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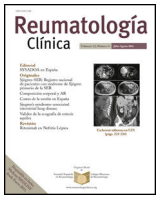

Letter to the Editor

Neurological manifestations of rheumatoid arthritis – Nearly 50 years of experience

Manifestaciones neurológicas de la artritis reumatoide: cerca de 50 años de experiencia

Dear Editor,

Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease that primarily affects synovial joints.[1] However, extra-articular manifestations may be present in up to 40% of RA patients, involving the central (CNS) and peripheral nervous systems (PNS) less frequently, with an estimated incidence of 11%.[2,3] Mechanical factors, vasculitis, accelerated atherosclerosis or the systemic illness itself may be involved in its pathophysiology.[1,2] Furthermore, iatrogenic events with neurological manifestations can also occur.[2,4] We aim to retrospectively characterize the neurological manifestations of RA patients referred to the Neuroimmunology outpatient clinic of a tertiary hospital.

An observational retrospective cohort study was conducted including patients referred to the Neuroimmunology outpatient clinic of Centro Hospitalar Universitário de Santo António between 1976 and 2023 with a diagnosis of RA. We collected demographic and clinical data regarding the patient, the rheumatic disease and the neurological manifestation and performed descriptive analysis.

From a total of 1979 patients observed in the Neuroimmunology outpatient clinic, 36 had RA, the majority being female ($n = 32$, 89%), with a mean age of 54.4 ± 13.7 years. Of these, 10 (28%) had neurological manifestations attributable to RA (Table 1), 5 (14%) had neurological autoimmune comorbidities and 21 (58%) suffered from another neurological illness. Among patients with neurological manifestations attributable to RA, the majority had seropositive ($n = 8$, 80%), prolonged disease (mean duration 13.5 ± 9.3 years) and it was in low activity or in remission ($n = 5/6$, 83.3%) at the time of the neurological condition. Excluding iatrogenic events, the PNS was the most frequently affected ($n = 5$ vs. $n = 3$ of CNS involvement), with distal sensory neuropathy and carpal tunnel syndrome (CTS) being the most prevalent manifestations. Regarding the three cases of CNS involvement, two were rheumatoid meningitis that implied an optimization of immunosuppression, and one was venous sinus thrombosis in a patient with other procoagulant risk factors, namely oestrogen contraceptive and recent breast cancer. Two cases of neurological events attributable to the use of anti-TNF were reported, which led to the suspension of the drug with improvement of the condition. Regarding neurological autoimmune comorbidities, four patients were followed for myasthenia gravis and one for multiple sclerosis. In the remaining patients, the symptoms can be categorized into the following groups: cognitive impairment ($n = 8$), headache ($n = 7$), vertigo ($n = 1$), epilepsy ($n = 1$), hypertensive encephalopathy ($n = 1$), diplopia ($n = 1$), gait disturbance ($n = 1$) and depressive syndrome ($n = 1$).

Neurological manifestations of RA, although experiencing decreasing incidence thanks to increasingly effective disease-modifying antirheumatic drugs, are still present in clinical practice and can be so severe that may impose optimizing immunosuppression or, in case of an iatrogenic event, to suspend therapy. They are more common in seropositive and longstanding disease and have scarce correlation with disease activity.[1–3] PNS is more frequently involved than CNS, usually comprising compressive neuropathies such as CTS, less reported in our cohort because it is rarely referred to Neurology.[2,5] Among non-compressive neuropathies, distal sensory, autonomic and sensorimotor neuropathies are other examples of PNS involvement, the latter often vasculitic.[2,3] When CNS is affected, it may involve atlantoaxial instability (also seldom referred to Neurology), meningitis, vasculitis and rheumatoid nodules.[1,6] Interestingly, most of the neurological symptoms exhibited by our cohort was not directly attributable to the rheumatic disease and a significant number of patients presented cognitive impairment, a condition more frequent in RA than in the general population.[2] To our knowledge, this is the first published data describing neurological manifestations in a RA cohort. A multidisciplinary cooperation between Rheumatology and Neurology is essential so that there is a correct recognition and appreciation of neurological complaints of patients with RA.

Table 1
Descriptive analysis of the neurological manifestations presented by patients with rheumatoid arthritis referred to the Neuroimmunology outpatient clinic.

ID	Sex	Age*	Rheumatoid arthritis				Neurological manifestation					
			RF/ACCP	Erosive	Disease activity*	Duration (years)*	Group	Type	Symptoms	Diagnostic tests	Treatment	Outcome
1	F	50	Y	Y	NR	20	CNS	Rheumatoid meningitis	Headache, dysphasia and altered state of consciousness	LP: pleocytosis (15 leukocytes) and ↑ IgG index; MRI: ↑ leptomeningeal enhancement; biopsy: lymphohistiocytic infiltrate of the leptomeninges	High dose steroid + cyclophosphamide	Improvement
2	F	52	Y	N	Low	13	CNS	Rheumatoid meningitis	Headache	MRI: thickening and ↑ dura mater contrast enhancement; LP: normal	High dose steroid	Improvement
3	F	47	NR	NR	NR	23	CNS	Venous sinus thrombosis	Severe sudden headache	MRI: venous sinus thrombosis; negative anti-APS	Anticoagulant	Improvement
4	F	68	Y	Y	NR	8	PNS	Rheumatoid vasculitis	Feet dysesthesias and paresthesias	EMG: mononeuritis multiplex	High dose steroid + azathioprine	Improvement
5	F	74	Y	N	NR	2	PNS	Distal sensory neuropathy CTS	Dysesthesias and paresthesias of the hands and feet	EMG: distal sensory neuropathy and bilateral CTS	Gabapentin	Stability
6	F	48	N	N	Low	1	PNS	Distal sensory neuropathy CTS	Hypoesthesia and paresthesias of the hands and feet	EMG: distal sensory neuropathy and bilateral CTS	Pregabalin	Stability
7	F	58	Y	N	Low	11	PNS	Distal sensory neuropathy	Right foot hypoesthesia	EMG: distal axonal sensory PNP; nerve biopsy: axonal PNP	Gabapentin	Improvement
8	F	60	Y	N	Moderate	22	PNS	CTS	Right hand nocturnal paresthesias	EMG: right mild CTS	–	Stability
9	F	54	Y	N	Low	7	Iatrogenic	Cognitive impairment associated with anti-TNF	Non-mnesic mild cognitive impairment after 17 months of anti-TNF	MRI: periventricular white matter inflammatory lesions; LP: normal	Stop etanercept + rituximab	Improvement
10	F	57	Y	Y	Remission	28	Iatrogenic	Transient neurological deficit associated with anti-TNF	Episode of paresthesias and hypoesthesia of the left hemibody after 15 days of anti-TNF	Brain MRI: two unspecific subcortical hypersignal foci on T2-weighted and FLAIR; negative anti-MOG and anti-AQP4; LP: normal; medullary MRI: normal	Stop etanercept	Improvement

ACCP: anti-cyclic citrullinated peptide antibody; APS: antiphospholipid syndrome; AQP4: aquaporin-4; CNS: central nervous system; CTS: carpal tunnel syndrome; EMG: electromyography; F: female; ID: identification; LP: lumbar puncture; MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging; N: no; NR: not registered; PNP: polyneuropathy; PNS: peripheral nervous system; RF: rheumatoid factor; TNF: tumour necrosis factor; Y: yes.

* At the time of the neurological manifestation.

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Conflict of interest

None declared.

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Evaluating the impact of the website campaign "A ti también te puede tocar" ("It could also be you") to spread awareness of systemic autoimmune rheumatic diseases

Evaluación del impacto de la web de la campaña "A ti también te puede tocar" para concienciar sobre las enfermedades reumáticas autoinmunes sistémicas

Dear Editor,

Health awareness campaigns draw attention to specific diseases, provide information for the general public, and engage people in the management of their diseases. During recent decades, the Internet has become a major source for information on health[1] and social network campaigns have increased the efficiency and effectiveness of public health communication campaigns.[2–4]

In 2021, the Spanish Society of Rheumatology launched an awareness campaign called "*A ti también te puede tocar*" ("*It could also be you*") in which its website formed the core of a broader digital strategy. The website hosted a digital video advert, as well as information and free downloadable materials about Behçet disease, systemic lupus erythematosus, vasculitis, scleroderma, Sjögren syndrome, and polymyositis. The website included a specific area for each disease. Users could share website content directly through social media channels. A link to the patients' website of the Spanish Rheumatology Foundation provided more information about SARDs (Systemic Autoimmune Rheumatic Diseases) and additional links to websites of other patients' associations.

Consistent with the approach of other researchers,[5,6] we evaluated the website in terms of engagement using Google Analytics.[7,8]

Data were collected from the Google Analytics dashboard in March 2022 for all website visits during the observation period (launch of the website in May 2021 to end of the campaign in December 2021). The overall reach of the website was measured by the number of users and sessions and the source of the users. We measured the engagement of users based on the following indicators: bounce rate, number of page views, pages per session, and session duration.

We recorded 107,657 single sessions by 87,059 new users involving 437,285 page views during the observation period. Fig. 1

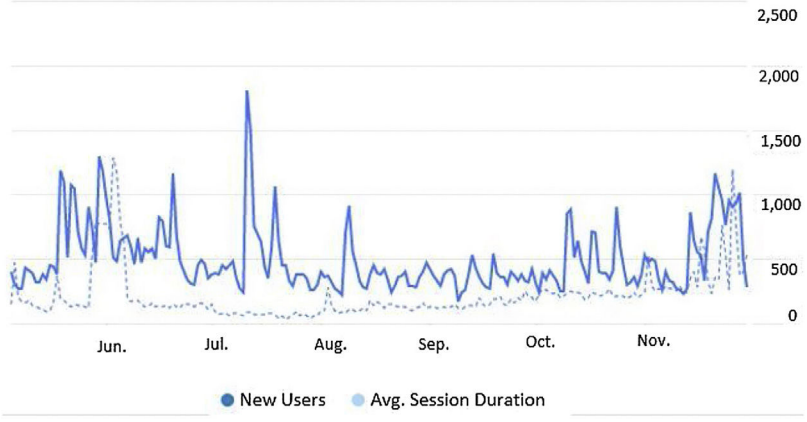

Fig. 1. Number of users and average duration of sessions over time.