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CASE REPORTS

Facioscapulohumeral muscular dystrophy (FSHD) and multiple sclerosis: a case report

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Facioscapulohumeral muscular dystrophy 1 (FSHD1) is an autosomal dominant neuromuscular disorder, associated with reduction of tandemly arrayed repetitive DNA elements D4Z4 (DRA), at 4q35. Few cases, especially carriers of 1-3 DRA show a syndromic form. Anecdotally the association of FSHD with multiple sclerosis (MS) is reported. Herein we report a 33 years old Caucasian with a molecular diagnosis of FSHD1 with classical phenotype (clinical category A2) and concomitant white matter lesions suggestive of MS. White matter lesions in patients with FSHD have often been described but rarely investigated in order to evaluate a possible diagnosis of MS. We think that MS and FSHD remain clearly distinct diseases, but growing evidences show a widespread and variable activation of the immune system in patients suffering from FSHD probably an hypotheses on a potential common pathogenetic mechanism between these two disorders could should be better investigated.

Key words: autoimmunity, myopathy, central nervous system

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Conflict of interest
The Authors declare no conflict of interest

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Introduction

Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant neuromuscular disorder characterized by progressive weakness of muscle in the face, shoulder girdle and arms. FSHD1 has been associated with reduction of tandemly arrayed repetitive DNA elements, D4Z4, at 4q35. Alleles with 1-3 D4Z4 repeats are generally associated with a syndromic form with extramuscular manifestations (i.e. central nervous system involvement with mental retardation and hearing loss) [1]. To our knowledge, there are only two cases, whose one is an autopsy case [2], of FSHD associated with multiple sclerosis [3]. Herein, we report another case of concomitant multiple sclerosis (MS) in a patient with FSHD1.

Case report

We evaluated a 33 years old Caucasian man referring a short episode of blurred vision in right eye occurs five months before and spontaneously resolved in fortnight period. At our visit he informs us that two years ago, over the course of 2-3 weeks, he developed also lower limb hypoesthesia and diplopia. However, he had a previous genetically confirmed diagnosis of FSHD1 (molecular analysis of DNA documented intermediate deletion

on 4q35 with 3 D4Z4 repeats). The muscle impairment started in the second decade of life with inability to bury the eyelashes, difficulty in pursing the lips, as well as whistling or puffing out the cheeks, winging of the scapulae and bilateral foot drop. In fact his neurologic examination showed a classic FSHD phenotype (Fig. 1), clinical category A2 [4]. Anyway, he presented right Babinski sign, moderate impairment of deep sensation and mild spasticity in the lower limbs, too. As there was centre nervous system involvement patient underwent a MRI brain that showed multiple demyelinating lesions both in the supratentorial and infratentorial white matter and several demyelinating lesions of the spinal cord. None of them demonstrated gadolinium enhancement (Fig. 2). White matter brain MRI alterations suggested a diagnosis of multiple sclerosis (MS). Then visual evoked potentials revealed mild delayed latencies bilaterally. Somatosensory and motor evoked responses both for upper and lower limb were altered [5-7].

Spinal fluid was acellular with normal protein and glucose level; however, oligoclonal bands were detected in CSF electrophoresis only, but not in the serum. Subsequently, the patient underwent an extensive work-up

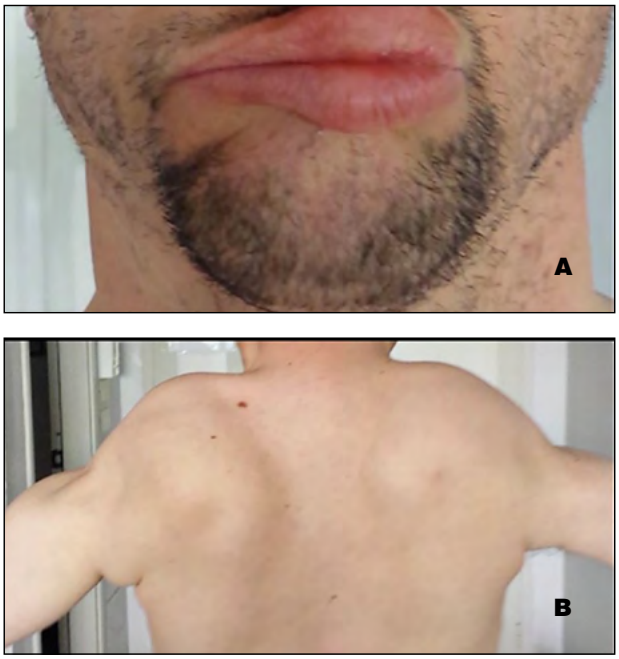

Figure 1. Weakness of lips' (A) and shoulder muscles (B) configuring a classic clinical phenotype of Facioscapulohumeral muscular dystrophy (clinical category A2).

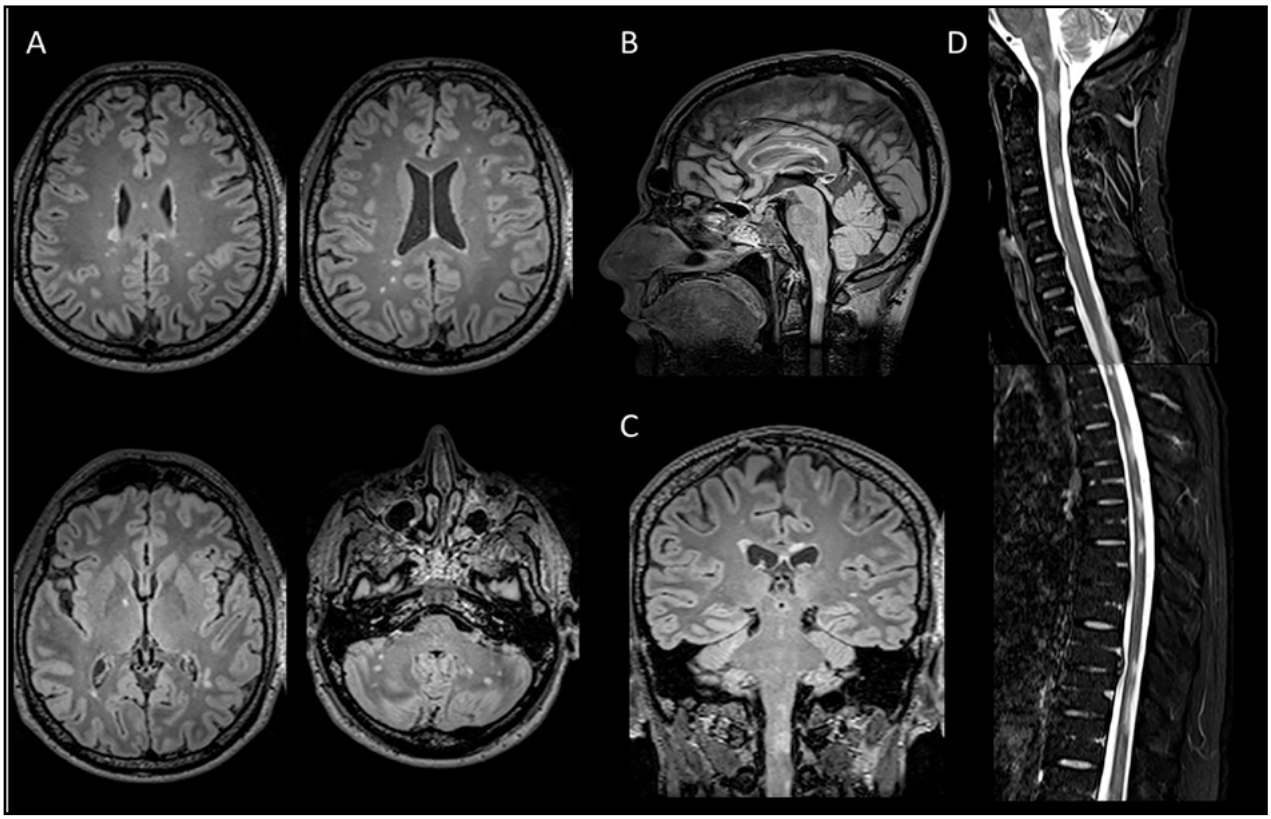

Figure 2. Axial FLAIR images (A) show multiple demyelinating lesions both in the supratentorial and infratentorial white matter. Sagittal (B) and coronal (C) FLAIR sequence depicts corpus callosum and medulla involvement. Sagittal STIR (D) demonstrates several demyelinating lesions of the spinal cord.

searching for metabolic, immune-mediated, infectious and vascular disorders that might simulate the working diagnosis of MS and all tests were either negative or normal. Neuropsychological evaluation using standard battery [8,9] showed no abnormalities. On the other hand, nerve conduction studies were within normal limits [10], whereas needle electromyography confirmed a myopathic pattern consistent with his previous diagnosis of FSHD. Finally, the patient fulfilled the Mc Donald criteria for the diagnosis of MS [11]. He started a disease modifying treatment with dimetilfumarate and non-pharmacological treatments were applied in an attempt to recover disability [12,13].

Discussion

White matter lesions in patients with FSHD have often been described but rarely investigated or correlated with the clinical and/or laboratory phenotype in order to evaluate a possible diagnosis of multiple sclerosis [14].

An autoptic case and a clinical case of association between FSHD and MS have been described [2,3] and hypotheses on a potential common pathogenetic mechanism between these two different disorders has been proposed. Obviously, MS and FSHD remain clearly distinct diseases, but growing evidences show a widespread and variable activation of the immune system in patients suffering from FSHD. Pathological data in muscle biopsy in FSHD patients are consistent with a significant presence of CD8+ T cells both in perivascular and endomysial infiltrates, together with macrophages. Moreover, an increased percentage of circulating CD14+T-bet+ cells and an increased spontaneous production of IL12/IL23p40, IFNγ, TNFα, IL6 and IL10 by PBMC have been described [15]. Furthermore, the presence of demyelinating lesions that have the characteristics of dissemination over time and space suggesting the diagnosis of multiple sclerosis, are increasingly noted in patients suffering from other genetically defined muscular diseases.

However, given the high prevalence of multiple sclerosis, we consider that the association between these two entities in our patient is casual. In the presence of signs or symptoms suggestive of involvement of the CNS in a primitively muscular pathology or the occasional finding of lesions of the white matter in the brain MRI, should always orientate a deep diagnostic screening in order to exclude a possible comorbidity with diseases such as multiple sclerosis.

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