This adjustment and the non-pharmacological measures were ineffectual for the control of OH, which improved after the introduction of midodrine. Nocturnal HBP in turn improved with clonidine and captopril with a single bedtime dose.

Midodrine is a selective 1-adrenergic alpha agonist causing venous and arterial constriction, with the subsequent increase in blood pressure. [6] Although there is some controversy about the aggravation of supine nocturnal HBP due to midodrine, its short half-life and the possibility of associating it with equally short half-life anti-hypertensives (for example clonidine and captopril) with a single bedtime dose are f ndings in favour of its administration in this kind of patient, particularly in diabetics with dysautonomic symptoms.[7] Although it was approved by the FDAin 1996 for this indication, the same agency has recently announced its possible withdrawal due to the lack of post-authorization studies after the clinical trial leading to its approval.[8] Other authors have already written of their concern over this and point to the existence of patients who might be left unprotected with this measure. [8] This will oblige us in the near future conduct controlled studies into this and other "orphan drugs" for neurogenic OH.

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Peripheral neuropathy as a f rst sign of microscopic polyangiitis ☆

Neuropatía periférica como forma de presentación de poliangeítis microscópica

Dear Editor:

The emergence of peripheral neuropathy is an important characteristic in both primary and secondary systemic vasculitides and is often observed during the f rst stages of the illness, thus giving it a major diagnostic valueAlterations in the peripheral nerve between the group of small-vessel vasculitides are highly variable; they make up a group with shared histological characteristics and frequently positive anti-neutrophil cytoplasmic antibodies (ANCA) in serum. The initial clinical characteristics of these vasculitides are very similar, and the differential diagnosis between them is on many occasions diff cult.

Microscopic polyangiitis (MPA) mainly affects the lungs and kidneys, and so has been studied particularly by rheumatologists and nephrologists; the criteria of the Chapel Hill Conference, however , do not limit MP A only to these organs, and alterations in the peripheral nervous system is no exception.

We report here the case of a 43-year-old woman without any signif cant history of pathology who attended our hospital as a result of a progressive condition lasting for two months and involving paraesthesias and mostly distal weakness in all four limbs, as well as asthenia, anorexia and slight fever The most signi f cant f ndings during systematic anamnesis were nicturia and occasional oliguria. The general examination was normal and the neurological examination revealed asymmetric weakness predominantly in the distal muscles of all four limbs, as well as hyporre f exia, distal tactile hypoaesthesia and distal abolition of sensitivity to vibration.

At the onset of her condition, the analytical studies showed her kidney function to be within the normal range (urea 34 mg/dL and creatinine 0.82 mg/dL), which slowly and gradually deteriorated until she presented, two months later, 64 mg/dL of urea and creatinine 1.4 mg/dL, with creatinine clearance of 48 mL/minute, as well as haematuria and proteinuria of 2.9 g/L that had not previously been present.

The neurophysiological study (tables 1 and 2) showed an axonal motor and sensory alteration in multiple nerves studied, compatible with multiple mononeuritis. The biopsy of the sural nerve showed evidence of severe axonal degeneration.

The initial determination of anti-nuclear antibodies, anti-DNA antibodies, anti-cardiolipins and ANCA, as well as angiotensin conversion enzyme and cryoglobulins was negative.

Treatment with oral corticosteroids (prednisone 1 mg/kg of bodyweight/day *per os*) gave rise to a slight increase in her neurological condition, without changes in her kidney

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Table 1 Involvement of the patient's motor nerves in the case study

Nerve/locations	Latency in ms	Amplitude in mV	Speed in m/s
Left median - abductor pollicis brevis (APB)			
1. wrist	3.45	7.7	
2. elbow		6.7	55.6
Right median - APB			
1. wrist	4.90	0.2	
2. elbow		0.2	67.6
Left cubital - abductor digiti quinti (ADM)			
1. wrist	2.70	1.7	
2. elbow		2.3	68.9
Right cubital - ADM			
1. Wrist	2.40	4.8	
2. Below elbow		4.0	54.4
3. Above elbow		4.6	72.0
Posterior right tibial - adductor obliquus hallucis (AH)			
1. Ankle	10.40	0.1	
2. Knee		0.2	34.5

function. It was decided to perform a renal biopsy that showed a type III extracapillary glomerulonephritis without immune deposits, so a bolus of methyl prednisolone (1,000 mg over 5 consecutive days) and oral cyclophosphamide at a dose of 50 mg/day was associated with the initial treatment, giving a clinical improvement neurological signs and symptoms and also in kidney function. After 12 months of treatment with cyclophosphamide, the patient is asymptomatic and free from infectious complications. Follow-up analytical studies gave positive ANCA f gures, without associated signs of activation, so the diagnosis of MPA was conf rmed.

Although MPA mainly affects the lungs and kidneys, the criteria of the Chapel Hill Conference do not limit it only to cases with renal and pulmonary alterations, as the def nition is based on the existence of a small-vessel vasculitis. General syndrome, arthritis, multiple mononeuritis and gastrointestinal

Table 2 Involvement of the patient's sensory nerves in the case study

Nerve/locations	Latency in ms	Amplitude in mV	Speed in m/s
Left median - abductor pollicis brevis (APB)			
1. wrist	3.45	7.7	
2. elbow		6.7	55.6
Right median - APB			
1. wrist	4.90	0.2	
2. elbow		0.2	67.6
Left cubital - abductor digiti quinti (ADM)			
1. wrist	2.70	1.7	
2. elbow		2.3	68.9
Right cubital - ADM			
1. Wrist	2.40	4.8	
2. Below elbow		4.0	54.4
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Posterior right tibial - adductor obliquus hallucis (AH)			
1. Ankle	10.40	0.1	
2. Knee		0.2	34.5

involvement are other frequent forms of clinical presentation of this illness as reported in the various series[1]. The peripheral nervous system is occasionally involved in this pathology and, in a percentage varying between 11 and 52% depending on the series, it may constitute the first manifestation of the condition,[2] as in the case of our patient.

The alteration of the peripheral nervous system in the initial phases of MPA is similar in both clinical and electrophysiological or histological terms to that present in a non-systemic vascular neuropathy.[3] The neuropathic symptoms are similar in terms of their progression, distribution and degree of weakness and sensory deficits, although the severity is considered greater in MPA.[2] Paraesthesias or pain in the limbs (85%) and weakness (15%)[3] have been described as the debut symptoms of axonal neuropathy, as occurred in the case reported here. Therefore, when the alteration in the peripheral nervous system is an early manifestation of systemic vasculitis, in the absence of other affected organs or systems, it is necessary to carry out a differential diagnosis with non-systemic vascular neuropathies, collagenosis or paraneoplastic syndromes.[4,5] In our case, the patient presented a multiple mononeuritis, apparently without any other accompanying clinical signs, which hindered the initial diagnosis, made possible thanks to the kidney involvement that gradually emerged and the result of the kidney biopsy.

The clinical presentation of patients diagnosed as having MPA is clearly defined but there are few studies describing this illness's progression. Savage et al. observed that general symptoms, arthralgias or minimal haemoptysis may occur months or years before the more defined phase of the illness[6]. Therefore, MPA cannot be considered an acute illness and the onset of symptoms in our patient was sub-acute. The long interval described between the first symptoms and their diagnosis (up to 12 years) illustrates the difficulty in recognizing this entity, especially when a single organ is affected.[7,8] Performing a biopsy on a peripheral nerve is recommended in these cases, with a view to the histological confirmation of the problem; on occasions, however, it is necessary to have a histological study of other organs in order to reach a definitive aetiological diagnosis, as occurred in our case.[9]

The pathogenic role of ANCA in these entities has not yet been clarified, and therefore the need to titre these for a diagnosis of MPA is controversial. Guillevin et al. are of the opinion that ANCA have a high diagnostic value for MPA.[1] Nonetheless, there is a minority of patients (approximately 10%) who are ANCA-negative despite having vasculitides defined by an association with ANCA; this may happen in early phases of the condition and may subsequently become positive as in the case we describe here, or this may be due to the production of antibodies below the threshold for detection in the tests.[10]

The start of treatment must not be delayed until the condition has been fully diagnosed as its prognosis depends on the speed with which therapy is started, and therefore which target organs, such as the lungs or the kidneys, are altered.[11]

In conclusion, and in accordance with the diagnostic criteria for MPA indicated in the introduction, we reached the suspected diagnosis of MPA in our patient as a consequence of the sub-acute presentation of a multiple mononeuritis and the alteration o small vessels in the kidney biopsy. The early start of treatment led to a recovery in both her neurological alteration and her kidney function. The conversion of ANCA results to positive months after the first symptoms meant that the diagnosis of MPA could be definitively established.

The onset of an isolated peripheral neuropathy should, then, make us think of the possibility of a small-vessel disease, and specifically MPA, in view of the variable clinical presentation of this pathology. We propose the serial monitoring of ANCA levels as the protocol for follow-up of these vasculitides.

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