

5. Niewiadomska M, Kulczycki J, Wochnik-Dyjas D, Szpak GM, Rakowicz M, Łojkowska W, et al. Impairment of the peripheral nervous system in Creutzfeldt-Jakob disease. *Arch Neurol.* 2002;59:1430–6.
6. Panegyres PK, Armari E, Shelly R. A patient with Creutzfeldt-Jakob disease presenting with amyotrophy: a case report. *J Med Case Rep.* 2013;7:218.
7. Allen IV, Dermott JH, Connolly JH, Hurwitz LJ. A study of a patient with the amyotrophic form of Creutzfeldt-Jakob disease. *Brain.* 1971;94:715–24.
8. Nowacki P, Kulczycki J, Narolewska A, Grzelec H. Amyotrophic form of Creutzfeldt-Jakob disease with rapid course in 82-year-old man. *Folia Neuropathol.* 2000;38:161–3.
9. Worrall BB, Rowland LP, Chin SM, Mastrianni JA, et al. Amyotrophy in prion diseases. *Arch Neurol.* 2000;57:33–8.
10. Meissner B, Kallenberg K, Sanchez-Juan P, Krasnianski A, Heinemann U, Vargas D, et al. Isolated cortical signal increase on MR imaging as a frequent lesion pattern in sporadic Creutzfeldt-Jakob disease. *Am J Neuroradiol.* 2008;29:1519–24.
11. Shiga Y, Miyazawa K, Sato S, Fukushima R, Shibuya S, Sato Y, et al. Diffusion-weighted MRI abnormalities as an early diagnostic marker for Creutzfeldt-Jakob disease. *Neurology.* 2004;63:443–9.
12. Moreno F, Arriola L. Neuroimagen en el diagnóstico de las encefalopatías espongiiformes transmisibles humanas. *Neurología.* 2006;2:428–36.
13. Ortega-Cubero S, Luquin MR, Domínguez I, Arbizub J, Pagola I, Carmona-Abellán MM, et al. Neuroimagen estructural y funcional en las enfermedades priónicas humanas. *Neurología.* 2011;27:27.

A. Díaz-Díaz*, M. Hervás-García, R. Amela-Peris, J.R. García-Rodríguez

Servicio de Neurología, Complejo Hospitalario Universitario Insular Materno-Infantil (CHUIMI), Las Palmas de Gran Canaria, Las Palmas, Spain

*Corresponding author.

E-mail address: abel.diaz88@gmail.com (A. Díaz-Díaz). 2173-5808/

© 2016 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Autoimmune necrotising myopathy: A case report[☆]



Miositis necrosante autoinmune: a propósito de un caso

Dear Editor,

We present the case of a 63-year-old woman with a history of obesity, arterial hypertension, dyslipidaemia, and diabetes mellitus who was being treated with losartan, hydrochlorothiazide, liraglutide, metformin, long-acting insulin, and rosuvastatin. She visited the neurology department due to a one-year history of slightly increased creatin kinase (CK) levels, which were initially symptomless, and were detected in routine blood tests. She subsequently presented progressive weakness in the proximal muscles of the lower limbs, displaying difficulties climbing stairs, and particularly standing up from the floor, which was associated with increased CK values (1932 IU/L). Both the patient's symptoms and the elevated CK levels persisted after discontinuation of statins. The neurological examination revealed normal cranial nerves; the upper limbs displayed preserved strength, slightly hypoactive stretch reflexes, and normal tactile perception; the lower limbs showed bilateral proximal loss of strength, especially in hip flexion (3/5) and adduction (4/5), and no deficit in knee flexion/extension, foot dorsiflexion, or plantar flexion bilaterally, positive

Gowers sign, and markedly hypoactive stretch reflexes (1/4); the patient's gait presented mild myopathic features.

Analytical studies showed persistently increasing CK levels, with initial figures of 300–500 IU/L, raising to 1932 IU/L, and finally 2195 IU/L, with increased aldolase levels (22.9 IU/L) and proportionally elevated transaminase levels (AST 55 IU/L and ALT 115 IU/L). The remaining parameters, including blood count, erythrocyte sedimentation rate, and kidney function, displayed normal values. The electromyography study (EMG) showed diffuse moderate myopathic involvement. A quadriceps biopsy revealed focal myophagocytosis, and fibre necrosis with no inflammatory infiltrates, vasculitis, or amyloid deposition. The tests performed revealed no evidence of viral infection, connective tissue disease, or neoplasm. The immunology study yielded positive results for anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) antibodies, confirming the diagnosis of autoimmune necrotising myopathy (ANM) secondary to statin use. The patient started treatment with prednisone at 1 mg/kg/day and azathioprine at 50 mg/12 h, which improved her clinical condition at 10 months of follow-up; regarding motor symptoms, she presented slightly impaired hip flexion (4+/5), with no impaired strength in other muscle groups; CK levels had decreased to 72 IU/L.

ANM secondary to statin use is a rare, recently described clinical entity; the antibody involved in its pathogenesis was identified in 2010.¹ It is characterised by persistence of muscle weakness even after discontinuation of treatment with statins; cellular necrosis in the muscle biopsy; and presence of anti-HMGCR antibodies.¹ Incidence is estimated at 2–3 cases per 100 000 patients treated with statins.² The condition is slightly more frequent in women and more common in patients aged 50 years or older.¹ The class II HLA-DRB1*11:01 allele is associated with the development of anti-HMGCR antibodies.³ In patients with a genetic predisposition, the use of statins causes overexpression of HMGCR through a

[☆] Please cite this article as: Navarro Pérez MP, Sanabria Sanchinell AA, Alfaro Torres J, Marquina Ibañez I, Larrodé Pellicer P. Miositis necrosante autoinmune: a propósito de un caso. *Neurología.* 2019;34:67–68.

currently unknown mechanism, resulting in the production of anti-HMGCR antibodies.⁴

ANM is clinically characterised by progressive muscle weakness (usually proximal and symmetrical), elevated serum CK levels, and persistence of weakness and elevated CK levels despite discontinuation of statins.⁵ EMG studies show decreased amplitude and duration of motor potentials with increased spontaneous activity. Histology studies show cellular necrosis with minimal inflammation and MHC-I overexpression in necrotic and non-necrotic muscle fibres.^{2,6} Diagnosis is confirmed by the presence of anti-HMGCR antibodies. Differential diagnosis includes other autoimmune necrotising myopathies, such as myopathy associated with anti-signal recognition particle antibodies and paraneoplastic necrotising myopathy.⁷ Although some authors report no increase in the prevalence of malignant tumours in patients with ANM, others recommend systematically performing imaging studies (chest radiography, mammography, endoscopy, etc.).⁸

Treatment starts with the discontinuation of statins⁵ and is subsequently based on immunosuppression; however, there are no controlled trials guiding therapeutic selection. Based on the available current clinical experience, we suggest starting treatment with oral prednisone dosed at 1 mg/kg/day, adding such immunosuppressants as methotrexate, azathioprine, or mycophenolate mofetil.^{2,5,7–10} If no clinical improvement is observed at 8–12 weeks of treatment with 2 drugs, treatment should be started with intravenous immunoglobulins, plasmapheresis, or such other agents as rituximab.² Response to treatment is generally good, although a relapse rate of 50% to 60% has been reported.⁸ These cases will require prolonged immunosuppressant treatment; intravenous immunoglobulins or corticosteroids may be used in relapses.^{2,5,8,9}

References

1. Christopher-Stine L, Casciola-Rosen LA, Hong G, Chung T, Corse AM, Mammen AL. A novel autoantibody recognizing 200-kd and 100-kd proteins is associated with an immune-mediated necrotizing myopathy. *Arthritis Rheum.* 2010;62:2757–66.
2. Mammen AL. Statin-associated autoimmune myopathy. *N Engl J Med.* 2016;374:664–9.
3. Mammen AL, Gaudet D, Brisson D, Christopher-Stine L, Lloyd TE, Leffel MS, et al. Increased frequency of DRB1*11:01 in

anti-hydroxymethylglutaryl-coenzyme A reductase-associated autoimmune myopathy. *Arthritis Care Res.* 2012;64:1233–7.

4. Mammen AL, Chung T, Christopher-Stine L, Rosen P, Rosen A, Doering KR, et al. Autoantibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase in patients with statin-associated autoimmune myopathy. *Arthritis Rheum.* 2011;63:713–21.
5. Grable-Espósito P, Katzberg HD, Greenberg SA, Srinivasan J, Katz J, Amato AA. Immune-mediated necrotizing myopathy associated with statins. *Muscle Nerve.* 2010;41:185–90.
6. Needham M, Fabian V, Knezevic W. Progressive myopathy with up regulation of MHC-I associated with statin therapy. *Neuromuscul Disord.* 2007;17:194–200.
7. Basharat P, Christopher-Stine L. Immune-mediated necrotizing myopathy: update on diagnosis and management. *Curr Rheumatol Rep.* 2015;17:1–12.
8. Kassardjian CD, Lennon VA, Alfugham NB, Mahler M, Milone M. Clinical features and treatment outcomes of necrotizing autoimmune myopathy. *JAMA Neurol.* 2015;72:996–1003.
9. Bergua C, Chiavelli H, Simon JP, Boyer O, Jouen F, Stenzel W, et al. Immune-mediated necrotizing myopathy. *Z Rheumatol.* 2016;75:151–6.
10. Hamann PD, Cooper RG, McHugh NJ, Chinoy H. Statin-induced necrotizing myositis—a discrete autoimmune entity within the statin-induced myopathy spectrum. *Autoimmun Rev.* 2013;12:1177–81.

M.P. Navarro Pérez^a, A.A. Sanabria Sanchinel^{b,c,*},
J. Alfaro Torres^d, I. Marquina Ibañez^d, P. Larrodé Pellicer^a

^a *Servicio de Neurología, Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain*

^b *Neuro-Clínica de Neurología, Ciudad de Guatemala, Guatemala*

^c *Sección de Neurología, CAMIP-Pamplona, Ciudad de Guatemala, Guatemala*

^d *Servicio de Anatomía Patológica, Hospital Universitario Miguel Servet, Zaragoza, Spain*

* Corresponding author.

E-mail address: abelsanabria2000@yahoo.es

(A.A. Sanabria Sanchinel).

2173-5808/

© 2017 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).