

# Bone Infarctions in a Patient with Systemic Lupus Erythematosus and Anti-phospholipid Syndrome

## Sistemik Lupus Eritematozus ve Anti-fosfolipit Sendromlu Bir Hastada Kemik İnfarktları

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**ABSTRACT** Avascular necrosis (AVN) is a well-known but rare complication in patients with systemic lupus erythematosus (SLE) and anti-phospholipid syndrome (APS), usually affecting weight-bearing bones and is most common in the femoral head. AVN has been reported in 2-30% of patients with SLE. In this article, I reported a 27-year-old man with a 6-year history of SLE, previously treated with high dose corticosteroids and cyclophosphamide pulse therapy for lupus nephritis presented to our clinic complaining of severe chronic pain in his bilateral knee and left ankle. X-rays and magnetic resonance imaging of knee and ankle revealed bone infarctions. We prescribed low-dose aspirin. The syndrome of multiple avascular necrosis and bone infarcts is a rare cause of musculoskeletal pain in patients with SLE.

**Keywords:** Lupus; bone infarct; musculoskeletal pain; anti-phospholipid syndrome

**ÖZET** Avasküler nekroz (AVN), sistemik lupus eritematozus (SLE) ve anti-fosfolipit sendrom hastalarında iyi bilinen, ancak nadir bir komplikasyondur. Genellikle ağırlık taşıyan kemikler etkilenir ve femur başı tutulumu yaygındır. AVN, SLE hastalarının %2-30'u olarak bildirilmiştir. Bu makalede 6 yıllık SLE geçmişi olan 27 yaşındaki erkek hasta sunuldu. Daha önce lupus nefriti için yüksek doz kortikosteroid ve pulse siklofosfamid ile tedavi edilen hasta, her iki diz ve sol ayak bileğinde kronik ağrı şikâyetiyle kliniğimize başvurdu. X-ray ve diz, ayak bileği manyetik rezonans görüntüleme ile dizler ve el bileklerinde kemik infarktları saptandı. Düşük doz aspirin reçete edildi. Birden fazla avasküler nekroz ve kemik infarktları SLE hastalarında kas iskelet ağrısının nadir bir nedenidir.

**Anahtar Kelimeler:** Lupus; kemik infark; kas iskelet ağrısı; anti-fosfolipid sendrom

**A**vascular necrosis (AVN) is a well-known but rare complication in patients with systemic lupus erythematosus (SLE) and antiphospholipid syndrome, usually affecting weight-bearing bones and is most common in the femoral head.<sup>1-3</sup> Systemic lupus erythematosus is an autoimmune, chronic inflammatory multisystem connective tissue disease and AVN of bone is a well-recognized complication of SLE. The musculoskeletal pain manifestation of SLE is diverse including arthralgia, synovitis, myositis, myopathy and AVN of bone which occurs in variable frequencies at various stages of the disease.<sup>4,5</sup> The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the American College of Rheumatology (ACR) SLE classification criteria to improve clinical relevance, meet stringent methodology requirements and incorporate new knowledge regarding the immunology of SLE.<sup>5</sup> Antiphospholipid syndrome (APS), also known as 'Hughes Syndrome,' is an autoimmune hypercoagulability disorder characterized by arterial and venous thrombosis and recurrent pregnancy losses in patients with antiphospholipid antibodies (aPL). aPL comprises three main

antibodies: anticardiolipin (aCL), lupus anticoagulant (LA), and anti-b2-glycoprotein-I antibodies (antib2GPI).<sup>6</sup> According to the Updated Classification Criteria for APS, as positive LA test, aCL IgG/IgM antibodies >99<sup>th</sup> percentile and aβ2GPI >99<sup>th</sup> percentile on two or more occasions at least 12 weeks apart.<sup>7</sup> AVN has been reported in 2-30% of patients with SLE.<sup>8</sup> AVN and bone infarctions are caused by a diminished blood flow to the bone.<sup>9</sup> In AVN early stages, plain radiography findings are unremarkable, and early lesions are detectable by magnetic resonance imaging (MRI).<sup>10</sup>

## CASE REPORT

The patient, a 27-year-old man with a 6-year history of SLE, previously treated with high-dose corticosteroids and cyclophosphamide pulse therapy for lupus nephritis presented to our clinic complaining of severe chronic pain in his bilateral knee and left ankle. He was under the treatment of hydroxychloroquine. His laboratory tests were hemoglobin 14 g/dl, white blood cells 7.8x10<sup>9</sup>/L, creatinine 1.04 mg/dl and erythrocyte sedimentation rate (ESR) 35 mm/h, c-reactive protein (CRP) 14.8 mg/l. Urinalysis revealed mild proteinuria without hematuria. Antinuclear antibodies and antibodies to dsDNA were positive. Previously, aCL antibodies, Ig G, and IgM were positive. There was no family history of connective tissue or other autoimmune condition. There was no trauma history in the patient. In the knee and ankle radiography (Figure 1), some fine smoky lines and irregular lesions, compatible with bone infarctions. Because of suspicion of bone infarct, we took an MRI of the patient. There were some signal changes in the metaphysis of the femur and distal tibia that was consistent with bone infarct in this area (Figure 2, 3). He referred to the rheumatologic clinic for AVN. He was prescribed low-dose aspirin and conservative treatment was given. Hydroxychloroquine treatment continued. After three months patient's pain was reduced.

## DISCUSSION

AVN of the bone is one of the leading causes of morbidity and disability in SLE patients.<sup>2</sup> AVN has been reported in 2-30% of patients with SLE.<sup>8</sup> Osteonecrosis (ON), is the cellular death of bone compo-



FIGURE 1: Plain bilateral knee and left ankle radiographs.



FIGURE 2: T1-weighted left knee magnetic resonance image showed geographic areas of decreased signal intensity within the medullary cavity of the left distal femur and proximal tibia, consistent with osteonecrosis.

nents due to interruption of blood supply, resulting in pain, bone destruction and loss of function or avascular necrosis of bone.<sup>11,12</sup> AVN in patients with SLE is most common in the femoral head, although the humeral head, tibial plateau, and scaphoid navicular can also be affected.<sup>13</sup> Many local and systemic factors have been implicated in the pathogenesis of AVN, involving corticosteroid therapy, systemic lupus erythematosus (SLE), hemoglobinopathies, alcohol abuse, Caisson disease, Gaucher disease, and hypercoagulability states.<sup>1,3,9,11,14,15</sup> Lupus activity, the presence of arthritis, vasculitis, aCL, corticosteroid and cytotoxic medication was associated with increased risk of avascular necrosis.<sup>1,3,16</sup> The association of AVN and aPL in patients with SLE has shown to be signif-



**FIGURE 3:** T2- weighted left ankle magnetic resonance image showed geographic areas of increased signal intensity within the medullary cavity of the left distal tibia, consistent with osteonecrosis.

icant in many studies.<sup>14,17</sup> However, the role of aPL in the pathogenesis of AVN is not proven yet as some studies have failed to establish the association.<sup>3,13,18</sup> Mok et al. a cohort of 265 SLE patients emphasizes that, during a 20-year follow-up, AVN was diagnosed in 11 (4%) patients with a mean of 9 years period after the onset of SLE.<sup>3</sup> Four (36%) of the 11 AVN patients were positive for aPL. Gladman and colleagues studied 744 SLE patients and noted that 70 (9%) patients developed AVN.<sup>13</sup> The affected sites varied between hips, knees, shoulders, ankles, elbows, and wrists. Although more AVN subjects (57.1%) had positive aCL compared to non-AVN subjects (44.3%), the difference did not reach statistical significance. Nagasawa et al. diagnosed AVN in 24 (22%) of 111 SLE patients. LA was positive in 25% of the AVN patients compared to 11% of 44 non-AVN patients.<sup>18</sup> Treatment of regular doses of prednisone greater than 20 mg/day,

another risk factor for osteonecrosis in SLE. AVN early stages, radiography findings are unremarkable.<sup>10,17,19</sup> Bone infarcts are only recognized late in their course on radiography, which shows dense, irregular shadows resembling puffs of smoke situated in the metaphyso-diaphyseal regions of the long bones. MRI examination is useful in these cases. MRI is the gold standard diagnostic method to detect both symptomatic and silent AVN.<sup>10,18</sup> Bone infarcts are verified early in their course by MRI, which reveals zones of reduced signal with irregular margins with scattered areas of increased signal of fat intensity.<sup>14,20</sup> In AVN advanced cases, surgery is the only option and frequently implies a joint replacement.<sup>10</sup> The present case and others suggest that SLE patients developing multifocal ON tend to be young, have several SLE clinical manifestations and serological abnormalities, and most have been exposed to CS and cytotoxic agents. Also, the possible association of antiphospholipid antibodies and corticosteroid therapy should alert physicians that these patients might be at higher risk for multifocal AVN.

### **Conflict of Interest**

*Authors declared no conflict of interest or financial support.*

### **Informed consent**

*Informed consent was obtained from patient included in the case report*

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