Both the patient's improvement with conservative treatment and the complete resolution of his symptoms indicate neurapraxia secondary to axonal damage as the probable aetiology; neurotmesis is less probable, as the damage to both nerves would have been irreversible. Furthermore, neurapraxia is the proposed aetiological mechanism in most of the reported cases of Tapia syndrome secondary to orotracheal intubation.[9]

References

1. Tapia AG. Un caso de paralisis del lado derecho de la laringe y de ungue, con paralisis del externo-cleidomastoidea y trapecio del mismo lado. Siglo Medica. 1905;52:211—3.
2. Bogousslavsky J, Fox AJ, Barnett HJ, Hachinski VC, Vinitski S, Carey LS, et al. Clinico-topo-graphic correlation of small vertebrobasilar infarct using mag- netic resonance imaging. Stroke. 1986;17:929—38.
3. Schoenberg BS, Massey EW. Tapia's syndrome. The erratic evolution of an eponym. Arch Neurol. 1979;36:257—60.
4. Rouvière H, Delmas A. Anatomía humana: descriptiva, topográfica y funcional. Tomo 1. Cabeza y Cuello. 11ª ed. Barcelona: Masson; 2005.
5. Lykoudis EG, Seretis K. Tapia's syndrome: an unexpected but real complication of rhinoplasty: case report and literature review. Aesth Plast Surg. 2012;36:557—9.
6. Nalladaru Z, Wessels A, DuPreez L. Tapia's syndrome — a rare complication following cardiac surgery. Interact CardioVasc Thorac Surg. 2012;14:131—2.
7. Tesei F, Poveda LM, Strali W, Tosi L, Farneti G. Unilateral laryngeal and hypoglossal paralysis (Tapia's syndrome) following rhinoplasty in general anaesthesia: case report and review of literature. Acta Otorhinolaryngol Ital. 2006;26:219—21.
8. Boga I, Aktas S. Treatment, classification and review of Tapia syndrome. J Craniofac Surg. 2010;21:278—80.
9. Coninckx M, Cardoen S, Hemelsoet D. Tapia's syndrome in the intensive care unit: a rare cause of combined cranial nerve palsy following intubation. Acta Neurol Belg. 2015;115:533—7.

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Myoclonus-dystonia and cerebellar ataxia in association with anti-glutamic acid decarboxylase autoimmunity☆

Distonía mioclónica y ataxia cerebelosa en la autoinmunidad antiglutámico-descarboxilasa

Dear Editor:

The main inhibitory neurotransmitter in the central nervous system is γ-aminobutyric acid (GABA). Autoimmunity against glutamic acid decarboxylase (GAD), a key element in the synthesis of GABA from glutamic acid, selectively inhibits GABAergic neurotransmission, causing such neurological conditions as stiff person syndrome, progressive encephalomyelitis with rigidity and myoclonus, epilepsy, and cerebellar ataxia. It may be associated with neoplasms, autoimmune polyglandular syndrome, type 1 diabetes mellitus, and autoimmune thyroiditis.[1–3] We present a case of myoclonus-dystonia and cerebellar ataxia in association with anti-GAD autoimmunity. The study was approved by our local healthcare research ethics committee, and the patient gave written informed consent.

Our patient was a 41-year-old man who 14 years earlier presented acute extension contracture of the right upper limb, which lasted several weeks. Sequelae consisted of involuntary movements of the hand and flexion of the wrist, which subsequently also appeared in the left upper limb. Symptoms remained stable until 2 years ago, when the patient's condition progressively worsened despite treatment with baclofen, tizanidine, and oxcarbazepine; the patient was left unable to write or use utensils.

The physical examination revealed dystonic upper limb posture, with arms in adduction and elbows in extension, and forced flexion of the wrists, and sudden, asynchronous jerks predominantly affecting distal muscles, both spontaneous and provoked by voluntary movement; the left lower limb showed abnormal posture in external rotation. Finger-to-nose and heel-to-knee tests showed dysmetria, stance and gait appeared broad-based, and the patient was unable to walk in tandem. During admission, the patient was clinically stable.

A blood analysis revealed anti-GAD65 antibodies at a titre of >1:30 000. The analysis of the cerebrospinal fluid (CSF) detected a positive band for anti-GAD65 antibodies; no other antineuronal antibodies were detected in the serum or CSF.

T1-weighted brain MRI sequences showed superior cerebellar vermis atrophy; T2-weighted FLAIR sequences displayed enlarged cerebellar fissures, reduced size of gyri, and hyperintensities in both cerebral hemispheres (Fig. 1). Chest and abdomen CT scan findings were normal. An electromyography study revealed involuntary muscle spasms in

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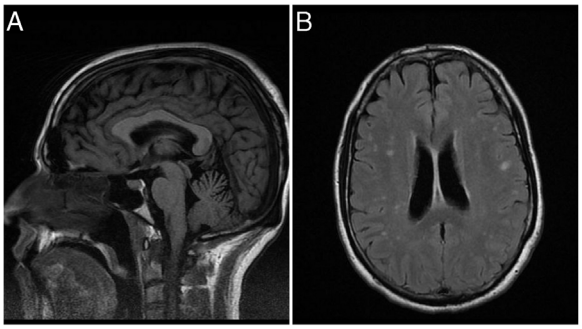

Figure 1 Brain magnetic resonance imaging study: (A) T1-weighted sequence showing superior cerebellar vermis atrophy. (B) T2-weighted FLAIR sequence showing hyperintensities.

the right triceps, which were compatible with myoclonus; an electroencephalography study did not reveal epileptiform activity.

We administered 2 cycles of intravenous methylprednisolone at 1 g/day for 5 days, and one cycle of intravenous immunoglobulins at 0.4 g/kg/day for 5 days; no improvement was observed. After treatment with 2400 mg/day gabapentin, the patient was able to walk in tandem, the posture of the limbs improved, and the amplitude and frequency of myoclonus decreased. We then added tiagabine at 15 mg/day and the patient regained the ability to perform such manual tasks as writing or using cutlery.

Myoclonus-dystonia, also known as DYT11 dystonia, is a syndrome characterised by dystonic limb posture accompanied by muscular jerks; the syndrome follows an autosomal dominant inheritance pattern. It manifests in the first or second decade of life; location in the body varies, intensity fluctuates, and symptoms improve with alcohol consumption. Our patient's symptoms resemble those of hereditary myoclonus-dystonia. Treatment consists of anticholinergics, pimozide, and tetrabenazine.[4–6] The improvement observed with gabapentin, which increases GABA concentration in nervous tissue in healthy volunteers,[7] and tiagabine, a synaptic GABA reuptake inhibitor,[8] may suggest a GABA deficiency, as this protein is abundant in the basal ganglia.[9]

Ataxia secondary to anti-GAD autoimmunity is explained by the inhibition of GABAergic neurotransmission due to the loss of Purkinje cells,[1,2,10] which use GABA as a neurotransmitter.[11] Gabapentin has been shown to improve ataxia in late cortical cerebellar atrophy,[12] in which the loss of Purkinje cells causes selective reduction of GABA in the dentate nuclei and CSF.[13,14] Also, in a case of adult-onset GM2 gangliosidosis, cerebellar ataxia improved with administration of tiagabine[12]; the drug also improved ataxia associated with anti-GAD autoimmunity in our case.

Initial treatment for anti-GAD autoimmunity consists of corticosteroids or immunoglobulins, followed by immunosuppressants for maintenance of remission.[3,15] This immunosuppressive treatment was probably ineffective because the disease was not at the active inflammation phase, as demonstrated by the absence of pleocytosis or high CSF protein levels and/or abnormal signal intensity on MRI, and the prolonged, gradual progression of symptoms. Nevertheless, ataxia, dystonia, and myoclonus considerably improved with gabapentin and tiagabine.

The association between anti-GAD autoimmunity and myoclonus-dystonia has not previously been reported in the literature, and it should be considered in sporadic cases of the disease. The improvement achieved with gabapentin and tiagabine in our case is noteworthy given the resistance to immunomodulatory treatment. Further studies with larger samples are therefore needed to confirm the efficacy of GABAergic agents in treating the different syndromes caused by anti-GAD autoimmunity.

References

1. Ishida K, Mitoma H, Mizusawa H. Reversibility of cerebellar GABAergic synapse impairment induced by anti-glutamic acid decarboxylase autoantibodies. J Neurol Sci. 2008;271:186–90.
2. Ishida K, Mitoma H, Wada Y, Oka T, Shibahara J, Saito Y, et al. Selective loss of Purkinje cells in a patient with anti-glutamic acid decarboxylase antibody-associated cerebellar ataxia. J Neurol Neurosurg Psychiatry. 2007;78:190–2.
3. McKeon A, Tracy J. GAD65 neurological autoimmunity. Muscle Nerve. 2017;56:15–27.
4. Kinugawa K, Vidailhet M, Clot F, Apartis E, Grabli D, Roze E. Myoclonus-dystonia: an update. Mov Disord. 2009;24:479–89.
5. Ritz K, Gerrits M, Foncke E, van Ruissen F, van der Linden C, Vergouwen M, et al. Myoclonus-dystonia: clinical and genetic evaluation of a large cohort. J Neurol Neurosurg Psychiatry. 2008;80:653–8.
6. Bhattacharyya KB, Roy A, Biswas A, Pal A. Sporadic and familial myoclonic dystonia: report of three cases and review of the literature. Ann Indian Acad Neurol. 2016;19:258–60.
7. Kuzniecky R, Ho S, Pan J, Martin R, Gilliam F, Faught E, et al. Modulation of cerebral GABA by topiramate, lamotrigine, and gabapentin in healthy adults. Neurology. 2002;58:368–72.
8. Ostergaard LH, Gram L, Dam M. Potential antiepileptic drugs. Tiagabine. In: Levy RH, Mattson RH, Meldrum BS, editors. Antiepileptic drugs. New York: Raven Press Ltd.; 1995. p. 1057–61.
9. Flórez J, Pazos A. Neurotransmisión en el sistema nervioso central. In: Flórez J, editor. Farmacología humana. Barcelona: Masson S.A.; 1997. p. 409–33.
10. Saiz A, Arpa J, Sagasta A, Casamitjana R, Zarranz JJ, Tolosa E, et al. Autoantibodies to glutamic acid decarboxylase in three patients with cerebellar ataxia, late-onset diabetes mellitus and polyendocrine autoimmunity. Neurology. 1997;49:1026–30.
11. Ottersen OP. Neurotransmitters in the cerebellum. Rev Neurol (París). 1993;11:629–36.
12. Gazulla J, Ruiz-Gazulla C, Tintoré M. GABAergic pharmacotherapy in the treatment of motor disorders of the central nervous system. Curr Pharm Des. 2015;21:4989–95.
13. Kanazawa I, Kwak S, Sasaki H, Mizusawa H, Muramoto O, Yoshizawa K, et al. Studies on neurotransmitter markers and neuronal cell density in the cerebellar system in olivopontocerebellar atrophy and cortical cerebellar atrophy. J Neurol Sci. 1985;71:193–208.
14. Ogawa N, Kuroda H, Ota Z, Yamamoto M, Otsuki S. Cerebrospinal fluid gamma-aminobutiric acid variations in cerebellar ataxia. Lancet. 1982;2:215.

15. Lauria G, Pareyson D, Pitzolu M, Bazzigaluppi E. Excellent response to steroid treatment in anti-GAD cerebellar ataxia. Lancet Neurol. 2003;2:634—5.

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Drug-resistant secondary headache associated with administration of biological drugs☆

Cefalea secundaria farmacorresistente asociada a fármacos biológicos

Dear Editor:

Headache has been reported as an adverse reaction to numerous biological drugs used to treat rheumatoid arthritis. More specifically, it is listed as an adverse reaction on the summaries of product characteristics for abatacept,[1] a human recombinant fusion protein that blocks the activation of T lymphocytes, and certolizumab pegol,[2] a Fab′ fragment of a humanised recombinant TNF antibody conjugated with polyethylene glycol.

We present the case of a 69-year-old woman who attended our headache unit due to exacerbation of existing tension-type headache. She consulted due to oppressive right temporal headache of moderate to severe intensity, with attacks occurring daily. She did not present nausea, vomiting, photophobia, or phonophobia, and headache was not aggravated by movement. The patient had history of asthma, treated with salmeterol and fluticasone; seronegative rheumatoid arthritis; and tension-type headache of mild intensity, which was well controlled with analgesics. Five days before consultation, she had started treatment with intravenous perfusions of 750 mg abatacept, to which she attributed the exacerbation of her headaches. She had history of arthritis, treated with hydroxychloroquine, methotrexate, leflunomide, rituximab, etanercept, adalimumab, and tocilizumab, which were withdrawn due to ineffectiveness or intolerance.

All neurological examination findings were normal, with no evidence of focal neurological signs; eye fundus and gait assessment and cranial palpation revealed no alterations. The results of a head CT scan, blood analysis, and a brain MRI scan were also normal. The patient was diagnosed with tension-type headache secondary to abatacept infusion; we started treatment with amitriptyline, observing no response at 4 months.

Given the temporal relationship between infusion of the drug and exacerbation of headache, we agreed with the patient to suspend abatacept for 3 months and subsequently reintroduce it with subcutaneous administration. The patient presented a distinct improvement in headache after the drug was suspended, and pain was controlled with pregabalin (75 mg every 12 hours), which she was using to treat pain associated with rheumatoid arthritis. With this treatment, pain became mild and the frequency of attacks reduced to less than 2 per month; headache did not interfere with the patient's daily life. When abatacept was reintroduced 3 months later, headache was reactivated. We therefore decided to withdraw the drug definitively and to maintain a watchful waiting approach with regard to the rheumatoid arthritis.

Three months later, arthritis worsened and we started treatment with golimumab. Response was good, with no effect on headache, but the drug had to be suspended a year later due to alopecia and weight loss of up to 7 kg. We subsequently started treatment with certolizumab pegol, which was also suspended due to continued weight loss and onset of facial flushing, palpitations, and pain of very similar characteristics to those of the headache associated with abatacept. Headache improved once more when the drug was withdrawn.

At 8 months without treatment, after a further worsening of the arthritis and with no further treatments available for the condition, the rheumatology department opted to administer abatacept once more. Treatment response was good but headache was exacerbated, despite trials with increased pregabalin dose (225 mg daily) and escitalopram, mirtazapine, and lacosamide.

Headache associated with rheumatoid arthritis is relatively common, either as the initial symptom,[3] associated with osteoarticular conditions, or secondary to cervical spondyloarthropathy or atlanto-axial subluxation.[4] As is the case with other biological drugs,[5] disease-modifying drugs for rheumatoid arthritis have been associated with headache. High incidence of headache is reported among patients receiving abatacept[6—8] or certolizumab pegol[9]; in both cases, pain is mild and is often associated with reactions when the infusion is administered.

Our patient had rheumatoid arthritis and presented headache with a clear temporal association with 2 disease-modifying treatments, with pain improving when the drugs were withdrawn and reappearing when they were reintroduced. The headache was drug-resistant, which influenced

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