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CASE REPORT

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Salmonella osteomyelitis complicating aseptic osteonecrosis: Don't forget about the antiphospholipid syndrome

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Abstract

Osteonecrosis in antiphospholipid syndrome is a diagnostic challenge for clinicians. Early diagnosis and intervention are important for better prognosis.

KEYWORDS

antiphospholipid syndrome, aseptic osteonecrosis, osteomyelitis, Salmonella

1 | INTRODUCTION

The antiphospholipid syndrome is characterized by arterial and/or venous thrombosis, and pregnancy morbidity in association with antiphospholipid antibodies. Osteonecrosis is one of the musculoskeletal manifestations. It can be rarely complicated with osteomyelitis. We present a case of bilateral aseptic osteonecrosis of the tibias complicated with Salmonella osteomyelitis, in antiphospholipid syndrome.

The antiphospholipid syndrome (APS) is a clinical-biological entity characterized by the association of thromboembolic events, classically recurrent, with obstetrical complications, and the permanent and significant presence of autoantibodies against the phospholipids of cell membranes at least 6 weeks.[1,2] It has a large clinical spectrum due to this thrombosis that can affect any vessels.

Though APS is a well-documented entity, certain manifestations of this syndrome such as osteonecrosis caused by thrombotic events in patients with secondary APS and SLE have been underappreciated. There are several risk factors for the genesis of osteonecrosis in patients with APS and SLE: glucosteroids used in the treatment of SLE and the presence of antiphospholipid antibodies.[3] This osteonecrosis predisposes secondarily to the local infections.

We present a case of bilateral osteonecrosis of the tibias in a 23-year-old patient suffering from secondary APS treated with low dose of glucosteroids. It was complicated with Salmonella osteomyelitis.

2 | CASE REPORT

A 23-year-old North African man has a history of APS secondary to a SLE evolving since 2015. The diagnosis of SLE was confirmed in the presence of erythema of the neckline, hemolytic anemia, lupus nephritis (extramembranous glomerulonephritis), and positive antinuclear antibodies (1/1600) associated with anti-DNA antibodies. The APS was diagnosed in the association of deep vein thrombosis of the right lower limb complicated with pulmonary embolism with positive anti-ß2GP1 and anticardiolipin antibodies. Other constitutional thrombophilias were excluded (protein C, protein S, and antithrombin 3 count was normal, and there was no resistance to activated protein C). The patient was initially treated with corticosteroids at the dosage of 1 mg/kg/day of prednisone associated with immunosuppressive therapy based on mycophenolate mofetil at the dosage of 3 gr per day. Anticoagulant treatment was also prescribed for 6 months. Then, no prophylactic treatment of thrombosis was prescribed.

A clinical and biological remission was obtained. The patient was treated by 10 mg of prednisone and 2 gr of mycophenolate mofetil.

After four years, in March 2019, the patient presented isolated inflammatory bone pain affecting both legs. There was no evidence for a clinical or biological outbreak of his systemic pathology.

The magnetic resonance imaging of both legs has shown an ancient bilateral multifocal infarction associated with acute metaphyseal epiphyseal infarction of distal right leg (Figures 1, 2, and 3). He was treated with painkillers.

Three months later, he consulted for the accentuation of the pain, especially on the right inferior extremity of limb, associated with a fever that had evolved for a week.

During his admission, he presented increased pain not calmed by high dosage of painkillers. At the physical examination, we objectified a fever at 40°C and inflammatory cutaneous signs on regard of the lower extremity of the left leg (Figure 4). We noted a lameness but without any signs of arthritis on both ankles.

At biological examinations, the C-reactive protein was elevated to 108 mg/L without elevated leukocytes. The platelet count was normal. Hemocultures and urinary cytobacteriological examination were negative. We did not check antiphospholipid antibodies or the thrombophilia profile.

There was a lytic image with peripheral condensation in the lower third of the tibia (Figure 5).

The ultrasound showed an irregular aspect of the bone cortex of the inner edge of the lower third of the right tibial diaphysis, without obvious subperiosteal collection, with significant infiltration on contact. The deep venous thrombosis in this same limb was confirmed by Doppler ultrasound.

An osteomyelitis was suspected. He was transferred to the orthopedic department where he had an exploration surgery.

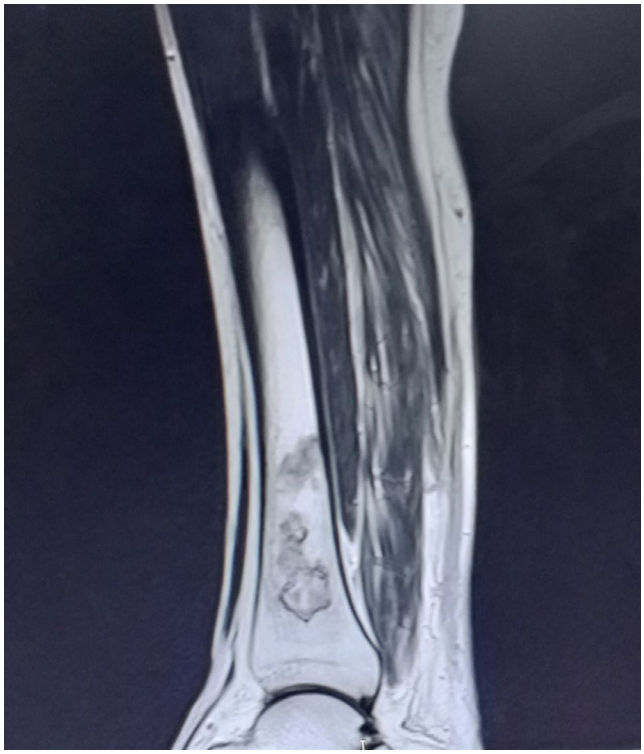

FIGURE 1 Large areas of necrosis in both tibias on magnetic resonance imaging

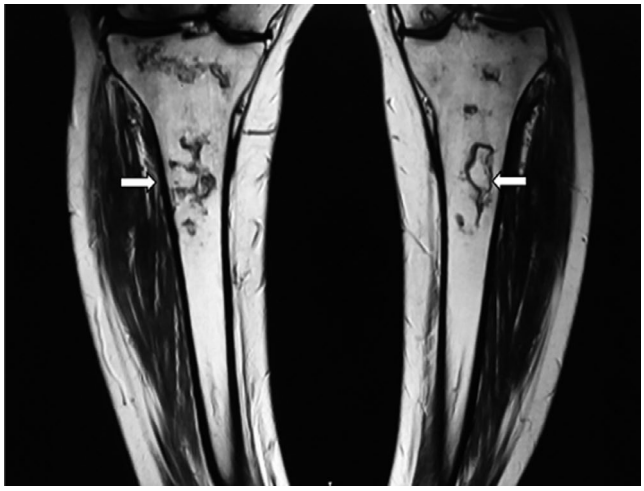

FIGURE 2 Large areas of necrosis in both tibias on magnetic resonance imaging

The diagnosis of osteomyelitis was confirmed on per operation (Figure 6). A Salmonella typhi was isolated in the per operation bacteriological examination. The patient was treated surgically (puncture and drainage of the pus) and received antibiotics (gentamycin for 5 days and amoxicillin-clavulanic acid for 30 days in intravenous way).

The evolution was good with desperation of fever and pain, and he started walking again. We decided to put him on anticoagulants for lifetime.

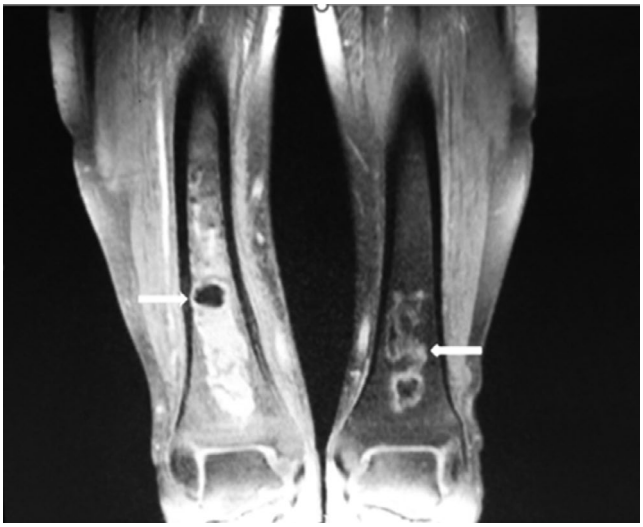

FIGURE 3 Large areas of necrosis in both tibias on magnetic resonance imaging

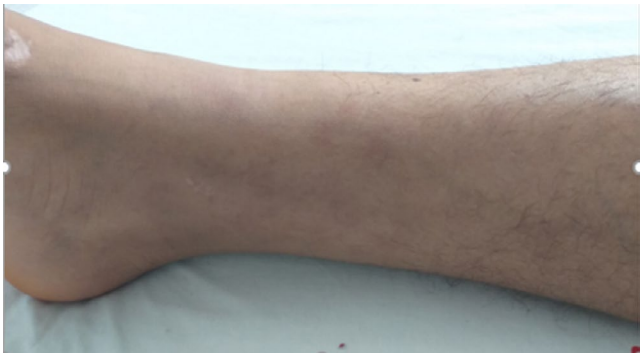

FIGURE 4 Macular erythematous lesions in the right leg

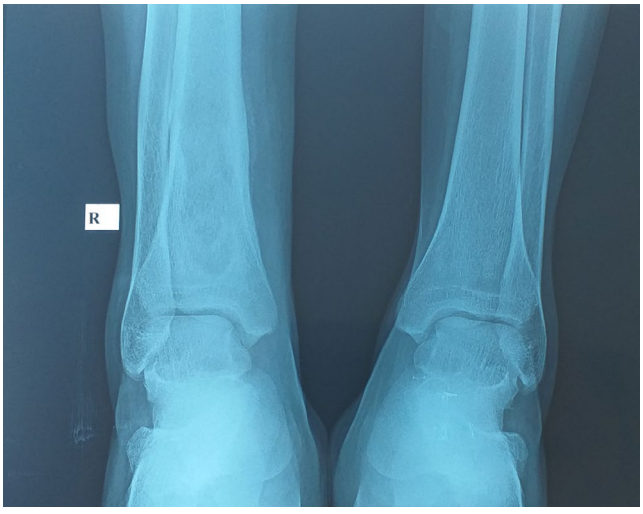

FIGURE 5 A lytic image with peripheral condensation in the lower third of the tibia

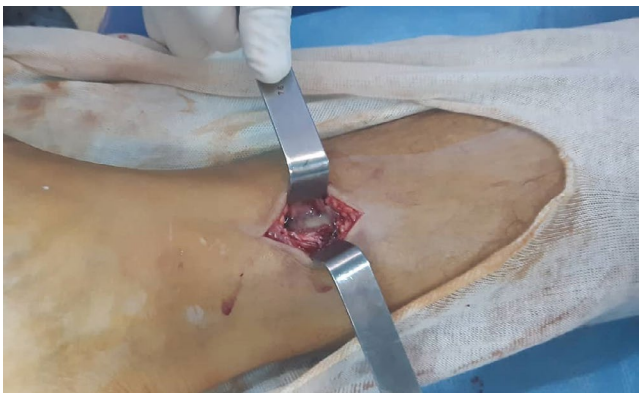

FIGURE 6 Per operation images showing the osteomyelitis

3 | DISCUSSION

The observation was characterized by the masculine gender of the patient, the multifactorial osteonecrosis (APS secondary to SLE and low dose of corticosteroids), an unusual localization in the lower third of the tibia, and the complication with Salmonella osteomyelitis.

In general, musculoskeletal manifestations of APS may be classified into three categories: pain/inflammation, necrosis, and fragility (osteoporosis, nontraumatic fractures). The avascular necrosis of bone is a significant threat to APL patients. It may even be among the presenting symptoms.[4] The prevalence rates ranged widely between 0.9% and 20%.[5,6]

The literature suggests that the cause of the clinical manifestations of APS is mostly the hypercoagulable state induced by these antibodies bound to various phospholipids on components of the coagulation system. The resulting dysregulation of the coagulation system induces the thrombotic events that characterize APS.[7]

The pathophysiology of osteonecrosis in patients with APS is not quite clear yet. Many mechanisms have been discussed. But, there are two main ideas: First, anticardiolipin antibodies are associated with thrombophilia, and second, these antibodies are associated with avascular necrosis of bone.[8,9] Osteonecrosis can be also caused by thrombosis induced by the hypercoagulable state set by the presence of antiphospholipid antibodies.

This thrombophilic and hypofibrinolytic state predisposes patients to venous thrombi. The resulting venous occlusion leads to venous sinusoidal hypertension within the cancellous bone.[10,11] The venous sinusoidal hypertension increases until arterial blood flow to the region is no longer able to deliver adequate oxygen to the bone. The resulting cellular hypoxia provokes bone and marrow cell death, thereby causing osteonecrosis.[12] This mechanism goes with the research finding that an elevated anticardiolipin antibody titer predisposes patients to osteonecrosis.[13]

To diagnose osteonecrosis, there are no efficient laboratory tests. However, it is necessary to eliminate more common etiologies such as sickle cell anemia and other hypercoagulopathies such as protein C and protein S deficiencies and factor V Leiden disease. The diagnosis of osteonecrosis is based on imaging modalities. Plain radiographs can help with the evolution of osteonecrosis. However, the magnetic resonance imaging provides high specificity and sensitivity, so that it detects the earliest signs of osteonecrosis, which are low signal intensity of the marrowfat on T1-weighted images (normally produces high signal intensity).[14] This radiologic abnormality was observed in our case.

There is no medical treatment for osteonecrosis. The surgical technics are inefficient so far. Anticoagulant treatment is necessary when thrombotic events are associated with bone complications. If there is no thrombosis, anticoagulation is not recommended in bone manifestations.[7]

One of the complications of osteonecrosis is infection, which is very rare. Only few cases are reported in the literature.[15,16] Unfortunately, our patient developed this complication with Salmonella.

Osteomyelitis risk factors are as follows: local infection (skin, muscle, and bone), advanced age, altered general state, hemodialysis, drug injection, sickle cell disease, vascularization disorders, and immunosuppressive therapy. The most common germs in cause are as follows: Staphylococcus aureus, Streptococcus, gram-negative bacillus from digestif origin, and anaerobic bacteria. Our patient had 2 risk factors: vascularization disorder and osteonecrosis, and immunosuppressive therapy.

Salmonella osteomyelitis is also a rare condition, accounting for 0.8% of all Salmonella infections and only 0.45% of all types of osteomyelitis.[17] It is commonly associated with sickle cell anemia and other hemoglobinopathies, malignancy, liver disease, alcoholism, diabetes, and surgery or trauma.

SLE predisposes to severe Salmonella infections.[18] Extradigestif manifestations are rare (4.87% of the nontypical salmonellosis in Prignet's series[19]). All serotypes can be isolated, but Salmonella typhimurium and Salmonella enteritidis are the most common.[19]

4 | CONCLUSION

Osteonecrosis in APS patients is an important threat; thus, suspicion of such a complication is a diagnostic challenge for clinicians for those who presented with inflammatory bone pain. Early diagnosis and intervention are important for better prognosis.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

I confirm that all persons designated as authors meet the criteria as outlined in the policy. FD: wrote the manuscript with support of IR and OF. FD, IR, OF, MBS, HZ, MS, KH, MK, and FB: contributed to the patient management. FD, IR, OF, MBS, SC, HZ, MS, KH, MK, CC, and FB: approved the final version. SC and CC: analyzed radiologic images.

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