Reviewer's report

Title: Facioscapulohumeral Muscular Dystrophy and Charcot-Marie-Tooth Neuropathy 1A - Evidence for “double-trouble” Overlapping Syndromes

Version: 4  Date: 24 May 2013

Reviewer: Mario Sabatelli

Reviewer’s report:

Authors describe a patient in whom two different genetic diseases occurred by chance.

This case report may have an educational value.

The paper needs some minor Essential revisions:
1. The introduction and the discussion are too long.
2. The following sentences should be changed:
   a. In the background section:
      “Due to the broad clinical diversity resulting from a shortened D4Z4 locus, it is often a diagnostic challenge to diagnose FSHD correctly.”
      This sentence should be rewritten.
   b. In the clinical data section
      “During the 5th decade, weakness of arm elevation and finger extensors and abductors occurred.”
      Which “abductors” were involved?
   c. In the clinical data section
      “Standing or walking on toes or heels was not impaired but mild ataxia was observed.
      Additionally, distal muscle weakness (extensor digitorum MRC 4/5, abductor pollicis MRC 4/5, tibialis anterior and gastrocnemius muscles MRC 2/5) along with marked muscle atrophy was found.”
      It is impossible for an individual with weakness 2/5 of both tibialis anterior and gastrocnemius to stand or walk on toes and heels.
      How do authors explain mild ataxia?
   d. In the clinical data section
      “EMG revealed neurogenic changes in the tibialis anterior muscles bilaterally without spontaneous activity.”
Which pattern was found in other muscles, namely in proximal ones?

e. In the clinical data section

“Nerve conduction velocity in upper limb motor nerves showed demyelinating neuropathy (median nerve 17 m/s, DML 9.5 ms; ulnar nerve 21 m/s, DML 7.2 ms).”

Amplitude of CMAPS should be reported

f. In the muscle biopsy section

“An open muscle biopsy of the left tibialis anterior muscle was performed at the age of 21. It showed moderate myopathic alterations with numerous hypertrophic type I fibres without necrotic fibres or inflammatory changes (see Fig. 4).”

Based on the figure provided, some neurogenic changes are present. How can authors state that hypertrophic fibers were type I? Was an ATPase staining performed? If yes was there type grouping?

g. In the discussion section

“In our patient, FSHD probably results from a de novo mutation ....”

This statement cannot be accepted as no clinical or genetic analysis could be performed on patient’s parents

h. In the discussion section

“In addition to stochastic effects and environmental influences, some of this variability might be caused by concomitant mutations in other genes for neuromuscular conditions.”

Variable expressivity of an autosomal dominant genetic disease may be due to other factors not mentioned here.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests