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Case report

A case with CMTX1 disease showing transient ischemic-attack-like episodes

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ABSTRACT

Charcot-Marie-Tooth (CMT) disease is a hereditary neurologic disease which affects the sensorial and motor fibers of the peripheral nerves. CMTX1 is an X-linked dominantly inherited subtype of CMT and is caused by mutations in gap junction beta 1 gene (*GJB1*). A small proportion of *GJB1* mutations are associated with recurrent central nervous system findings. We describe a 15-year-old male patient with CMTX1 who had stroke-like findings along with foot deformities and peripheral neuropathy. Strokes and stroke-like attacks are rarely seen in children and adolescents. Herein, neurological signs, MRI findings and genetic results of a CMTX1 case are presented and discussed.

1. Introduction

Charcot-Marie-Tooth (CMT) disease, which affects the sensorial and motor fibers of the peripheral nerves, comprises a group of hereditary neuropathies and is among the most commonly seen hereditary neurologic diseases. CMTX1, an X-linked dominantly inherited type of the disease, comprises 7–10% of all CMT cases [1]. CMTX1 results from mutations taking place in gap junction beta 1 (*GJB1*), which encodes connexin32 protein (Cx32) [2].

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As in the classical CMT presentation, lower extremities typically become affected early in the course of CMTX1, and in its slow progression, the disease causes distal muscular weakness, atrophy, sensorial loss, foot deformities, and areflexia [1]. Unlike in other types of CMT, reversible white matter lesions can be detected in CMTX1 [2]. CNS involvement is thought to be a result of the expression of Cx32 both in oligodendrocytes and Schwann cells [3].

2. Case report

A 15-year old male presented to the Emergency Department with acute right-sided hemiparesis, which recovered within 8 h. On the second day he experienced anarthria and left-sided hemiplegia, which recovered within 12 h. On the third day, he suffered from various acute neurological problems as follows: transient anarthria, upward gase paresis, pseudobulbar findings, right hemiplegia, and trunk ataxia. Neurological examination revealed that deep tendon reflexes were hypoactive/abolic, and hammer toe/pes cavus deformity was remarkable (Fig. 1). Brain MRI showed that there were bilateral periventricular deep white matter, capsula interna, and corpus callosum involvement. These lesions had a tendency to confluency, showed diffusion limitation, and appeared hyperintense in the T2 and FLAIR sequences, but there was no contrast enhancement (Fig. 2). Intra and extra-cranial CT angiographies were normal. Level of protein in the CSF was 77.3 mg/dl (15–45 mg/dl) and that of IgG was 8.4 mg/dl (3.6–6.1 mg/dl). CSF was free of cells, and the lactate levels both in CSF and blood were within normal limits. EMG showing demyelination combined with axonal degeneration. Hearing and eye tests as well as cardiac examination were normal. Genetic testing revealed a hemizygous mutation, c.542T>C; p.V181A (NM_001097642), in *GJB1* gene. Lesions were noticed to regress in the MRI taken two weeks later. During the 2-year follow-up, the complaints of the patient resolved and did not reoccur.

3. Discussion

Compared to adults, strokes and stroke-like attacks are rarely seen in children and adolescents. Besides, their etiologies are not the same as those in adults [4]. Among the vascular and intravascular etiologies are Moyamoya, vascular malformations, sinus thrombosis, cardiac diseases, trauma, collagen vascular diseases, sickle cell anemia, thrombocyte pathologies, genetic factors resulting in strokes like Factor V Leiden and prothrombin gene mutations, as well as encephalitis and meningitis with an autoimmune or infectious etiology. All these factors should be investigated within a specific algorithm in children with transient acute hemiparesis or focal neurological deficits. Migraine and mitochondrial diseases may lead to similar episodes. Nevertheless, these two are among the principal etiological factors with limited laboratory indicators. What can be determined in the case of migraine are non-specific signals and in that of mitochondrial diseases, transient, patch-like T2, FLAIR hyperintensities. Family history and accompanying clinical symptoms may be very helpful and guiding when algorithms for diagnosis are evaluated.

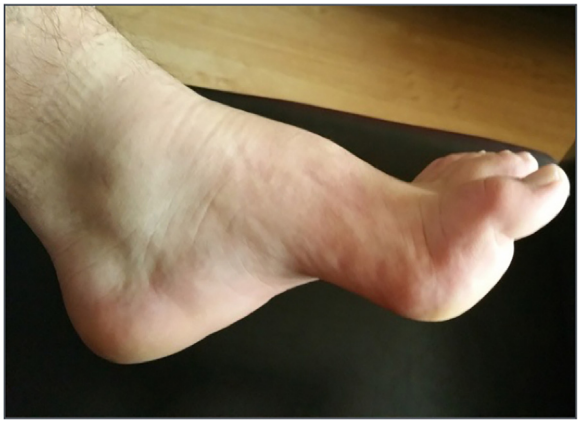

Fig. 1 – Pes cavus deformity.

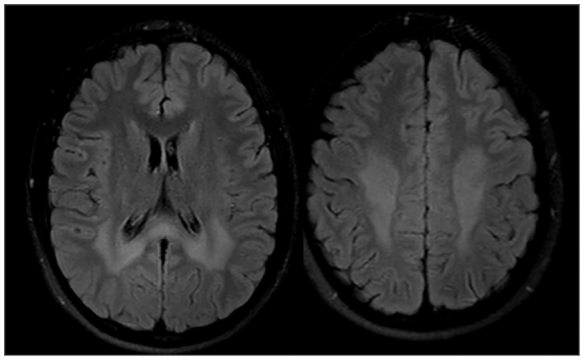

Fig. 2 – Bilateral periventricular, symmetrical and confluent hyperintense lesions during the stroke-like attack at axial FLAIR MR images. The hyperintense lesions are marked in the posterior regions, and subcortical U-fibers are preserved.

Symptoms in CMTX1 usually occur during late childhood and adolescence. The age interval at which the disease is most frequently seen is between 7 and 26 years. Compared to women, CMTX1 has a tendency to occur earlier in men and its course is more severe [1,5,6]. Gait disturbance is the most frequently encountered initial symptom [5]. It is when this symptom begins that a slight decrease in nerve conduction velocity occurs along with a mild lengthening in distal latency and F-latency, as well as a decrease in amplitude. EMG findings indicate the presence of both axonal and demyelinating involvement. Apart from its typical clinical features, CMTX1 has been reported to cause the below conditions in a small proportion of patients: sensorineural hearing loss, tremor in hands, pathologic fractures, recurrent CNS findings, and reversible changes in white matter [2].

Nicholson et al. are the first to demonstrate that evoked potential anomalies are the indicators of the CNS involvement in CMTX1 [7]. Severe CNS dysfunction in this disease is rather rare. Neurological deficits with an acute or subacute onset, or with a fluctuating course are often episodic and reversible. The severity of CNS involvement does not correlate with that of peripheral neuropathy [2]. Some of the predisposing factors are as follows: fever, exercise, traveling to higher or lower

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