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Short Communication

Diabetic Cidp-Like Neuropathy in a Pazient With Becker's Myotonia

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Abstract

Becker's disease (BM) is an autosomal recessive congenital myotonia, characterized by impaired muscle relaxation after voluntary contraction and variable degrees of muscle weakness. BM is caused by mutations in CLCN1 gene on chromosome 7q35 encoding the major skeletal muscle chloride channel CLC-1. Although neuropathy has been associated with myotonic dystrophy, to date no case of neuropathy during the course of BM has been reported. Herein we describe the case of a patient with BM and diabetes who progressive gait disturbance, distal paresthesias, muscle weakness. Neurophysiological assessment and diagnostic lumbar puncture revealed the presence of a chronic inflammatory demyelinating neuropathy. The case here presented developed a diabetic chronic demyelinating inflammatory neuropathy resembling CIDP during the course of BM. The most consistent hypothesis explaining such an unusual association is that the inflammatory neuropathy is related to the concomitant occurrence of diabetes.

Keywords: Chronic inflammatory demyelinating neuropathy; Myotonia; Becker's Disease; Diabetes

Abbreviations

Becker's disease (BM); Peripheral neuropathy (PN); Myotonic dystrophy (MD); Chronic inflammatory

demyelinating neuropathy (CIDP); CIDP associated with diabetes (DM-CIDP)

Becker's disease (BM) is a recessive congenital myotonia, characterized by impaired muscle relaxation after voluntary contraction and variable degrees of muscle weakness [1]. BM is caused by mutations in CLCN1 gene on chromosome 7q35 encoding the major skeletal muscle chloride channel CLC-1 [1]. Although peripheral neuropathy (PN) both primary or secondary to other cause may develop in up to 50% of cases during the course of myotonic dystrophy, no case of chronic inflammatory demyelinating neuropathy (CIDP) during the course of BM has been reported.

A 54-year-old man suffering from diabetes by many years (in therapy with oral anti-diabetic drugs), hypercholesterolemia (without statin use) and obesity presented with progressive gait disturbance, distal paresthesias, muscle weakness of lower limbs in the last two years.

Since childhood, he also presented prolonged muscular contraction after voluntary movement, especially after rest, involving upper limbs and face. Genetic testing highlighted in the patient and his brother homozygous mutation 1598C>T in the CLCN1 gene. On admission, neurological examination revealed diffuse muscle hypertrophy, with slight proximal weakness, generalized areflexia and diminished perception of touch, pain, vibration and position sense at the four limbs. Grip-release myotonia was evocable. Complete blood count, thyroid, liver and kidney function tests, cobalamin, folate, C-reactive protein level, thyroid and renal function, anti-gangliosides, antinuclear antibodies, creatine kinase, serology for HCV, HBV, EBV, HIV, and immunofixation were normal. Total-Cholesterol was 271mg/dL, Glycated hemoglobin was 7.9%. Electromyography revealed chronic denervation, myopathic motor unit potentials, with fibrillations, myotonic discharges in the four limbs muscles. Nerve conduction studies showed diffuse slowing of motor and sensory conduction with conduction blocks. (figure) Lumbar puncture demonstrated increased cerebrospinal fluid proteins (90mg/dl), increased CSF albumin ratio and normal cell count. Treatment with intravenous immunoglobulin (5-day 0.4gr/kg/die) was started with a moderately positive response.

Herein we report on a patient with BM and diabetes who developed a chronic demyelinating inflammatory neuropathy resembling CIDP. The most consistent hypothesis explaining such an unusual association is that the inflammatory neuropathy is related to the concomitant occurrence of diabetes. The relationship between CIDP and diabetes is not completely understood but the odds ratio of the occurrence of CIDP was reported to be up to 11 times higher in diabetic than in non-diabetic subjects [2]. CIDP associated with diabetes (DM-CIDP) and Idiopathic CIDP patients present similar clinical and electrophysiological features and response rate to treatment [3]. Another less feasible explanation is that such an association is not casual. There is a growing evidences that a mutation in a structural gene can provoke an intense inflammatory reaction [4]. Inflammatory foci with both T cells, macrophages, and B cells at the site of muscle degeneration have been observed in muscle samples of patients with Duchenne's Muscular Dystrophy, a disease caused by

mutations in the structural muscle protein dystrophin [5]. Inflammatory neuropathy resembling CIDP has been observed in patients with myotonic dystrophy type 1, and a toxic RNA gain-of-function of the mutated DMPK gene which can directly affect the innate immune system has been hypothesized [6]. In children with X-linked adrenoleukodystrophy there is an intense inflammatory demyelinating neuro-pathology in the brain, with many features of acute disseminated encephalomyelitis and multiple sclerosis. The disease is caused by a mutation in ABCD1, a peroxisomal membrane protein (ALDP) that is part of a small family of related peroxisomal membrane proteins [7]. All these findings emphasize how genetic or epigenetic disorders in structural genes can lead to inflammation and even autoimmunity. Although the most likely hypothesis underlying the clinical feature in our patient is a casual association, genetic mutations can lead to an immune response which is indistinguishable from autoimmunity, as exemplified from other genetic disorders. Further studies however are needed on large cohort of BM patients to clarify these aspects.

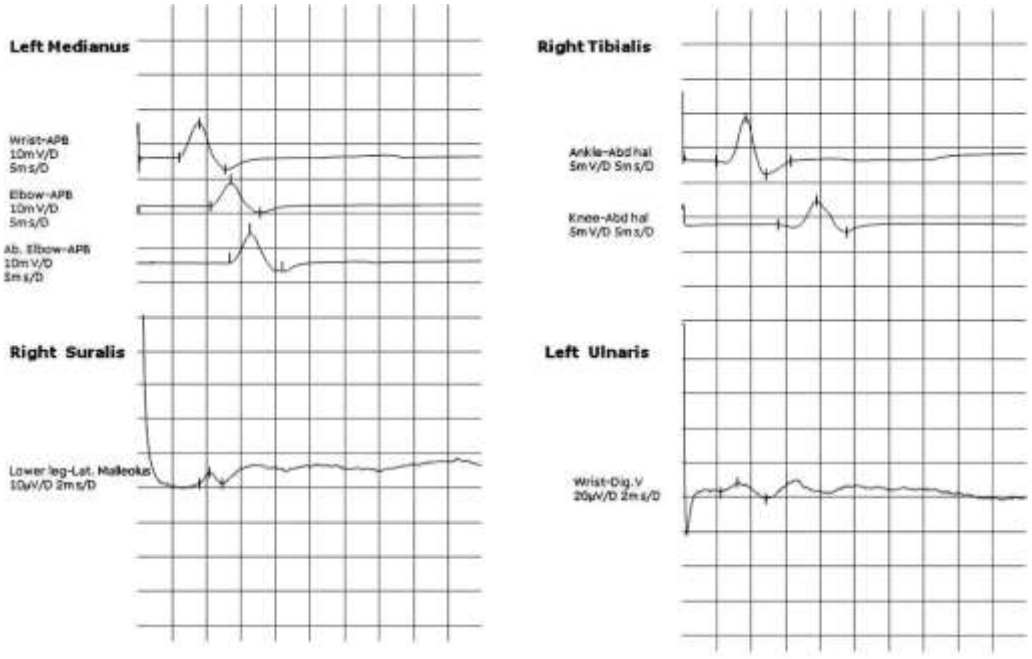

Figure: Motor conduction studies showing slowing of conduction with partial conduction block in the right tibial nerve (conduction velocity (cv): 39m/sec, normal: 54.9 ± 7.6; Map amplitude ankle: 8.2mV; Knee: 4.5mV; normal value 15 ± 3.2) and in the left medianus (Below elbow-wrist vc: 45.5m/s; normal: 56.7 ± 3.8; below-above elbow vc: 42.5m/s, normal: 57.5 ± 3.4;Wrist amplitude: 13.5mV, normal: 13.2 ± 5.0; below elbow amplitude: 8.7, normal: 13.5 ± 4.1; above elbow: 9.0, normal: 13.7 ± 4.1).

Sensory conduction studies showing slowing of conduction and reduced potential amplitude in the right suralis nerve (cv: 37.9, normal: 46 ± 0.5, amplitude: 3.3µV; normal: 3.5 ± 0.2) and in the left

ulnaris (cv: 41.9, normal: 57 ± 5; amplitude 9.6μV; normal: 15-50).

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