Spastic paraparesis revealing celiac disease

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To the Editor,

Celiac disease (CD) is a chronic immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Neurological symptoms in CD patients remain rare occurring approximately in 6 to 10% of cases (1). They may precede the diagnosis or occur during the course of the disease. They must be sought systematically, given the therapeutic and prognostic implications. Spastic paraparesis is rarely reported during CD.

We report the case of a 16-year-old girl issued from a non consanguineous marriage with no particular medical history, with a good psychomotor development. She developed, since the age of 3 years, progressive gait disorders causing frequent falls. Neurological examination disclosed spastic paraparesis .Sensation and coordination were normal. General physical examination showed staturo-ponderal delay and mucocutaneous pallor.

Cranial and spinal Magnetic Resonance Imaging (MRI) was normal.

Biological investigations revealed signs of malabsorption : hypocholesterolemia, hypochromic microcytic anemia and decreased serum levels of both iron and ferritin. Infectious serology (Lyme, brucellosis, HIV, hepatitis B and C), serum vitamin*'s* levels and cerebrospinal fluid analysis were normal.

Immunologic studies were negative except for CD (anti-transglutaminase 2 antibodies (AT2) were positive and gastro- esophageal endoscopy and duodenal biopsy objectified a grade IV villous atrophy). The diagnosis of CD was made. The patient was put under Gluten Free Diet (GFD). The evolution was marked by an improvement of gait disorders. The patient regained walking autonomy after 18 months of gluten free diet.

Recognizing CD can be sometimes challenging. In fact, it was reported that large proportions of those with the disease are not diagnosed until adulthood. One of the reasons of diagnostic delay is that the classic gastrointestinal way may be missing and masked by symptoms that seem to be unrelated to a gastrointestinal disease, especially the neurological manifestation.

Causality is now well established for certain neurological manifestations such as gluten ataxia or peripheral neuropathy.

The originality of our observation consists in the nature of the neurological impairment : spastic paraparesis. In fact, paraparesis has been exceptionally reported in CD. Only 6 cases have been published (2-6) having an association of CD and paraparesis (see table 1).

There is no particular physiopathological mechanism explaining this neurological impairement but rather physiopathological hypotheses common in neurological damage during Celiac Disease:

– Nutritional deficiencies (vitamin B12, B9, A, E, D, K, iron, calcium, zinc and copper). However, the occurrence of such complications in subjects without any nutritional deficiency concluded that malabsorption' signs alone could not explain the neurological disorders.

– Autoimmunity was also evoked : Anti transglutaminase 2 antibodies (AT2), anti-gliadin antibodies and more recently anti-tissue transglutaminase **6** antibodies would be implicated in the pathogenesis of neurological complications. Indeed, tissue transglutaminase is widely expressed in the central nervous system and plays a major role in the maintenance of vascular endothelial integrity and in the regulation of cellular apoptosis. AT2 induced therefore neuronal degeneration and alteration of the blood- brain barrier responsible for autoimmune angiopathy. (7)

In our patient, spastic paraplegia was initially suspected; but the absence of consanguinity and similar cases in the family as well as the improvement of gait disorder with GFD were against this diagnosis .For us, celiac disease seems to be at the origin of spastic paraparesis. The effectiveness of the GFD strengthens our hypothesis.

In conclusion, because CD is a potentially treatable cause of neurologic manifestation, tests for CD should be included in the evaluation of neurological syndrome of unknown etiology ; whatever its nature ; even in the absence of typical gut symptoms.

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Table 1. — **Summary of the different cases of the literature presenting paraparesis and celiac disease**

Reference (Year)	Age (years)	Personal History	Symptomatology/Clinical examination	Biology	Cranial and spinal MRI	Diagnosis	Treatment
(2) 2016	5	Biotinidase deficiency	Inability to walk, Paraparesis, strabismus, and back pain	Biotinidase deficiency	Hyperintensities in the T2-weighted image of the periaqueductal region and the cervical spinal cord	Biotinidase Deficiency associated to CD	GFD Biotinidase
(3) 2006	20	CD since the age of 2 years	Progressive gait disorder since the age of 3 years CE : spastic paraparesis staturo-ponderal delay	Normal	Normal	CD	GFD
	20	Congenital cataract/ CD since the age of 8 years	Progressive gait disorder since the age of 3 years. CE : spastic paraparesis	Normal	Subcortical hyperintensities in the T2 weighted image	CD	GFD
(4) 2004	46	CD since the age of 12 years	Spastic paraparesis, Posterior cordonal syndrome			Myelopathy-Peripheral neuropathy associated to CD	GFD
(5) 2017	17 months	No personal medical history	Paraparesis, Disturbed sensibility, Areflexia	Iron deficiency Elevated immunoglobulin A antibodies against gliadin and tissue transglutaminase	Abnormal high signal intensity on T2-weighted images in the cord on the thoracic level, transverse myelitis	Transverse myelitis associated to CD	GFD Methyl-prednisolone
(6) 2015	3	No personal history	Diarrhea, Vomiting, Dehydration then appearance of a flaccid paraparesis	Severe hypokalemia		hypokalemia due to CD (malabsorption)	*Potassium correction but no improvement of paraparesis *GFD *Steroids

Abbreviations : GFD : Gluten free diet ; CD : celiac disease ; CE : clinical examination, MRI : Magnetic Resonance Imaging.

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