Neurophysiologic Features of Carpal Tunnel Syndrome in Adults with an Isolated Elevated Plasma Level of Homocysteine

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Abstract—Carpal tunnel syndrome (CTS) is a mono-neuropathy of the median nerve at the wrist. CTS can be caused by a variety of pathophysiological conditions and can also be an early scenario of the underlying peripheral neuropathy. We recently reported that an elevated plasma level of homocysteine (eHcy) is an independent risk factor for development of peripheral neuropathy. However, the neurophysiologic features of CTS in subjects with an isolated eHcy have not been studied. We retrospectively reviewed clinical charts and neurophysiology databank to identify subjects with a clinical diagnosis of CTS with isolated elevated plasma levels of homocysteine, who had received electrodiagnostic evaluation. Subjects with a clinical diagnosis of neuropathy or with an identifiable etiology, other than isolated eHcy, for neuropathy were excluded. From 361 subjects with electrodagnostically confirmed CTS, 7 subjects (age: 57±8 year-old, mean±SD) were included. Nerve conduction study on median nerve showed a mildly increased distal latency (4.5±1.1 ms) but normal amplitude (8.4±2.4 mV) and conduction velocity (53.6±4.7 m/s) in motor median nerves; and mildly slowed velocity (41.4±28.2 m/s), but normal amplitude (19.4±16.9 µV) in sensory median nerves. Electromyography showed normal findings in all subjects. The electrodiagnostic studies suggested demyelination in nature. Our findings showed that the neurophysiologic features of CTS in adults with isolated eHcy were demyelinating in nature, which may suggest a favorable outcome with appropriate treatment.

Keyword — carpal tunnel syndrome, homocysteine, hyperhomocysteinemia, median nerve, neuropathy, neurophysiologic features.


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I. INTRODUCTION

Carpal tunnel syndrome (CTS) is a median nerve mono-neuropathy at the wrist typically manifested with numbness of the thumb, index, long and radial half of the ring finger [1]. Although many pathophysiologic conditions are recognized as contributing factors, CTS can be idiopathic because of absence of an identifiable etiology. On the other hand, CTS can be an early symptom of an underlying peripheral neuropathy [2]. We recently reported that an elevated plasma level of homocysteine (eHcy) is an independent risk factor for development of peripheral neuropathy [3]. However, the electrophysiologic features of CTS in subjects with an isolated eHcy have not been studied. In this article, we reported the neurophysiologic features of CTS in subjects with isolated eHcy.

II. METHODS

Retrospective review of the clinic charts and neurophysiology databank from 1/1/05 to 6/30/2014 was performed to identify subjects with a diagnosis of CTS. Demographic data, laboratory and electrodiagnostic findings were recorded. Inclusion criteria were 1) subjects was a clinically diagnosed CTS; 2) subjects had received an electrodiagnostic study at least on one arm and one leg; 3) subjects had laboratory studies performed with simultaneous measurements of B12, folic acid, homocysteine, and methylmalonic acid; and 4) laboratory studies showed an isolated eHcy but other findings including methylmalonic acid, B12, folic acid, homocysteine, and methylmalonic acid; and laboratory studies showed an isolated eHcy but other findings including methylmalonic acid, B12, folic acid, hematocrit, chemistry, liver, function tests, thyroid-stimulating hormone, inflammatory screen, angiotensin converting enzyme antinuclear antibody panel, hepatitis profile, rapid plasma reagin, Lyme titers, and human immunodeficiency virus, were normal. Exclusion criteria were 1) subjects with a presentation of symptoms or signs suggestive of a clinical diagnosis of a generalized neuropathy; 2) subjects with an identifiable etiology, other than the isolated eHcy, for neuropathy; 3) subjects with a history of traumatic injury to the neck, arm or wrist; and 4) subjects did not receive electrodiagnostic evaluation. This study was approved by the Temple University Institutional Review Board.

Neurophysiologic studies and data acquisition

Conventional nerve conduction studies (NCS) and electromyography (EMG) were performed in at least one arm.
and one leg [4]. In brief, motor NCS on median, ulnar, fibular (peroneal) and tibial nerves; and sensory NCS on median, ulnar, radial and sural nerves were performed using a Nicolette Biomedical EMG machine (Viking Select, version 10, Madison, WI). The skin temperature was monitored and maintained at 32°C or above for the arm; and 30°C or above for the leg. Data of NCS including distal latency, amplitude, duration and area of the action potentials, and conduction velocity of individual nerves were obtained. EMG was performed in deltoid, biceps, triceps, first dorsal interosseous, and abductor pollicis brevis muscles in one arm; and in medial vastus, tibialis anterior, medial gastrocnemius, and pedis first dorsal interosseous muscles in one leg. Data of EMG including insertional, spontaneous, and volitional activities; configuration of motor unit potentials and recruitment pattern were collected. The electrodiagnostic findings of CTS were analyzed.

III. RESULTS

From 361 subjects with an electrodagnosis of CTS, seven (age: 57.0±8.4 year-old, mean±SD, range: 47-68, male/female: 2/5), who fulfilled the inclusion criteria, were included. Their plasma level of homocysteine was elevated (17.2±6.8 μmol/L, normal: <11.5), but with normal plasma levels of other findings including B12 (335±136 pg/mL; normal: 200-1100), folic acid (16.6±4.2 ng/mL; normal: >5.4), methylmanolic acid (159.6±20.1 nmol/L; normal: 73-376), and a normal mean corpuscular volume (98.4±21.4 fl; normal: 80-100) of red blood cells. NCS on median nerve showed a slightlly increased distal latency (4.5±1.1 ms) but normal amplitude (8.4±2.4 mV) and conduction velocity (53.6±4.7 m/s) in motor; and mildly slowed velocity (41.4±8.2 m/s) but normal amplitude (19.4±16.9 µV) in sensory nerves (Table 1). EMG showed normal findings in all muscles sampled in the arms and legs of all subjects (data not shown). These findings provided electrodagnostic evidence indicative of a mild demyelination of the median mononeuropathy at the wrist.

IV. DISCUSSION

Our study showed that the neurophysiologic features of CTS in adults with an isolated eHcy may be a mild demyelination in pathology.

CTS can be caused by various etiologies, including traumatic (i.e. recurrent micro-injury at wrist, heavy manual work or work with vibrating tools); systemic diseases such as metabolic (i.e. diabetes mellitus), inflammatory (i.e. rheumatoid arthritis), endocrinologic (i.e. hypothyroidism, obesity, pregnancy), malnutritional (i.e. Vitamin B deficiency), toxic (i.e. alcohol, medicine, intoxication), structural (i.e. ganglion, lipoma,
mucopolysaccharidoses), paraneoplastic or autoimmunemediated (i.e. multiple myeloma), genetic (i.e. family cluster, primary amyloidosis, hereditary neuropathy with liability to pressure palsies); and others. CTS can also be manifested as an early symptom of peripheral neuropathy [2]. eHcy has been recognized as a risk factor associated with many neurologic conditions including stroke, cognitive decline, dementia, and Alzheimer’s disease. We recently reported that isolated eHcy is an independent risk factor for the development of peripheral neuropathy [3]. We termed this entity as isolated eHcy-induced neuropathy (IHIN). The electrophysiologic features of IHIN are a large fiber neuropathy with mild demyelination and minimally distal axonal denervation [4].

It is well known that eHcy occurs in the conditions of either B12 and/or folic acid deficiency, or with a genetic variation. The electrophysiologic features of B12 deficiency-induced neuropathy have been reported as either axonal degeneration and/or demyelination [5-8]. In contrast, IHIN is a large fiber neuropathy with mild demyelination and minimally distal axonal denervation [4]. To our knowledge, there is no published report on electrophysiologic findings of isolated eHcy-related CTS.

Our current study provided evidence that the electrophysiologic features of the isolated eHcy-related CTS are mildly demyelinating in nature. Importantly CTS can be an early symptom of an underlying peripheral neuropathy [2] and isolated eHcy may predispose susceptible individuals to develop IHIN [3] and CTS. Notably, none of the subjects with concomitant peripheral neuropathy was included in our study. Increased occurrence of CTS has been reported in diabetics [9-11], women [12-19], in pregnancy [20], obesity [15,19,21-25], and genetic predisposition [26,27]. Interestingly, eHcy has also been observed in these conditions [28-31]. eHcy can cause peripheral neuropathy [3] or exacerbate pre-existing diabetic neuropathy [32-34].

The electrodiagnostic findings of demyelinating features in the subjects with CTS with isolated eHcy may suggest a reversible pathology, because of absence of neurophysiological evidence indicating an axonal loss. Therefore, a favorable outcome may be expected with appropriate treatment.

This study had limitations. It was with a small number of subjects, given the fact that only a strict small population suffers from an isolated eHcy who has only “pure CTS”. Another drawback was the lack of a histologic confirmation on demyelination of CTS, which is an invasive modality and usually not routinely performed for the diagnosing CTS.

In summary, we showed in this pilot study that eHcy may be associated with the development of CTS. The neurophysiologic features of eHcy-related CTS are mildly demyelinating in nature, which may predict a favorable outcome with appropriate treatment. A large scale study is warranted to validate these findings.

V. ACKNOWLEDGMENTS

We are grateful to Dr. Sonya Knight who was involved in the initial data collection.

References

Questions (please choose a single answer):

1. Elevated plasma level of homocysteine can be caused by deficiency of
   
   A. B12
   B. Folic acid.
   C. Methylmalonic acid.
   D. A and B.
   E. A and B and C.

2. Increased occurrence of carpal tunnel syndrome (CTS) has been reported in all the following medical conditions except:
   
   A. Diabetics.
   B. Men more than women.
   C. Obesity.
   D. Genetic predisposition
   E. eHcy.

3. Which of the following statement is incorrect:
   
   A. CTS is a median nerve mono-neuropathy at the wrist.
   B. CTS typically presents with numbness of the thumb, index, and long and ulnar half of the ring finger.
   C. The neurophysiologic features of eHcy-related CTS are axonal loss in nature.
   D. CTS can be an early symptom of an underlying peripheral neuropathy.

   Answers:
   1. D; 2. B; 3. C