Experience with immunotherapy in 3 patients with cerebellar ataxia associated with anti-glutamic acid decarboxylase antibodies

Dear Editor,

High levels of glutamate decarboxylase enzyme (anti-GAD) are frequently detected in stiff person syndrome (SPS), and they have also been reported more recently in a group of patients with cerebellar ataxia. As these syndromes are probably of autoimmune origin, several immunomodulatory regimens have been employed, and these treatments have yielded variable results. However, there are no studies describing long-term outcomes for these patients.

We describe the initial clinical response and long-term outcome after immunomodulatory treatment in 2 patients with cerebellar ataxia with anti-GAD antibodies. We also present a third case with long-standing SPS and cerebellar ataxia associated with anti-GAD antibodies and describe how the 2 clinical manifestations responded differently to treatment.

Case 1

We present the case of a 75-year-old woman with a history of Graves disease and diabetes mellitus type 1 (DM1). At the age of 60, she began to experience symptoms of instability, dysarthria, and nystagmus which progressed for several months. Brain MRI study showed mild cerebellar atrophy. Anti-GAD antibody titres in serum were measured by radioimmunoassay, which yielded a level of 39 500 U/mL; CSF analysis revealed positive oligoclonal bands (OCB). The patient was treated with intravenous immunoglobulins (IVIG) dosed at 0.4 g/kg/day for 5 days, and symptoms improved slightly. Treatment with IVIG has since been administered every 3-4 months, and the patient’s condition remains stable to date. This case report has already been published.

Case 2

The second case is a 55-year-old woman with no relevant personal history who developed pancerebellar syndrome at the age of 50. At the same time, she was diagnosed with DM. The brain MRI study revealed atrophy of the cerebellar vermis (Fig. 1). Anti-GAD antibody titres in serum were measured by radioimmunoassay, which yielded a level of 23 000 U/mL. The patient was treated with methylprednisolone (1000 mg/day for 5 days), and clinical symptoms ...

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Figure 1 Case 2: Brain MRI scan, sagittal T1-weighted sequence displaying vermian atrophy.

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improved somewhat. Since that phase, she has been treated with prednisone (2.5 mg/day) and azathioprine (50 mg/day) and no symptom progression has been observed.

Case 3

Woman aged 65 years with a history of exophthalmos secondary to prior Graves disease. At the age of 50, she began experiencing symptoms of leg rigidity and spasms. At the age of 52, she underwent an examination in another centre, which revealed scanning dystarthis, limb ataxia, generalised hyperreflexia, and increased tone of the lower limbs. She was attended for the first time at our hospital at the age of 65, and we observed exacerbated symptoms, including inability to remain standing without help. Anti-GAD antibody titres in serum and CSF were 0.99 and 0.97 respectively (in this case we used another technique whose reference value is < 0.027); CSF was OCB-negative. At the same time, she was diagnosed with pernicious anaemia, and levels of vitamin B₁₂ were corrected with intramuscular vitamin supplementation. Brain MRI study revealed overall cerebellar atrophy (Fig. 2). The patient was treated with IVIG (0.4 g/kg/day for 5 days), which improved leg spasms and rigidity, but the cerebellar syndrome displayed no changes.

The video provided as additional online material shows the following: pretreatment (0 to 45 seconds): (1) upper-limb dysmetria, more severe on the right side, and dyssyndactochokinesia, (2) generalised hyperreflexia and increased tone of the lower limbs, especially the right leg, and (3) pronounced rigidity of the legs, and difficulty walking; post-treatment (46 to 90 seconds): (1) dysmetria and dyssyndactochokinesia, which remains unaltered, (2) decreased tone of the legs, and (3) decreased rigidity of the legs during walking with improved ability to take steps. Cerebellar ataxia, however, remains unchanged.

Nevertheless, other authors have reported a good response to immunological therapy. It seems reasonable to think that treatment may be effective when administered early, before irreversible neuronal loss has occurred. Therefore, early diagnosis and treatment of patients with cerebellar ataxia with anti-GAD antibodies are essential.

Although it is difficult to make a long-term forecast due to the spontaneous and fluctuating course of the disease, long-term immunomodulatory treatment could help stabilise the patient's condition. Further studies are needed to establish the most appropriate strategies for both initial and long term treatment.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.nrleng.2013.06.018.

References


Figure 2 Case 3: Brain MRI scan, sagittal T1-weighted sequence displaying atrophy of the vermis and cerebellar hemispheres.
Diaphragmatic flutter: A case report and literature review

Aleteo diafragmático. Descripción de caso y revisión de la literatura

Diaphragmatic flutter is a rare condition characterised by rhythmic involuntary contractions of the diaphragm and other respiratory muscles innervated by cervical nerve roots. It has been described in people of all ages and both sexes. Its clinical presentation varies greatly and clinical symptoms are quite unusual, which may result in late diagnoses and ineffective treatments. Symptoms include thoracic or abdominal pain and dyskinetic movements in the thorax and abdominal wall. Idiopathic diaphragmatic flutter is the most common presentation, although it has also been described in association with other clinical and surgical entities. Diagnosis is based on strong clinical suspicion in addition to fluoroscopy or electrophysiological studies showing diaphragm movement. No clinical studies have addressed treatment options for this disorder. Current treatment relies on expert opinion and case reports and may be pharmacological or non-pharmacological.

We present the case of a 17-year-old adolescent who experienced sudden onset of pain in the right lumbar region and right iliac fossa which radiated to the back and lasted 45 days. Pain was associated with involuntary movements of the trunk. She was referred to the emergency department by the neurology department due to exacerbation of pain, presence of predominantly right-sided rhythmic involuntary movements of the trunk, nausea, vomiting, and a burning feeling in the right facial and brachial regions and right hemithorax. Our patient had previously been evaluated by several departments at an outpatient clinic, including the neurology, internal medicine, psychiatry, psychology, and rehabilitation and physical medicine departments. She had also undergone neural therapy and physiotherapy, but symptoms did not improve. Findings from contrast and non-contrast MRI studies of the cervical and thoracic spine were normal (Fig. 1). She was treated with fluoxetine 20 mg/day and with clonazepam drops; the latter improved her symptoms slightly. Our patient had a history of recurrent

Figure 1  Gadolinium-enhanced sagittal T2-weighted MRI sequences of the cervical (A) and thoracic (B) spine, with normal results.

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