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Letters to the Editor

Posterior Ankle Impingement Syndrome

Síndrome del choque posterior del tobillo

Dear Editor,

We present a case of a 38-year-old female with a history of right posterior ankle pain for 2 months which worsened with walking and standing up for a long time. There were no complaints in other joints. On physical examination the patient presented swelling of the posterior ankle and complained of pain with forced flexion of the right feet. There was no increase of inflammation parameters in blood tests. Radiographic lateral view of the right ankle demonstrated an enlarged Stieda's process (Fig. 1). The magnetic resonance imaging (MRI) of the right ankle confirmed the Stieda's process (Fig. 1) being able to originate posterior conflict, with a subtle bone marrow edema. A slight effusion was observed in the anterior and posterior compartments of the tibiotalar joint as well as edema of the subcutaneous fat. The patient was told to rest and NSAID were prescribed with resolution of the hindfoot pain.

The posterior ankle impingement syndrome is a condition resulting from soft tissue compression between the posterior process of the calcaneus and the posterior tibia during ankle plantar flexion.[1] An important cause of the syndrome is a prominent posterolateral talar process (Stieda's process) or the presence of os trigonum, due to its impact on adjacent structures.[2] Patients usually report chronic or recurrent posterior ankle pain caused or exacerbated by forced plantar flexion.[3] Other causes of this syndrome may result from flexor hallucis longus tenosynovitis, ankle osteochondritis, subtalar joint disease, and fracture. Diagnosis of posterior ankle impingement syndrome is based primarily on clinical history and physical examination. Radiography, computed tomography, and MRI are useful to detect associated bone and soft-tissue abnormalities.[3] MRI can identify the presence of a Stieda's process or a separate os trigonum in addition to secondary findings that suggest posterior ankle impingement as well as: increased signal intensity in the soft tissues posterior to the ankle, thickening of the posterior joint capsule, posterior and subtalar synovitis, flexor hallucis longus tenosynovitis and bone marrow edema pattern in the os trigonum and posterior talus.[4•7] Symptoms typically improve with nonsurgical management but surgery may be required in refractory cases. A literature review on conservative treatment of the posterior ankle impingement syndrome suggests that the initial treatment should aim at decreasing inflammation with non-steroidal anti-inflammatory drugs and activity restriction (avoidance of forced plantar flexion).[8] Furthermore, a physiotherapy program that includes soft tissue therapy, stretching and mobilizations of restricted joints of the lower kinetic chain should be implemented in conjunction with a progressive strengthening, balance and proprioception enhancement program.[8,9] Cortisone injections can be performed in patients with higher levels of pain. These injections into the affected area may reduce the pain and allow the patient to progress into a rehabilitation program.[10] It is also suggested to tape or brace the ankle in a protective dorsiflexion position when the patient undertakes intense activities, such as sports.[2]

This case emphasizes the importance of considering posterior ankle impingement due to a Stieda's process of the talus as a cause of hindfoot pain. In fact, it is an underrecognized cause of posterior ankle pain but imaging can easily make the diagnosis and guide appropriate treatment.

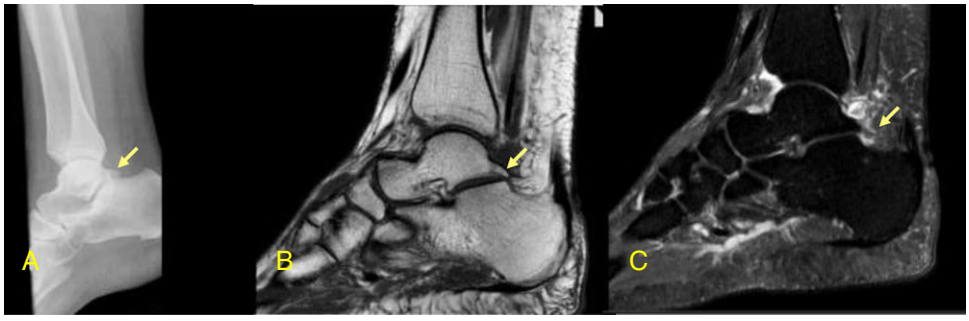

Fig. 1. Lateral right ankle radiography (A), T1 weighted sequence (B) and sagittal STIR MRI sequence (C) images demonstrating an enlarged Stieda's process (arrows) with mild bone marrow and soft tissues edema.

Conflict of interest

The authors declare that they have no conflicts of interest.

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2173-5743/

Response to: Tropical Arthritogenic Alphaviruses☆

Respuesta a: Alfavirus tropicales artritogénicos

To the Editor,

We read the complete review recently reported by Mejía and López-Vélez on tropical arthritogenic alphaviruses with interest.[1] However, based on our experience in Colombia, a country that is significantly affected by arboviruses, such as Chikungunya virus and Zika virus infections, there are certain aspects of the review that should have been mentioned.[2]

Latin America is seeing the emergence of new tropical viral agents, transmitted by arthropod vectors (arboviruses). They have been classified into 4 groups, A, B, C and D, the first 2 being of greater clinical importance.[2] Group A is comprised of the genus alphavirus, involving Chikungunya virus and Mayaro virus, both arthritogenic; whereas group B includes other tropical arthritogenic viruses of other genera and families, also of considerable clinical importance, including their rheumatological manifestations, such is the case of Zika and dengue viruses.[2] The title of the article makes one think that it refers only to arthritogenic alphaviruses, but that does not occur in Table 1, where there is a broad spectrum of viruses that cause musculoskeletal manifestations, which makes one think that the authors are dealing in general with viruses of rheumatological importance. However, in this case, they should have mentioned, for example, Zika virus, which not only provokes arthralgia and other rheumatological manifestations, but has recently been detected directly in synovial fluid, where it can even remain for several weeks.[3]

Speaking specifically of Chikungunya virus, one of the most important arthritogenic alphaviruses in terms of its acute and chronic morbidity and its persistence for long periods of time, in Colombia, between 2014 and 2015, there were more than 3 million new cases, and a proportion of nearly 50% of those patients developed chronic post-Chikungunya inflammatory rheumatism (pCHIK-CIR). This has been documented in a number of cohorts in the departments of Sucre,[4] Tolima[5] and Risaralda,[6] since the beginning of 2016, following along the lines of estimates[7] and meta-analyses of observational studies conducted in other countries.[8] Thus it is surprising that, when discussing pCHIK-CIR, the authors refer only to studies dealing with Reunion Island in France, but there is absolutely no mention of Latin America.

It is important to call attention to the relatively high frequency observed in certain reports, with ranges from 14.4% to 87.2%, as well as a mean persistence of 20.12 months in 47.57% of the patients (95% confidence interval: 45.08–50.13), and a duration of even more than 5 years.[7,9] Thus, pCHIK-CIR has been established as a challenge for Latin American rheumatology.

Finally, it is also surprising that there is such a limited reference to Mayaro virus, especially since, after Chikungunya, this arthritogenic alphavirus could be important not only because of its acute morbidity, but also chronic as well, in many Latin American countries. New outbreaks have recently been reported in Venezuela and in Haiti, among others. Thus, this virus should also be considered in the differential diagnosis.[10]

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2173-5743/

Lupus Nephritis Associated With Cytoplasmic Anti-neutrophil Cytoplasmic Antibodies☆

Nefritis lúpica asociada con c-ANCA

To the Editor,

Systemic lupus erythematosus (SLE) and the vasculitides associated with antineutrophil cytoplasmic antibodies (ANCA) are well-differentiated diseases; although approximately a third of the patients with SLE are ANCA-positive,[1] this is rarely associated with vasculitis. The presence of ANCA in patients with SLE seems to predispose them to lupus nephritis (LN), low levels of complement C3 and a higher rate of complications.[2]

We present the case of a 55-year-old man from Mexico City, who presented with a 5-month history of arthralgia in shoulders, wrists and ankles, that was bilateral and symmetrical; moreover, he had episodes of recurrent sinusitis, weight loss and edema arising from the lower limbs; there were no lesions affecting the skin. In the initial examination he underwent urinalysis which showed proteinuria of 200 mg/dL, innumerable erythrocytes, leukocytes 20 to 25 per field, red blood cell and leukocyte casts; creatinine: 1.66 mg/dL (reference range 0.6–1.3 mg/dL). Blood tests revealed hemoglobin concentration of 9.1 g/dL (reference range 13–17 g/dL), normocytic and normochromic; the remaining cell lines were normal; erythrocyte sedimentation rate (ESR): 55 mm/h (reference range 0–15 mm/h); C-reactive protein (CRP): 6.24 mg/dL (reference range 0–3 mg/dL). Immunological profile with a 1:160 titer of antinuclear antibodies (ANA), which had a homogeneous/fine speckled pattern by immunofluorescence and 78.0 IU/mL in enzyme-linked immunosorbent assay (ELISA) (reference range for high positive >60 IU/mL), anti-double stranded DNA (anti-ds DNA) by chemiluminescence: 1.4 IU/mL (reference range for negative <20 IU/mL), antiproteinase 3 (cytoplasmic [c-ANCA]) positive with titers reaching 1:320, granular pattern by immunofluorescence and higher than 100 IU/mL by ELISA (reference range 0–3.5 IU/mL), myeloperoxidase (perinuclear [p-ANCA]) were negative using the same technique, complement C3 was 71.7 mg/dL (reference range 90–180 mg/dL) and complement C4 was 17.6 mg/dL (reference range 10–40 mg/dL); human immunodeficiency virus (HIV) antibodies, cryoglobulins and hepatitis B and C negative; subsequently, 24 h urine was collected and revealed a proteinuria of 1.77 g.

Given the presence of data compatible with nephritic syndrome, the patient underwent renal biopsy. The result was membranoproliferative and active diffuse extracapillary glomerulonephritis (crescents 80%) due to immune complexes, interstitial fibrosis, tubulointerstitial nephritis with mononuclear infiltrate, with no evidence of vasculitis; direct immunofluorescence with deposits of immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM), complement C1q, complement C3 with a focal granular pattern (Fig. 1). With these data associated with the clinical presentation, the diagnosis was LN class IV-S (A), with an activity score of 18 and chronicity of 7.

Treatment was begun with 1 g intravenous cyclophosphamide every 30 days for a total of 6 doses, 1 g intravenous methylprednisolone every 24 h the first 3 days, followed by 60 mg of oral prednisone every 24 h for 4 weeks, 24-hour monitoring of proteinuria 1 month after treatment of 870 mg, creatinine of 1.54 mg/dL, at which time a trend toward a partial response was established.[3] The patient continued with cyclophosphamide and steroids were tapered. During follow-up, there was an increase in proteinuria, persistence of dysmorphic erythrocytes at 0–5 per field, monitoring of positive c-ANCA at a titer of 1:160 in immunofluorescence, aside from a reduction in the glomerular filtration rate, with an increase >1 mg/dL in creatinine, leading to renal relapse.[3] Table 1 summarizes the 6-month follow-up. In line with the diagnosis of LN, given the symptoms of chronic sinusitis and positive c-ANCA, we studied a possible associated vasculitis. We performed computed tomography of the paranasal sinuses 20 days after the initiation of treatment (Fig. 2), which revealed swelling of the nasal mucosa, with slight bone erosion in left maxillary antral wall and turbinates justified by the chronic sinusitis process; chest radiograph was normal (Fig. 2C), and a biopsy of the nasal mucosa showed the absence of granulomas or other data suggesting a process of vasculitis.

This case corresponds to LN with failure of the first line of treatment, associated with high titers of positive c-ANCA, with no evidence of solid elements enabling the parallel diagnosis of vasculitis. A number of authors have observed that SLE patients can present these antibodies; that is the case of Galeazzi et al.,[4] who evaluated 566 patients with SLE in 11 European centers, presenting a prevalence of 16.4% (15.4% with p-ANCA and 1% with c-ANCA) in individuals in whom that relationship was detected; other reports demonstrate a highly variable relationship with prevalence of up to 37.3%,[5,6] predominantly with p-ANCA positivity.

We recommend that all the patients with LN should undergo an intentional search for ANCA, because they have a higher positivity rate than SLE patients with no renal involvement; Pradhan et al.[7] recorded a prevalence of 54.5%, and all of these individuals were positive for p-ANCA; subsequently, Pan et al.[2] evaluated 60

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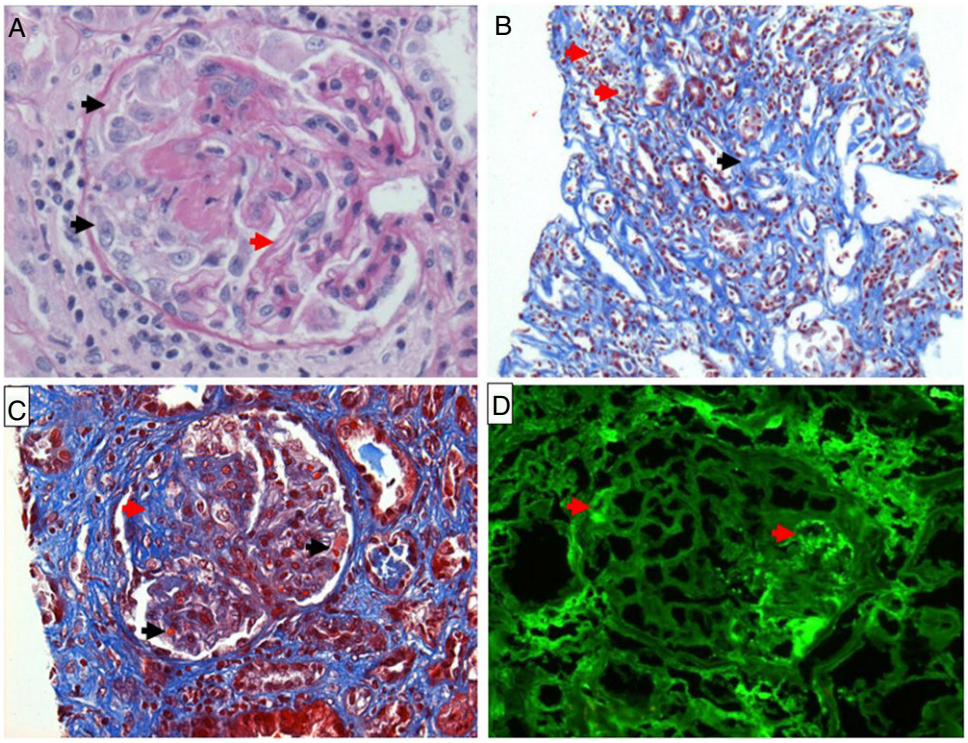

Fig. 1. Renal biopsy. (A) Hematoxylin–eosin staining 40×; observe the membranoproliferative pattern with an image showing double contour (red arrow), formation of crescents (black arrows). (B) Masson trichrome staining 10×; observe tubulointerstitial nephritis with mononuclear infiltrate (red arrows) and interstitial fibrosis (black arrow). (C) Masson trichrome staining 40×; with presence of thrombi and fibrinoid necrosis in capillary loops (black arrows), segmental glomerular fibrosis (red arrow). (D) Immunofluorescence 40×; positive for immunoglobulin G with a focal granular pattern and only a few segments of capillary loops (red arrows).

Table 1
Changes in 24-hour Proteinuria, Serum Creatinine, Cytoplasmic Antineutrophil Cytoplasmic Antibodies and Complement Over a 6-month Follow-up Period.

	Diagnosis	First month	Third month	Sixth month
24-Hour proteinuria (mg)	1770	870	4055	2967
Serum creatinine (mg/dL)	1.66	1.54	2.57	2.48
C-ANCA by immunofluorescence	1:320		1:160	
Complement C3 (90–180) (mg/dL)	71.7	85.6	73.2	106.0
Complement C4 (10–40) (mg/dL)	17.6	26.8	18.4	28.2

C-ANCA, cytoplasmic antineutrophil cytoplasmic antibodies.

patients with a diagnosis of SLE, 28 of them with LN, observing a prevalence of ANCA of 53.6% and concluding that said association was related to higher activity and a poorer prognosis. Nasr et al.[8] reported 10 patients with LN associated with the presence of ANCA and described the histopathological features of the renal biopsy. It revealed a greater formation of crescents in our patient, involving 80% of the glomeruli, and areas of necrosis were also demonstrated by the histopathological study (Fig. 1). This suggests that their presence precipitated those findings, although the role they play in the pathophysiology of LN has not been made clear.

With regard to treatment, the population with LN and ANCA-positivity should undergo follow-up studies of the scheme for the induction of conventional remission; given the failure of complete remission with first-line treatment in our patient, an alternative strategy should be proposed for initial treatment for patients of this type.

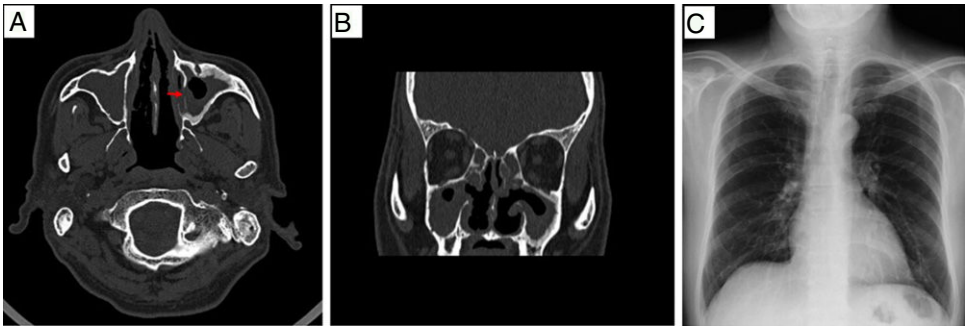

Fig. 2. (A and B) Computed tomography images of paranasal sinuses in simple phase: axial scan (A), coronal scan (B), swollen nasal mucosa, slight bone erosion involving left maxillary antral wall (red arrow) and inferior turbinates. (C) Normal posteroanterior chest radiograph; no lesions on lung parenchyma.

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2173-5743/

Rituximab in Refractory Autoimmune Hemolytic Anemia in Systemic Lupus Erythematosus☆

Rituximab en la anemia hemolítica autoinmune refractaria en lupus eritematoso sistémico

Dear Editor,

Autoimmune hemolytic anemia (AIHA) is a common manifestation in systemic lupus erythematosus (SLE), and is often refractory to standard treatment. Corticosteroids constitute the first-line treatment, with a rate of initial response of 70%–85%, although the response is maintained 1 year later in less than 20%.[1,2] In cases of refractory AIHA, splenectomy has traditionally been the second-line treatment, with a response rate of 60%–70%, resulting in a considerable increase in the risk of severe infections.[2] In cases of refractory disease or in which splenectomy is contraindicated, immunosuppressive agents such as azathioprine, cyclophosphamide, cyclosporine A and, in recent years, rituximab (anti-[cluster of differentiation] CD20 monoclonal antibody) can be employed with a good response.[3,4] We report two cases of refractory AIHA secondary to SLE treated with rituximab.

Case no. 1: The patient was a 37-year-old woman who had been diagnosed with SLE 10 years ago, and was being treated with hydroxychloroquine (200 mg/day). She came to the emergency department with severe weakness, arthralgia and mucocutaneous pallor. Laboratory studies revealed a hemoglobin (Hb) level of 5 g/dL and a mean corpuscular volume of 81 fL, and thus required a transfusion of packed red cells. We found her total bilirubin (TB) to be 2.3 mg/dL at the expense of indirect bilirubin, haptoglobin of 1 mg/dL, lactate dehydrogenase (LDH) of 856 U/L and positivity on direct and indirect Coombs tests. The patient was diagnosed with AIHA and treatment was begun with corticosteroids (1 mg/kg body weight/day) and azathioprine (50 mg/12 h). The disease became chronic, with corticosteroid-dependent flares.

Case no. 2: The patient was a 19-year-old woman who had recently been diagnosed with SLE and was being treated with azathioprine (50 mg/day) and hydroxychloroquine (200 mg/day). She came to the emergency department with a fever of 38.5 °C, deterioration of her general health status, polyarthralgia and weakness. Laboratory studies revealed a Hb level of 7.5 g/dL, TB of 2.16 mg/dL with a predominance of indirect bilirubin and LDH was 678 U/L. She was diagnosed with AIHA and was treated with corticosteroids at a dose of 1 mg/kg body weight/day. She progressed favorably, but subsequently had further hemolytic crises upon corticosteroid tapering.

In both cases, given the persistence of relapses despite corticosteroid and immunosuppressive therapy, it was proposed to initiate treatment with rituximab at a weekly dose of 375 mg/m^2 for 4 weeks, and the outcome was favorable and rapid. The treatment maintained Hb levels over 12.5 g/dL after 10 and 12 months, respectively (Fig. 1). In the first patient, we administered a second course of rituximab 1 year later; however, the second patient achieved a response that she continues to maintain.

The efficacy of rituximab in autoimmune hematologic disorders is probably due not only to the elimination of the pathogenic autoantibody, but to B-cell depletion as antigen-presenting cells and their conversion to producers of cytokines.[5] Although the

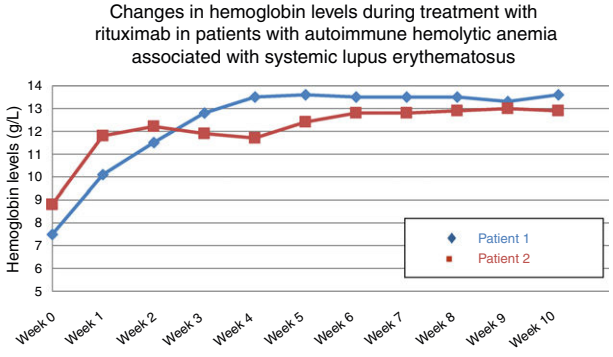

Fig. 1. Changes in the hemoglobin levels with rituximab (375 mg/m^2/weekly for 4 weeks). Stabilization in week 3 of treatment and tapering of corticosteroids to 5 mg/day.

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impact of rituximab as the first-line treatment of patients with AIHA is still unknown, it has been found to be effective as second-line therapy in prospective and retrospective studies,[6–8] with rates of relapse-free survival that range from 64% to 100% at 36 months. Moreover, the rate of response to therapy with a combination of rituximab and corticosteroids is significantly higher than that of corticosteroid monotherapy.[8,9]

Autoimmune hemolytic anemia is a serious pathological condition. Thus, an early diagnosis is important, as is intensive treatment to detain the hemolytic process. In our experience, the use of rituximab resulted in a rapid and durable response that continued over time in two patients of similar characteristics. We consider, in this respect, and according to the literature reviewed, that the initiation of this drug should not be delayed.[6,7,10] Given the safety and tolerability of rituximab,[8,9] its use as the second-line of treatment should be recommended, instead of the utilization of immunosuppressive agents that have a greater toxicity or rather than splenectomy.[8]

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