Anti-Hu associated paraneoplastic neuropathy simulating an axonal variant of Guillain-Barré syndrome☆,☆☆

Neuropatía paraneoplásica asociada a anti-Hu simulando una variante axonal de Guillain-Barré

Dear Editor:

Acute motor/motor-sensory axonal neuropathy (AMAN/AMSAN) is a rare, severe form of Guillain-Barré syndrome (GBS).[1] Although it is usually triggered by infection, on exceptional occasions it may present as a paraneoplastic syndrome.[2] We present one such case of paraneoplastic neuropathy simulating axonal GBS.

Our patient was a 53-year-old man with personal history of arterial hypertension and smoking (100 packs/year). Two weeks before admission to hospital he presented dysaesthesia in a glove and stocking pattern, subsequently extending up to the elbows and knees; as dysaesthesia progressed, the patient also presented weakness, diplopia, and urinary retention. The neurological examination revealed paresis of both lateral rectus muscles, left tonic pupil, paresis of the distal muscles of the lower limbs, and hypoaesthesia to proprioceptive and nociceptive stimuli. The patient also displayed generalised hyporeflexia with normal plantar reflexes, postural instability during the Romberg test, and ataxic gait. He did not display anhidrosis.

A blood test revealed no alterations, with normal erythrocyte, leucocyte, and platelet counts; normal kidney and liver function; and tumour marker levels (CEA, Ca 19.9, AFP, and PSA) within the normal range. Immune tests yielded negative results, except for an antinuclear antibody titre of 1/160. A chest and abdomen CT scan revealed right hilar adenopathy and isodense nodular lesions in the liver parenchyma. The initial neurophysiological study revealed signs of predominantly sensory axonal involvement. A CSF analysis revealed albuminocytologic dissociation, with high protein levels (202.80 mg/dL) and no red blood cells; the remaining CSF findings were normal. Anti-Hu antibodies were detected in the CSF and serum (Western blot and indirect immunofluorescence). Transbronchial biopsy was performed to obtain a sample of the hilar adenopathy, and the patient was diagnosed with small-cell lung cancer.

Immunoglobulin treatment (5 days' duration) was ineffective. The symptoms worsened, with the patient presenting permanent dysaesthesia, allodynia, increased weakness of distal muscles, bilateral tonic pupils (with response to pilocarpine), ophthalmoparesis, and severe dysautonomia (orthostatic hypotension, constipation, urinary retention, nocturnal hyperhidrosis, and recurrent syncope). Ten days after immunoglobulin treatment, he received 5 cycles of plasmapheresis, which stabilised the neurological symptoms. However, the patient died of respiratory complications a month after diagnosis.

GBS is usually caused by a demyelinating polyneuropathy. Since its initial description, several rare forms have been reported, including the axonal subtype, encompassing AMAN and AMSAN, with the latter being the more severe form.[1,3]

From a neurophysiological viewpoint, the axonal subtype is characterised by axonal degeneration and reversible nerve conduction block, which progress in parallel with clinical symptoms over the course of days to weeks.[1,4]

The literature includes very few reports of axonal forms of GBS associated with antineuronal antibodies and presenting as a paraneoplastic syndrome.[5–7] Anti-Hu antineuronal antibodies are usually associated with small-cell lung cancer, but have also been detected in such other cancers as breast and prostate tumours.[8] Anti-Hu antibodies can be determined in the serum or the CSF.[9] Unlike GBS, sensory and sensorimotor neuropathies are often associated with presence of anti-Hu antibodies due to direct immune-mediated damage to the neuronal cell body.[8,10,11] In these cases, a sural nerve biopsy reveals axonal degeneration and occasionally inflammatory cells in the epineurial space.[4] Dysautonomia secondary to paraneoplastic neuropathies, as in the case presented here, may present in isolation or combined with other symptoms.[12] It is frequently associated with anti-Hu antibodies and may be a key finding in screening for paraneoplastic syndromes: paraneoplastic origin should be suspected when the initial symptoms are severe.[2,13,14] Presence of dysautonomic symptoms suggests poorer prognosis given the potential for severe complications.

As in other paraneoplastic syndromes, management of paraneoplastic neuropathies focuses on treating the underlying neoplasia. Plasmapheresis and various immunosuppressants have been tested, including corticosteroids, rituximab, and intravenous immunoglobulins; these treatments seem to be effective in demyelinating forms.[1] In cases of axonal degeneration, however, they are often ineffective or may stabilise progression with severe sequelae due to the aggressive course of axonal forms, especially when associated with anti-Hu antibodies. Non-responders may benefit from cyclophosphamide or rituximab pulse therapy, although the effectiveness of these approaches has only been tested in isolated cases.[14]

References

1. Kuwabara S, Yuki N. Axonal Guillain-Barré syndrome: concepts and controversies. Lancet Neurol. 2013;12:1180–8.
2. Koike H, Tanaka F, Sobue G. Paraneoplastic neuropathy: wide-ranging clinicopathological manifestations. Curr Opin Neurol. 2011;24:504–10.
3. Dimachckie MM, Bahron RJ. Guillain syndrome and variants. Neurol Clin. 2013;31:491–510.
4. Oh SJ, Gürtekin Y, Dropcho EJ, King P, Claussen GC. Anti-Hu antibody neuropathy: a clinical, electrophisiological and pathological study. Clin Neurophysiol. 2005;116:28–34.

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☆☆ This study was presented in poster format at the 37th Annual Meeting of the Andalusian Society of Neurology (2014).

5. López JL, Amezcua S, Pascual J, Algara M. Acute motor axonal neuropathy associated with anal carcinoma: paraneoplastic neurological syndrome or coincidence? Rep Pract Oncol Radiother. 2011;16:54—7.
6. Nokura K, Nagamatsu M, Inagaki T, Yamamoto H, Koga H, Sugimura K, et al. Acute motor and sensory neuronopathy associated with small-cell lung cancer: a clinicopathological study. Neuropathology. 2006;26:329—37.
7. Bishay RH, Paton J, Abraham V. Variant Guillain-Barré syndrome in a patient with non-Hodgkin's lymphoma. Case Rep Hematol. 2015;2015, 979237.
8. Rudniki SA, Dalmau J. Paraneoplastic syndromes of peripheral nerves. Curr Opin Neurol. 2015;18:598—603.
9. Schwenkenbecher P, Chacko LP, Wurster U, Pars K, Pul R, Sühs KW, et al. Intrathecal synthesis of anti-Hu antibodies distinguishes patients with paraneoplastic peripheral neuropathy and encephalitis. BMC Neurol. 2016;16:136.
10. Camdessanché JP, Antoine JC, Honnorat J, Vial C, Petiot P, Convers P, et al. Paraneoplastic peripheral neuropathy associated with anti-Hu antibodies. A clinical and electrophysiological study of 20 patients. Brain. 2002;125:166—75.
11. Blaes F, Tschernatsch M. Paraneoplastic neurological disorders. Expert Rev Neurother. 2010;10:1559—68.
12. Höftberger R, Rosenfeld MR, Dalmau J. Update on neurological paraneoplastic syndromes. Curr Opin Oncol. 2015;27:489—95.
13. Palao S, Corral I, Vera R, Alonso de Leciñana M. Progressive dysautonomia as initial manifestation of anti-Hu antibody-related syndrome. Neurologia. 2007;22:899—902.
14. Graus F, Dalmau J. Paraneoplastic neuropathy. Curr Opin Neurol. 2013;26:489—96.

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Evaluation of the duration of the effect of botulinum toxin in clinical practice☆

Evaluación de la duración del efecto de la toxina botulínica en la práctica clínica

Dear Editor:

Focal dystonia is the most frequent form of primary dystonia, with a prevalence of 110 cases per million population.[1] Cervical dystonia and blepharospasm are the most frequent forms of focal dystonia.

The treatment of choice for focal dystonia consists of periodic injections of botulinum toxin (BTX).[2,3] In clinical practice, BTX is administered at fixed intervals, generally longer than 3 months. For more than 2 decades, these intervals have been recommended with a view to reducing the risk of the patient developing neutralising antibodies against BTX. However, although the highly purified type-A botulinum toxins currently used present practically no association with the development of clinically relevant neutralising antibodies,[4] these prolonged intervals are maintained. The duration of the clinical improvement induced by BTX may be shorter than 3 months in patients with focal dystonia.[5,6]

In this letter, we present the results of a study conducted at our centre to evaluate the duration of the effect of BTX in patients with focal dystonia. From September 2015 to March 2016, we evaluated 90 consecutive patients diagnosed with blepharospasm and cervical dystonia and treated with BTX. Using a structured questionnaire, we collected data on the duration of the effect of the last injection of BTX, as well as the actual duration of the intervals between the last 3 treatment sessions. We also collected data on disease duration, duration of treatment with BTX, the dose used, the type of BTX, and patients' demographic data (sex and age).

Data were analysed using descriptive statistics and the one-way ANOVA test was used to compare means.

Women accounted for 73% of the patients, and mean age (standard deviation) was 67.8 years (14.0); 31 patients presented cervical dystonia and 59 blepharospasm. Mean disease duration was 11.5 years (8.4). Botulinum toxin A was administered to 77.8% of patients and 22.2% received incobotulinumtoxin A. The mean dose was 46.3 units (11.8) in patients with blepharospasm and 191.3 units (62.1) in patients with cervical dystonia. The duration of the effect of BTX was 11.6 weeks (4.0), with actual infiltration intervals being 15.3 weeks (3.2) ($P < 0.02$). Overall, symptoms reappeared before 3 months in 38 patients (42.2%). In these patients, the mean duration of the effect of BTX was 8.4 weeks (2.1), with the actual infiltration interval being 14.2 weeks (2.7) ($P < 0.05$). Symptoms reappeared before 3 months in 44% of the 59 patients with blepharospasm and in 42% of the 31 patients with cervical dystonia. After analysing the duration of the effect in patients presenting symptom

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