent compression of the anterior cervical cord during
In supporting this view, findings in our case demonstrated transient engorgement of the dorsal epidural venous during flexion displacing the cervical cord anteriorly. As the displacement occurs repetitively, it may cause anterior compression of the cervical cord against the ventral dura, thereby compromising its vascular supply and resulting intermittent ischemia and subsequent development of the anterior cervical spinal cord atrophy. Additionally, HD may result from a mismatch in the growth of the cervical dura to the growth of the vertebral bodies, which causes deficient laxity. In such cases, neck flexion causes the abnormally taut dura to separate from the lamina creating negative pressure within the epidural space which contains adipose tissue and veins. The negative pressure results in distention of the epidural venous plexus, which in turn produces a mass effect on the thecal sac and anterior displacement of the cervical cord with eventual compression on the ventral spinal cord against the anterior cervical dura and vertebral bodies. Effects from those factors, either alone or in combination, may lead to recurrent subclinical ischemia of the anterior horn cells in the cervical spinal cord, resulting in weakness and atrophy of the affected upper extremity.

Conventional MRI is a useful tool in the evaluation of HD. However, utility of DTI in evaluating the integrity of the spinal cord and white matter pathway related to HD remains yet to be explored. DTI is a promising modality for in vivo mapping of the organization of deep tissues. It allows observation of the microstructural and architectural properties of the white matter by measuring the stochastic movement of water molecules within tissue. By quantifying the degree of diffusion of water molecules in each voxel of an image in directions parallel and transverse to the plane of neuronal axons, DTI can be used in evaluating spinal cord in vivo as FA is a measure of the degree of directionality of diffusion. Its values range from 0, indicating isotropic or no directional dependence of the diffusion, to 1, indicating diffusion occurs only along one axis and is fully restricted along a single direction. FA can be obtained from DTI calculations and reflects the magnitude of anisotropy along the spinal cord tracts. The unique anisotropic characteristics of the spinal cord may allow DTI to localize white matter, separate white from gray matter and assess structural damage of the cord. Previous studies showed changes in diffusion characteristics along injured spinal cords and difference in the FA parameters between the normal and injured spinal cord, indicating the ability of DTI to differentiate normal from injured spinal cord. Acquisitions of DTI in our patient demonstrated reduced FA values in the left aspect of the spinal cord, which correlates well with the clinical presentations of muscular symptoms and signs in the left arm, and the MRI findings of the left sided spinal cord atrophy. Previous studies have attempted to use DTI in HD in evaluation of lower and upper motor neuron involvement, but, to our knowledge, there were no reported FA values of the spinal cord particularly during the neutral and flexed positions. Utilization of DTI may aid in defining functional and structural differences between the progressive and static phases of HD. FA values may serve as a surrogate functional biomarker in the cervical spinal cord for HD and DTI may play a role in facilitating the diagnosis and classifying the stage of HD. To prove it, serial DTI imaging studies in a cohort of HD patients with age-matched controls are needed.

There is no cure for HD. Treatment consists of muscle strengthening exercises and training in hand coordination. Recent anecdotal reports showed that surgical interventions may produce promising therapeutic outcome but their long-term effects must be validated in a large scale clinical trial. The HD symptoms usually progress slowly for a few years before reaching a plateau, and then remain stable for many years. Disability is generally slight. Rarely, the weakness progresses to the opposite limb.

References


Questions:

1) What type of neuronal disease is Hirayama?
   a. Upper motor neuron.
   b. Lower motor neuron.
   c. Mixed upper and lower motor neuron.
   d. Mixed upper and lower sensory neuron.

2) What age and gender are most commonly affected by Hirayama Disease?
   a. Males, 2-5 years of age.
   b. Males, 15-25 years of age.
   c. Females, 20-30 years of age.
   d. Both genders, 50-70 years of age.

3) Which ethnic group is Hirayama Disease most common in?
   a. Caucasian.
   b. African American.
   c. Hispanic.
   d. Asian.

4) What is the typical clinical presentation for Hirayama Disease?
   a. Rapid onset with progressive deterioration.
   b. Insidious; initially static then progressive.
   c. Insidious; initially progressive then static.
   d. Insidious; static.

Answers:
   1) a; 2) d; 3) b; 4) c.