Amyotrophic Chorea-acanthocytosis: a rare presentation of a rare disease

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Introduction

Chorea-acanthocytosis is a severe neurodegenerative disease characterized by cognitive decline, involuntary movements and the presence of **thorny red blood cells** known as acanthocytes. It is caused by a mutation of the chorein (**VPS13A**) gene, and is inherited in an autosomal recessive pattern. In some cases, central symptoms may be accompanied by **myopathy and axonal neuropathy**.
We describe the case of a patient affected with chorea-acanthocytosis that we have been following for over ten years.

Presentation and history

This patient came to medical attention for the first time at the age of 40, for the insidious onset of **muscle cramps and progressive weakness of the upper and lower limbs**. His older brother was also affected by a similar condition.
At the time of his first admission, the strength deficit was confirmed; **diffuse fasciculations** were observed, in absence of other involuntary movements. Serum CK was over 3000 U/L and a neurophysiological evaluation showed diffuse signs of axonal neuropathy and active denervation.
Over the years, the weakness had made autonomous gait impossible; the patient had also developed **dysarthria and mixed dysphagia**, impairing speech and feeding.
We admitted the patient at the age of 52 for a new evaluation.

General and Neurological Examination

At the time of our most recent observation, the patient was bedridden. His clinical picture was dominated by severe weakness, with paresis of the upper limbs (2/5 score on the Medical Research Council scale) and plegia of the lower limbs. There was a **striking degree of muscular atrophy**, with occasional fasciculations.
His speech was hypophonic and severely dysarthric, with the frequent occurrence of **spontaneous vocalizations**; his mixed dysphagia had progressed to the point that a percutaneous endoscopic gastrotomy had to be performed in order to ensure safe and appropriate nutrition. **Bucco-oro-lingual choreic movements** were present; however self-harming behavior, a common feature of chorea-acanthocytosis, was not observed.
His cognitive state could not be properly assessed due to the severe dysarthria, but the patient appeared to be wakeful, aware of his surroundings and able to interact with relatives and with the medical staff.

Diagnostic Work-up.

- Brain MRI showed a **marked volume reduction of the lenticular and caudate nuclei** in T1-weighted sequences (**fig. 1A**), with ex vacuo dilatation of the lateral ventricles; in T2-weighted and FLAIR sequences (**fig 1B, C**), the lenticular nuclei also appeared hyperintense, as an expression of neurodegeneration and gliosis. A moderate degree of cortical atrophy was also present.
- Electroneuromyography confirmed a severe axonal neuropathy in all limbs, with **secondary neurogenic changes** in the muscle.
- Muscle biopsy, performed on the left deltoid, showed an **extreme degree of variability in fiber size (fig 2A)**, with a majority of mostly type-II atrophic fibers surrounding highly hypertrophic type-I ones (with diameters reaching 190 micrometers) **(fig 2B)**. An increase in the connective tissue could also be observed.
- **17% of his red blood cells** were acanthocytes. **Chorein was undetectable.**
- Genetic testing for **VPS13A** mutations is ongoing.

Conclusion

This case underlines the importance of suspecting chorea-acanthocytosis even in cases presenting with **mainly peripheral symptoms**, in which the extrapyramidal involvement is relatively minor.

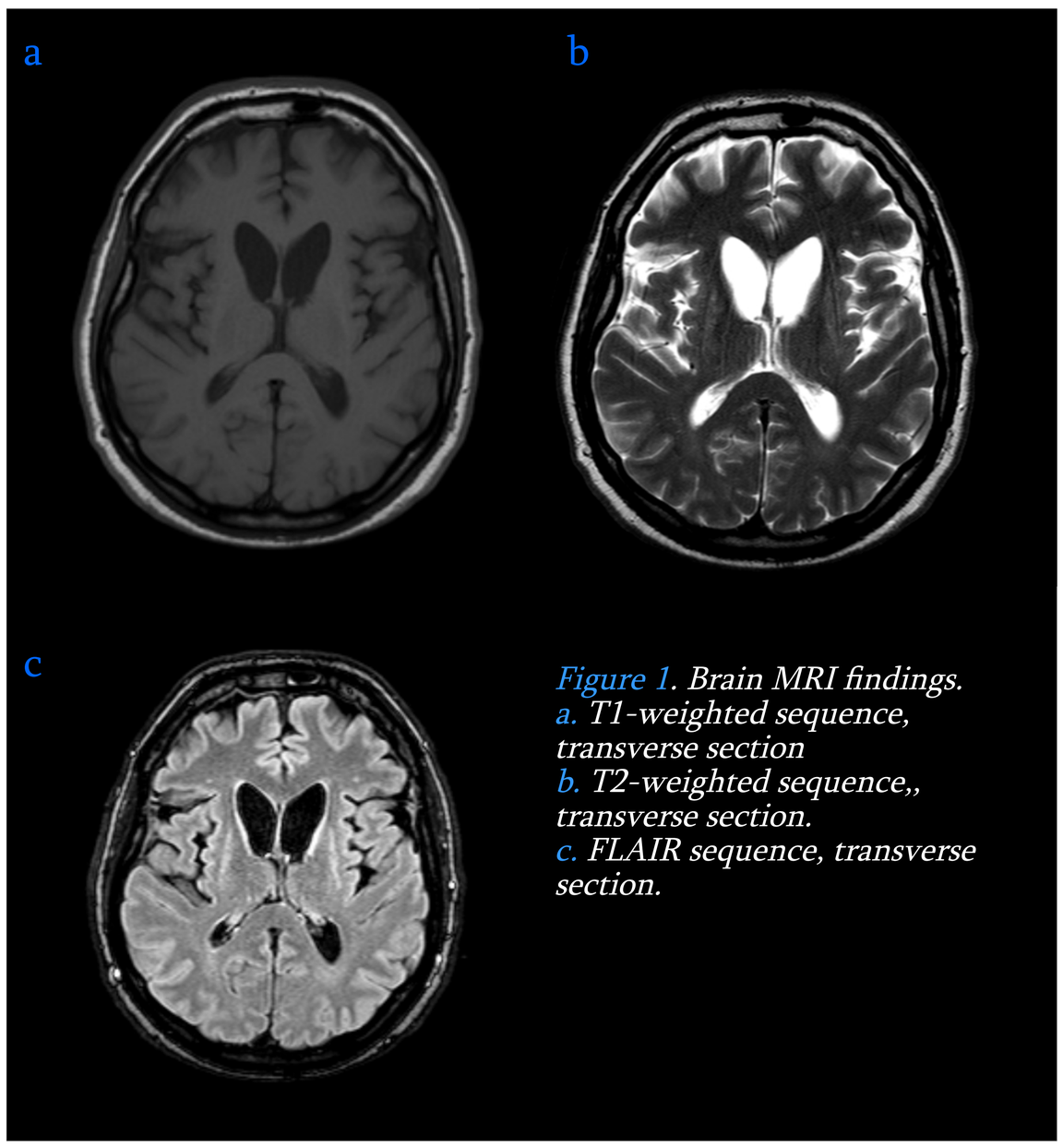

Figure 1. Brain MRI findings.
a. T1-weighted sequence, transverse section
b. T2-weighted sequence,, transverse section.
c. FLAIR sequence, transverse section.

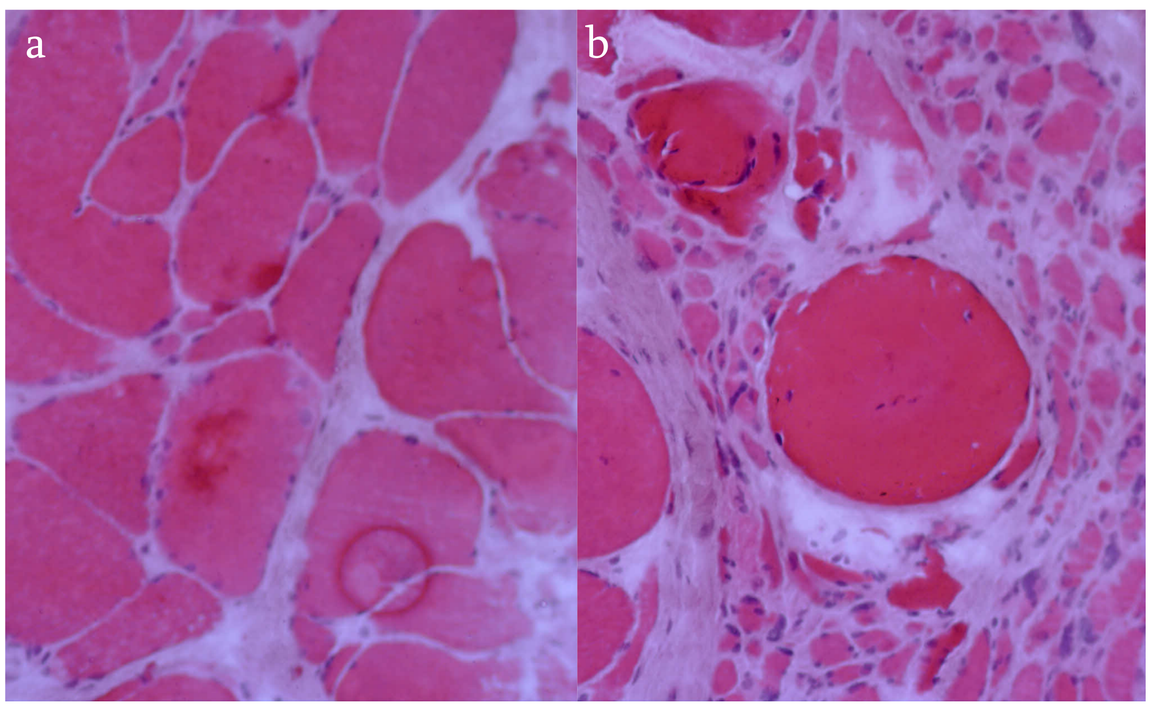

Figure 2. Muscle Biopsy of the left deltoid.
a. Variability in fiber size, with most fibers presenting an angular shape.
b. A giant hypertrophic fiber surrounded by atrophic ones. An overabundance of connective tissue can also be observed.
(Hematoxylin-Eosin staining, 20x magnification).