Cerebellar ataxia and coeliac disease

Howard W Sander, Paul Magda, Russell L Chin, Anita Wu, Thomas H Brannagan III, Peter H R Green, Norman Latov

A 37-year-old woman presented in July, 2002, with a 12-year history of progressive dysarthria and ataxia. Her symptoms became noticeably worse during pregnancy in 1999 and 2001. She had also been anaemic for the past 7 years, and coeliac disease had been diagnosed in 1997. At that time, she had high serum concentrations of IgG and IgA antibodies to gliadin, an endomysial titre of 1:32, and duodenal atrophy on endoscopy; a duodenal biopsy showed subtotal villous atrophy. Neurological tests were done at the same time; median somatosensory evoked potentials showed a delay between the lower brainstem and cortex. She underwent tests for spinocerebellar ataxia,1–3 brainstem auditory and visual evoked potentials, and cerebral MRI, none of which showed any abnormalities. Cervical spine MRI showed mild degenerative changes. For 5 years, she had followed a strict gluten-free diet, but on examination in 2002 she had severe dysarthria, left finger-to-nose dysmetria, poor right rapid-alternating and fine-finger movements, diminished oculomotor, sensory, or bladder dysfunction.1 The ataxia of limb, station, and gait, and/or dysarthria, occasionally improves after a prolonged gluten-free diet.2 Ataxic patients also have a higher incidence of gluten-sensitivity, defined as the presence of antibodies to gliadin or transglutaminase in the absence of histological evidence of coeliac disease.1 IVIg has had a beneficial effect in patients with sporadic cerebellar ataxia, in the context of GAD antibodies,3 and gluten sensitivity, defined as the presence of antibodies to gliadin, purkinje cells, and voltage-gated calcium channels. The only abnormal results were increased IgA antibodies to transglutaminase, and glutamic acid decarboxylase (GAD). Cerebral MRI showed superior vermis atrophy, whereas lumbosacral MRI was normal. H reflexes were absent. Electromyography showed prolonged durations of motor unit potentials distally. We did not do a nerve biopsy, and we do not have the facilities to do indirect immunohistochemistry or immunofluorescence.

We treated her with intravenous immunoglobulin (IVIg) 2 g/kg initially, and 0.5 g/kg 2 weeks later. Within a month, she reported substantial improvements in her speech and gait. She was able to safely hold her children. Acquaintances noted that the audible slap of her walk disappeared. Squatting, walking, stair-climbing, tandem gait, and standing on one leg all became much easier, and she no longer spilt cups of liquid. On examination, we found that all the neurological signs had improved; she still had slight dysarthria and left finger-nose dysmetria, an unsteady gait with a widened base and very slight slapping, and impaired tandem walking, and we calculated a modified ICARS score of 3/96. She developed a slight rash, so we stopped IVIg and gave her a single dose of methylprednisolone. However, 5 weeks later, she deteriorated, and 8 weeks after the last IVIg infusion, her modified ICARS score had worsened to 17/96. We changed to another brand of IVIg and again started with 2 g/kg after hydrocortisone pretreatment. 3 weeks later, she was much improved, with a modified ICARS score of 3/96. When last seen in September, 2003, she had been stable for 6 months, on maintenance doses of IVIg, 0·5 g/kg/month.

Coeliac disease occurs in approximately 9% of patients with idiopathic cerebellar ataxia. Patients can present with ataxia of limb, station, and gait, and/or dysarthria, oculomotor, sensory, or bladder dysfunction.1 The ataxia occasionally improves after a prolonged gluten-free diet.2 Ataxic patients also have a higher incidence of gluten-sensitivity, defined as the presence of antibodies to gliadin or transglutaminase in the absence of histological evidence of coeliac disease.1 IVIg has had a beneficial effect in patients with sporadic cerebellar ataxia, in the context of GAD antibodies,3 and gluten sensitivity,4 but has not yet been shown to work for the combination of ataxia and coeliac disease. It would be interesting to test plasma-apheresis or corticosteroids, as an alternative to costly IVIg, and to ascertain whether all ataxic patients with coeliac disease eventually respond to therapeutic long-term immunosuppression.

References