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CORRESPONDENCE

Non-traumatic metatarsal fracture: Uncommon complication of primary antiphospholipid syndrome

Fractura metatarsiana no traumática: Una complicación rara del síndrome antifosfolípido primario

To the Editor

Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by recurrent venous or arterial thrombosis and/or pregnancy morbidity associated with persistently elevated levels of antiphospholipid antibodies (aPL).[1]

A number of non-thrombotic manifestations are associated with APS, including chorea, epilepsy, transverse myelitis, multiple-sclerosis-like syndrome or cutaneous manifestations.[2] Very few reports have described orthopaedic manifestations in APS patients.[3,4] Avascular necrosis is the most frequent orthopaedic complication described in these patients.[3,4] More exceptional complications include algodystrophy and bone marrow necrosis.

Stress fractures of the metatarsals occur as a result of repetitive, long-term loading and are more common in military recruits, athletes, dancers and in patients with metabolic diseases such as osteoporosis or diabetes mellitus. Metatarsal fractures have been reported in rheumatoid arthritis, polymialgia rheumatica and chronic bronchitis. Associated risk factors in these conditions were long term treatment with corticosteroids and low bone density.[5] Sangle el al.[6] reported on metatarsal fractures in 17 female SLE patients associated with aPL and in 2 patients with primary APS, without history of trauma. We here describe the case of a primary APS patient who developed spontaneous metatarsal fracture despite anticoagulation therapy.

A 43-year-old female was admitted at the Clinical Immunology Unit because of development of an episode of central retinal vein occlusion. Thrombosis was confirmed by ophthalmic evaluation and fluorescein fundus angiography. The patient did not have risk factors for thrombosis. Family history: the mother had polymyositis and a sister autoimmune thyroiditis. Her physical exam was normal. IgM aPL determined by a standardized commercial enzyme-linked immunosorbent assay [anticardiolipin (15, 45 and 16 MPL units/ml) and anti-beta-2-glycoprotein-I (11, 30 and 60 units/ml)] were positive in more than 2 separated evaluations (at least 12 weeks apart). Lupus anticoagulant was negative. Serum concentrations of glucose, creatinine, urea, cholesterol, HDL-cholesterol, LDL cholesterol, triglycerides, protein C, protein S, homocysteine and coagulation factors were normal. Platelet counts were normal. APS was diagnosed and acenocoumarol therapy started to maintain an international normalized ratio between 2 and 3. An extended immunological study revealed the presence of elevated antithyroid antibody titers (869–1553 IU/ml) with normal T3, T4 and TSH levels and without clinical manifestations. Low titer positive antinuclear antibodies (1/80 homogenous pattern) were observed on only one occasion with negative values in further studies. Anti-DNA antibodies were persistently negative. Complement factors and haemolytical activity of complement were within normal values. During a 7-year clinical follow-up the patient did not show any clinical criteria of SLE or other autoimmune diseases that could be associated with APS. There was no recurrence of ocular thrombosis during follow-up.

Two years after the diagnosis of APS, the patient complained of foot pain without any other symptoms. Foot X-rays disclosed the presence of a third metatarsal fracture on the right foot (Figure 1). Serum calcium levels, phosphataemia, alkaline phosphatase, metabolic profile and her bone mineral density were within normal ranges. The patient had no physical stress or repetitive-overuse injuries, and she had never received steroid

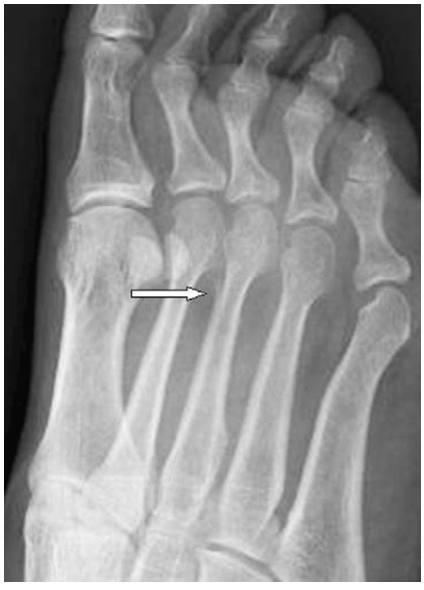

Figure 1 Foot X-rays disclosed the presence of a third metatarsal fracture on the right foot.

treatment. There was no evidence of malignancies or haemoglobinopathies.

aPL are associated with arterial and venous thrombosis, but their role in the pathogenesis of orthopaedic complications is unknown.[7] It has been suggested that bone microinfarcts caused by reaction of the aPL with endothelium could lead to bone damage and fracture.[7] Several risk factors such as glucocorticoid therapy or osteoporosis might explain development of osteonecrosis or bone fractures. The fact that our patient did not have these conditions supports the hypothesis that this complication might have been associated with APS, as reported by Sangle et al.[6] in APS patients using warfarin. A relationship between long-term warfarin therapy and osteoporotic fractures has been reported[8] and a degree of deterioration of bone structure has been also associated with acenocoumarol and low molecular weight heparin therapy,[9] but it remains unclear whether the antithrombotic therapy plays a role in the development of metatarsal fractures.

Proper diagnosis of metatarsal fractures requires a thorough clinical evaluation, and an early diagnosis is important since these fractures may require treatment such as nonweight-bearing immobilization coupled with therapy and often surgery.[10]

As orthopaedic involvement could be considered an underrecognized feature of APS, physicians dealing with these patients should consider metatarsal fractures as a possible cause of foot pain. The idea that these fractures could be the first manifestation of APS should also be taken into account.

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D. Alecsandru, E. Fernandez-Cruz and J. Carbone*

Immunology Department, Hospital Gregorio Marañon, Madrid, Spain

*Corresponding author.
E-mail address: jcarbone.hgugm@salud.madrid.org (J. Carbone).

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Hipotiroidismo primario autoinmune en pacientes con anemia perniciosa

Primary autoimmune hypothyroidism in patients with pernicious anemia

Sr. Editor:

La anemia perniciosa (AP) se define como el déficit de vitamina B12 causado por la ausencia de factor intrínseco debida a una atrofia gástrica de naturaleza autoinmune, aun cuando no exista anemia. Se ha descrito clásicamente que la AP puede asociarse a otras enfermedades autoinmunes, como la enfermedad tiroidea autoinmune[1–3]. No obstante, la frecuencia de dicha asociación ha sido poco estudiada[1–7]. En este artículo se describen los casos de AP con hipotiroidismo primario autoinmune (HPA) en una serie de pacientes diagnosticados en una consulta de medicina interna.

En nuestro estudio, el diagnóstico de AP se estableció por la existencia de un nivel plasmático de vitamina B12 inferior a 197 pg/ml (límite inferior del rango de normalidad de nuestro laboratorio), la presencia de anticuerpos (Ac) antifactor intrínseco y/o gastritis crónica atrófica demostrada en las biopsias gástricas y la respuesta al tratamiento con vitamina B12 en los casos en que hubiese manifestaciones hematológicas o neurológicas de la AP. El diagnóstico de HPA se estableció por la existencia de un hipotiroidismo primario bioquímico y Ac antiperoxidasa y/o antitiroglobulina.

Trece pacientes fueron diagnosticados de AP en un periodo de 4 años en una consulta de medicina interna de un hospital comarcal del norte de Extremadura (España). El seguimiento medio de los pacientes tras el diagnóstico de AP fue de 15,6 meses (rango 3–36 meses). Cuatro (30,8%) de esos 13 pacientes