13. Urban DL, Scholle LM, Alt K, Ludolph AC, Rosenbohm A. Camptocormia as a novel phenotype in a heterozygous POLG2 mutation. Diagnostics. 2020;10:8—11.

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Idiopathic hypereosinophilic syndrome presenting as mononeuritis multiplex. Lessons learned after 18-months of follow-up☆

Mononeuritis múltiple como forma de presentación de un síndrome hipereosinofílico idiopático. Lecciones aprendidas tras 18 meses de seguimiento

Dear Editor:

Hypereosinophilic syndrome (HS) is a rare systemic disease included in the group of myeloproliferative disorders. It is diagnosed in patients presenting elevated eosinophil counts below 1500 cells/μL for over 6 consecutive months and eosinophilic infiltration of tissues and organs after excluding such secondary causes of eosinophilia as drug reactions, infections, immune disorders, or allergies.[1]

Several subtypes have been described, including a myeloproliferative and a lymphoproliferative form; diagnosis of these subtypes is based on the detection of genetic mutations (in *BCR-ABL* and *FIP1L1/PDGFRA* fusion genes) and expression of eosinophil membrane proteins. However, idiopathic HS does not meet these diagnostic criteria.[2]

From a neurological viewpoint, idiopathic HS is characterised by involvement of both the central nervous system (venous thrombosis and encephalopathy) and the peripheral nervous system (peripheral neuropathy).[3,4] The pathogenic mechanism of peripheral neuropathy is unclear. Although nearly all affected tissues present eosinophil infiltration, histopathology studies of the damaged nerves do not reveal direct infiltration, inflammation, or vasculitis. The role of eosinophils as secretory cells and mediators of the cytotoxic response seems to explain the pathophysiology of peripheral neuropathy, particularly major basic protein and eosinophil-derived neurotoxin, which are responsible for neuropathic axonal damage through disruption of vasa vasorum permeability and perineuronal oedema, respectively.[5,6]

We present the case of a 49-year-old woman with no relevant medical history who presented mononeuritis multiplex as the initial manifestation of idiopathic HS. She consulted due to one month's history of acute pain beginning in the left forearm, and subsequently affecting the right elbow and the anterior aspect of the right thigh. Pain progressed to persistent paraesthesia and weakness in the areas previously mentioned. The examination confirmed mild motor weakness in the left arm (flexor digitorum profundus muscle of the fourth and fifth digits, adductor minimi digiti, first dorsal interosseous, and adductor pollicis) and right leg (posterior tibialis, triceps surae, flexor digitorum longus, and flexor digitorum brevis); absent right Achilles reflex; and hypoaesthesia and hypalgesia in the territories of the left ulnar and saphenous nerves and the posterior aspect of the right leg.

A complete blood count revealed an elevated eosinophil count (2100 cells/μL), mild thrombocytopaenia (99 000 platelets/μL), and a white blood cell differential with 26% eosinophils. A possible adverse drug reaction was ruled out; serology studies for Epstein Barr virus, cytomegalovirus, hepatitis C virus, HIV, *Borrelia*, and syphilis yielded negative results, and stool examination detected no parasites. Antibody testing detected a low titre of antinuclear antibodies with a homogeneous pattern, and normal immunoglobulin levels (IgE: 2.45 kU/L; normal range, < 100 kU/L); the patient tested negative for the remaining parameters (complement, anti-dsDNA, anti-RNP, anti-Scl-70, anti-SN, anti-Ro, anti-La, ANCA, anti-CCP, cryoglobulins, antineuronal antibodies). Cytochemical analysis and a monoclonal antibody study of the CSF yielded normal results. Electromyography revealed multiple mononeuropathy, with mild involvement of the left ulnar nerve and extremely severe involvement of the right peroneal and posterior tibial nerves. Bone marrow biopsy yielded normal results. Cytogenetic testing of the *BCR-ABL* and *PDFGRA* genes revealed no pathological alterations. Peripheral nerve biopsy was not performed.

Suspecting idiopathic HS as the cause of mononeuritis multiplex, we started treatment with high-dose corticosteroids (methylprednisolone dosed at 1 g/day) for 5 days, which improved our patient's symptoms and laboratory parameters within weeks. We subsequently started treatment with prednisone, tapering the dose to 15 mg/day. A follow-up examination at 6 months revealed no motor or sensory impairment, with the patient presenting a normal blood eosinophil count. At 18 months, a decrease in the dose

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of prednisone to 5 mg/48 hours resulted in an elevated blood eosinophil count (> 3000 cells/μL) and acute limb ischaemia in the right leg. We increased the dose to 30 mg/day and started treatment with hydroxycarbamide.

Hypereosinophilia may cause bilateral, symmetrical sensory and motor symptoms affecting the distal part of the limbs; asymmetrical involvement in the form of mononeuritis multiplex is extremely rare.[6] Our patient presented idiopathic HS manifesting as mononeuritis multiplex, with an initially complete response to corticosteroid therapy. Following tapering of the corticosteroid, she presented severe systemic symptoms and required immunosuppresive therapy; this underscores the need for strict monitoring of eosinophil levels and early onset of corticosteroid-sparing immunosuppressive therapy due to the risk of relapse.

Idiopathic HS should be included in the differential diagnosis of mononeuritis multiplex: although the condition is a rare cause of multiple mononeuropathy, it responds well to specific treatment.

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Conflicts of interest

The authors have no conflicts of interest to declare

References

1. Ben-Hur T, Agmon Y, Rund D, Steiner I. Hypereosinophilic syndrome presenting as recurrent benign mononeuritis multiplex. Isr J Med Sci. 1994;30:709—11.
2. Curtis C, Ogbogu P. Hypereosinophilic syndrome. Clin Rev Allergy Immunol. 2016;50:240—51.
3. Arnaud A, Lagueny A, Hermosilla E, Ferrer X, Vital C, Julien J. Multinévrite au cours d'un syndrome d'hyperéosinophilie essentielle. Rev Neurol (Paris). 1997;153:785—9.
4. Titlić M, Kodzoman K, Loncar D. Neurologic manifestations of hypereosinophilic syndrome-review of the literature. Acta Clin Croat. 2012;51:65—9.
5. Moore PM, Harley JB, Fauci AS. Neurologic dysfunction in the idiopathic hypereosinophilic syndrome. Ann Intern Med. 1985;102:109—14.
6. Pardal-Fernández JM, Sáez-Méndez L, Rodríguez-Vázquez M, Godes-Medrano B, Iñíguez-De Onzoño L. Mononeuritis múltiple y fascitis eosinofílica en una paciente con síndrome hipereosinofílico idiopático. Rev Neurol. 2012;54:100—4.

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Improvement of walking ability in patients with adrenoleukodystrophy treated with fampridine as compassionate use☆

Mejoría de la marcha en pacientes con adrenoleucodistrofia tratados con fampridina como uso compasivo

Dear Editor:

Adrenoleukodystrophy is an X-linked genetic disease caused by a mutation that dysregulates metabolism of very long-chain fatty acids. This leads to a defect in axonal myelination and white matter involvement, with neurological symptoms varying according to the form of disease presentation[1]; in some cases, it manifests with symptoms of spastic paraparesis.[2] Furthermore, it is associated with damage to the adrenal cortex, with subsequent hormonal involvement.

Due to its X-linked inheritance pattern, it predominantly affects boys, although girls may also present a certain degree of involvement, which is generally milder but in some cases it may be as disabling as in boys.[2,3]

The clinical spectrum includes:

- A classic form, with onset during childhood, which clinically presents as learning and behavioural problems with psychomotor developmental regression. It also manifests with visual alterations due to optic atrophy, auditory deficits, and progressive motor impairment, causing spastic tetraparesis that generally leads to dependence within a short period (2-3 years).
- A form with onset during young adulthood (approximately in the third decade of life), known as adrenomyeloneuropathy. It generally manifests as a progressive gait disorder with spastic tetraparesis and sensory ataxia. It may be associated with neurogenic bladder, sexual dysfunction, and occasionally adrenal insufficiency, which may also precede the other symptoms. Psychiatric symptoms, such as depression and psychosis, have also been described. Although it inevitably presents a progressive course, progression is slower than in the childhood-onset form.
- Lastly, in cases of predominantly hormonal involvement, symptoms coincide with those of classic Addison syn-

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