Gluten sensitivity in a patient with late onset Friedreich ataxia: diagnostic and pathogenetic implications

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Introduction

- Gluten Ataxia (GA) is an immune-mediated sporadic cerebellar ataxia defined by the presence of antigliadin antibodies in ataxic patients
- GA as a clinical entity has often been debated being the causative role of antibodies in triggering cerebellar damage still controversial, in fact they have also been found in hereditary ataxias and healthy controls (about 15%)
- Friedreich Ataxia (FA) is one of the most common autosomal recessive cerebellar ataxias, caused by mutations in the FXN gene
- Herein we describe a case of late-onset cerebellar ataxia with positive celiac-associated antibodies

Case report

- 61 years-old woman (consanguineous parents) complaining, since the age of 55 years, of progressive unsteadiness while walking, difficulty in manipulating objects, speech disorders and urinary incontinence
- Neurological examination: ataxic gait with positive Romberg sign, square-wave jerks during eye pursuit movements, dysartria, muscle hypotonia, brisk deep tendon reflexes (DTRs) and dysmetria. SARA score: 13
- Laboratory screening: complete blood count, immunoglobulins, complement, erythrocyte sedimentation rate (ESR), auto-antibodies (ANA, ENA, nDNA, cardiolipin), folate, vitamin B12, vitamin E, thyroid hormones and anti-Tg, anti-TPO antibodies, alpha-FP, CEA, Ca 15.3, Ca 125, Ab anti Hu, anti-Yo, anti-Ri, anti-amphifisin, anti-CV2, anti-Ma2 were normal
- Tilt test : normal
- Echocardiography: normal (no IVS hypertrophy)
- Brain MRI: small subcortical T2-hyperintense gliotic lesions with no cerebellar atrophy (Figure 2)
- EMG: normal
- Evocated Potentials (PEV: absence left P100; BAEP and PESS: normal; PEM: abnormal CCT bilaterally)
- Laboratory screening revealed a gluten sensitivity (anti-gliadin antibodies 15.4 U/ml (n.v. < 9.6 U/ml), positive anti-endomysium antibodies and negative anti-transglutaminase antibodies)
- HLA-DQ typing showed the DQB1*02/DQA1*05 combination and DQ8
- The patient did not refer any gastro-intestinal symptom and the duodenal biopsy revealed no abnormalities
- Genetic analysis of frataxin gene (FXN) : large GAA expansion in intron 1 of FXN, compatible with a diagnosis of (VLOFA): 127/77 (n.v. < 38)
- The patient starts gluten free diet but after 8 months clinical condition was unchanged

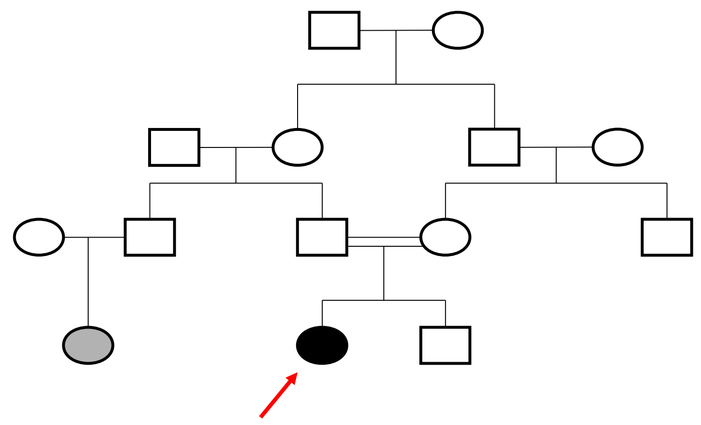
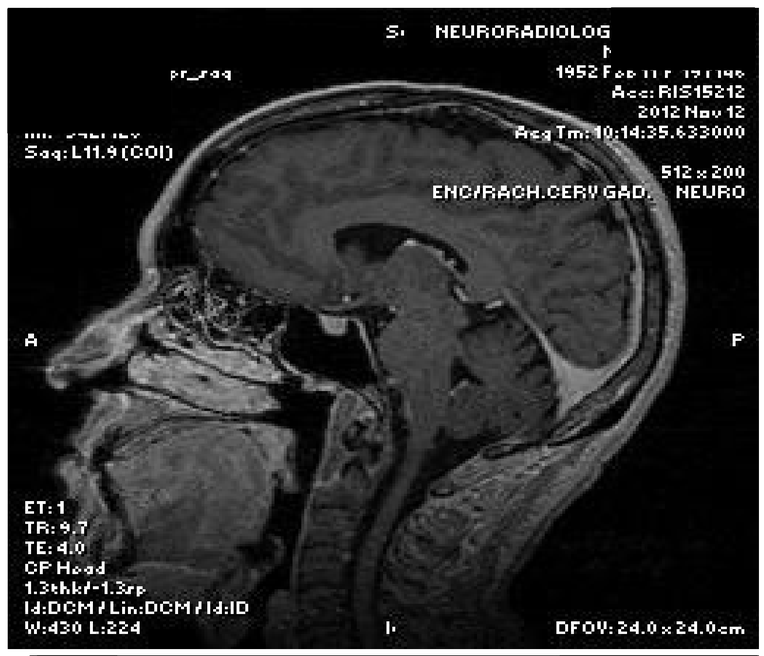


Figure 1: Family tree



b

a

Figure 2: Brain MRI small subcortical T2-hyperintense gliotic lesions (a) with no cerebellar atrophy (b)

Discussion

- We described a FA case in whom laboratory screening revealed also a gluten sensitivity indicating a possible double contribution to cerebellar degeneration
- Gluten sensitivity have been rarely reported in patients with hereditary ataxia (SCAs) but no one in association with FA.
- The role of gluten sensitivity in the patogenesis of cerebellar damage is not yet clearly elucidated. Patients with SCA2 with associated positive AGA , showed not improvement to dietary restrictions raising the question of whether cerebellar degeneration might induce the synthesis of anti-gliadin antibodies as a secondary event.

References

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