

Cerebellar ataxia associated to anti-glutamic acid decarboxylase autoantibody (anti-GAD)

Partial improvement with intravenous immunoglobulin therapy

José Luiz Pedroso, Pedro Braga-Neto, Livia Almeida Dutra, Orlando G.P. Barsottini

High levels of glutamic acid decarboxylase (GAD) autoantibody may be observed in a few patients with sporadic ataxias, supporting an autoimmune pathogenesis of the cerebellar syndrome¹.

We describe a patient with GAD autoantibody (anti-GAD) ataxia and type 1 diabetes with partial improvement of neurological symptoms after immunoglobulin therapy.

CASE

A 51 year-old man presented to our hospital with nine-years history of progressive gait instability, difficulty walking and insulin dependent diabetes. Family history was unremarkable. On examination, there was ataxic gait, severe limb and trunk ataxia, and dysarthria. He scored 65 in International Cooperative Ataxia Rating Scale (ICARS) and 20 in Scale for Assessment and Rating of Ataxia (SARA), an objective toll for evaluating ataxia severity. Electroneuromyography was normal. Blood tests, thyroid function, antibodies and serologic tests were normal, except for high serum anti-GAD: 3.2 U/mL (normal range: <1.0 U/mL). Brain magnetic resonance imaging (MRI) disclosed mild cerebellar atrophy. Genetic tests for spinocerebellar ataxias type 1, 2, 3 and 6 were negative. Immunoglobulin therapy was started, 0.4 g/Kg daily, for five consecutive days every month, during three months. Partial improvement of motor symptoms was observed four months after the beginning of treatment: he scored 37 in ICARS and 16 in SARA.

DISCUSSION

GAD is the enzyme that catalyses the conversion of glutamic acid to the neurotransmitter gamma-amino butyric acid. Neurological disorders related to GAD antibodies include cerebellar ataxia, palatal myoclonus, stiff-person syndrome, drug-resistant epilepsy and also limbic encephalitis^{1,2}. Experimental data have suggested a direct excitotoxic effect of GAD antibodies on Purkinje cells to explain cerebellar involvement, although there is controversy regarding the exact pathogenic role of neurological disorders related to GAD antibodies².

The clinical spectrum of anti-GAD ataxia comprises slowly progressive cerebellar ataxia syndrome evolving in months or years, associated with cerebellar atrophy

on brain MRI in about half of cases. Cerebrospinal fluid analyses frequently detects oligoclonal bands^{2,3}. Diagnosis is supported by high serum GAD antibodies. Association with late-onset type 1 diabetes and other autoimmune disorders is frequently seen². On the other hand, a Brazilian series have demonstrated that around 50% of long-duration type 1 diabetes subjects without neurological symptoms presented high titers of GAD antibodies⁴. Although positive, our patient presented lower levels of anti-GAD antibodies compared to other case reports².

Other case reports have suggested that immunotherapy might be useful in autoantibody-positive cerebellar ataxia, but this still subject of controversy. Recently, Nanri et al. described a clear improvement in ICARS in two patients with anti-GAD ataxia using immunoglobulin. Additionally, steroids and immunosuppressive agents might also be used⁵.

This short report and analyses of previous data suggest that testing for GAD antibodies may be indicated in patients with sporadic cerebellar ataxia, particularly when type 1 diabetes is present. Treatment with immunoglobulin or other immunosuppressive agents might be considered in these cases.

REFERENCES

- Honnorat J, Saiz A, Giometto B, et al. Cerebellar ataxia with anti-glutamic acid decarboxylase antibodies: study of 14 patients. *Arch Neurol* 2001;58:225-230.
- Vianello M, Tavolato B, Armani M, Giometto B. Cerebellar ataxia associated with anti-glutamic acid decarboxylase autoantibodies. *The Cerebellum* 2003;2:77-79.
- Abele M, Weller M, Mescheriokov S, Burk K, Dichyons J, Klockgether T. Cerebellar ataxia with glutamic acid decarboxylase autoantibodies. *Neurology* 1999;52:857-859.
- Pardini VC, Mourão DM, Nascimento PD, Vívolo MA, Ferreira SRG, Pardini H. Frequency of islet cell autoantibodies (IA-2 and GAD) in young Brazilian type 1 diabetes patients. *Braz J Med Biol Res* 1999;32:1195-1198.
- Nanri K, Okita M, Takeguchi M, et al. Intravenous immunoglobulin therapy for autoantibody-positive cerebellar ataxia. *Intern Med* 2009;48:783-790.

ATAXIA CEREBELAR ASSOCIADA AO ANTICORPO ANTI-ÁCIDO GLUTÂMICO DESCARBOXILASE (ANTI-GAD): MELHORA PARCIAL APÓS TRATAMENTO COM IMUNOGLOBULINA ENDOVENOSA

Department of Neurology and Neurosurgery- Division of General Neurology and Ataxias, Universidade Federal de São Paulo, São Paulo SP, Brazil.

Correspondence: José Luiz Pedroso - Rua Botucatu 740 - 04023-900 São Paulo SP - Brasil. E-mail: zeluzpedroso@yahoo.com.br

Received 17 May 2011, received in final form 14 July 2011. Accepted 21 July 2011.