Avascular necrosis of the right femoral head in female patient with Systemic Lupus Erythematosus

A Sinaga[1], H Nufus[1], B Setiyohadi[2]

[1] Department of Internal Medicine, University of Indonesia School of Medicine/ Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; [2] Division of Rheumatology, Department of Internal Medicine, University of Indonesia School of Medicine/Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Avascular necrosis (also known as osteonecrosis, aseptic necrosis, or ischemic necrosis) represents collection of pathologic conditions from various etiologies causing impairment of blood supply to particular bone resulting in bone cellular death. Avascular necrosis remains a significant cause of morbidity in patients with systemic lupus erythematosus (SLE).[1] It often involves multiple joints in SLE, in which the femoral head is involved in most of these patients. Corticosteroids use is known as a major risk factor in the development of this complication.[2-3] We report this case due to its quite common occurrence in SLE patients. The early recognition of avascular necrosis is essential to prevent morbidity.

CASE REPORT

A 24 year-old female patient presented to Emergency Department of Cipto Mangunkusumo General Hospital with chief complaint of pain in right hip two weeks prior to admission. She was difficult to move her right thigh and walk due to the severity of the pain. The pain was aggravated with movement and relieved by rest; thus, she had limitation of daily activities. There was no history of trauma or thrombotic episodes. She did not smoke cigarette and drink alcohol. She was not married. There was no family history of similar illness in her family.

The patient was diagnosed with SLE two months prior to admission. Her chief complaint was dark rashes all over her extremities. She was given methylprednisolone 32 mg/day, omeprazole 20 mg bid, folic acid qd, and vitamin D3 tid. Her rashes were improved with the medication, but she did not regularly visit the Allergy and Immunology Clinic in Cipto Mangunkusumo General Hospital.

The physical examinaton revealed moderately ill-looking. Her body weight was 45 kg and her height was 152 cm with body mass index (BMI) of 18.6 kg/m^2. Her blood pressure was 110/70 mmHg, without tachycardia and tachypnea. Her body temperature was 37ºC. She had no malar rash or stomatitis, but she had hyper-pigmented macula all over her extremities and an ulcer in sacral region 3 cm in diameter with clean base and no pus. There was no limb length discrepancy. She was difficult to move her right leg out and unable to raise that. Her physiological reflexes were intact. No pathological reflexes noted during the examination. Other physical examinations were within normal limits.

Laboratory examination revealed hemoglobin of 10.2 gram%; haematocrit of 31%; white blood count (WBC) of 10,200 u/L, and platelet count of 314,000 u/L. The blood urea was 27 mg/dL and creatinine was 0.4 mg/dL. The electrolytes and liver transaminases were within normal limits. ANA was positive and anti-ds-DNA was 360.79. The erythrocyte sedimentation rate (ESR) was 110 mm/h. Her activated partial thromboplastin time (aPTT) was 35.4 sec (control 33.5 sec) and prothrombin time (PT) 14.1 sec (control 11.6 sec), which were normal. Radiography of the chest, pelvis, and lumbo-sacral were revealed no abnormalities. Her electrocardiography (ECG) was also within normal limits.

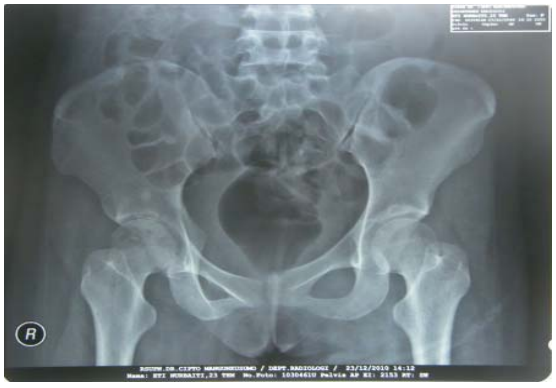

Figure 1 : Pelvic radiography showed no abnormality on both femoral heads

The working diagnoses were suspected fracture of the right femoral head caused by suspected avascular necrosis, SLE, anemia, low intake, pressure ulcer, and immobilization. Then, she was given intravenous normal saline and Triofusin E 1000 per 24 hours, 1700 kcal diet per day, methylprednisolone tablets 8 mg bid, folic acid tablet qd, vitamin D3 tid, omeprazole 40 mg injection qd, tramadol 100 mg injection bid, heparine UFH 5000 units subcutaneously bid, ceftriaxone 2 g injection qd, and metronidazole 500 mg infusion tid. The patient was planned for pelvic magnetic resonance imaging (MRI) and consulted to the Department of Orthopedic and Traumatology. On fourth day of hospitalization, patient and her family decided to go home due to financial problems.

Four days after the discharge, patient went for pelvic MRI. The test revealed collapse of the right femoral head which suggested avascular necrosis of the right femoral head. She was then lost to follow-up and had never visited the hospital ever since.

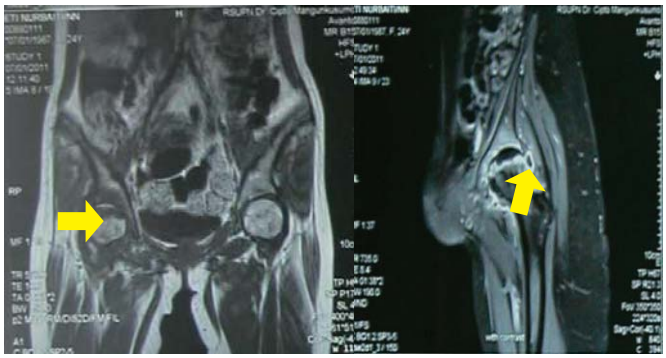

Figure 2 Patient's MRI showed collapse of the right femoral head (yellow arrow)

DISCUSSION

Systemic lupus erythematosus is a multisystem, autoimmune disease of unknown etiology. It is characterized by immune dysregulation that results in the production of autoantibodies, generation of circulating immune complexes, and activation of the complement system. Pathogenesis of the disease is apparently multifactorial with genetics, environmental, hormonal, and possibly viral influences playing a role.[4]

Avascular necrosis (also known as osteonecrosis, aseptic necrosis, or ischemic necrosis) represents conditions that result in impairment of blood supply to particular bone resulting in bone cellular death. Avascular necrosis can lead to architectural collapse of the subchondral bone, joint incongruency, and degenerative arthritis. A definite association between avascular necrosis and SLE was first documented in 1960 by Dubois and Cozen. Avascular necrosis has continued to be a significant cause of morbidity in patients with SLE.[1] The incidence of avascular necrosis in SLE patients is 4-16% and often involves multiple joints. The femoral head is involved in 80% of these patients. Corticosteroids use is a major risk factor in the development of this complication.[1,5] A researcher, named Zizic concluded on the rarity of avascular necrosis in other steroid-dependent populations, such as asthma, dermatological disorder, and inflammatory bowel disease, when compared to SLE.[5-7] This finding suggests that additional factors specific to SLE itself may be responsible for avascular necrosis. Other features which have been associated with development of avascular necrosis in SLE include arthritis, central nervous system disease, vasculitis, hematologic abnormalities, Raynaud's phenomenon, and antiphospholipid antibodies.[2-3,5]

The pathogenesis of avascular necrosis in SLE is multifactorial. Some factors that may contribute are blood flow to the bone, vasculitis, and corticosteroid itself. The femoral head derives its blood supply from three sources: intraosseus cervical vessels, retinacular vessels, and the artery of the ligamentum teres. There are only few anastomoses to the femoral head. Therefore, any disruption to the blood flow of one artery above cannot be compensated by the collateral vasculature.[2,8]

It is believed that vasculitis and increased tendency to thrombosis as components of lupus syndrome contribute to avascular necrosis in SLE.[5] Vasculitis is characterized by inflammation of the vessel wall and intravascular activation of polymorphonuclear (PMN) leukocyte and release of reactive oxygen species. These events may stimulate aggregation of PMN resulting in intravascular thrombus.[2] Mont et al found a high incidence of thrombophlebitis and vasculitis in patients with avascular necrosis. This suggests that the pathophysiological mechanisms of thrombotic and endothelial damage are involved in the development of avascular necrosis.[9,10] From history taking, patient mentioned no history of any thrombotic events, more over from blood examination revealed normal hemostatic examination.

The mechanism of steroid induced avascular necrosis is still not fully understood. Corticosteroids use at least 30 mg/day is a major risk factor in the development of this complication. McFarland and Frost suggested that corticosteroids may suppress osteoblastic function of the bone; and therefore impairs the host response to micro-fractures. Corticosteroids also exert some effect to fat metabolism, storage, and asymptomatic systemic fat emboli. Two hypotheses have been proposed in an attempt to explain the mechanism by which changes in fat metabolism after steroid administration can lead to avascular necrosis. The first suggests that altered fat metabolism causes an increase in the size of intraosseous adipocytes, leading to increased intraosseous pressure which compromises perfusion (through activation of the coagulation pathway) and results in ischemia. The second proposed mechanism is that altered fat metabolism results in increased serum lipid levels with subsequent occlusion of subchondral vessels by fat emboli. Animal studies have proposed that increased levels of serum lipids leads to lipid deposition in the femoral head, causing femoral hypertension and ischemia. Fisher and Bickel concluded that systemic fat emboli caused a mechanical vascular obstruction on avascular necrosis.[1-2,5]

Studies investigating avascular necrosis and steroid treatment yielded conflicting results concerning cumulative steroid dose, maximum daily steroid dose, route of administration, and duration. Aranow et al screened 62 SLE patients by MRI for avascular necrosis. Fourty three of 62 patients took □30mg/day of prednisone and nine patients (19%) had evidence of avascular necrosis. Patients who had taken <30mg/day had no evidence of avascular necrosis. From another descriptive study done by Castro et al concluded that there was no significant difference between the avascular necrosis and non-avascular necrosis group in relation to the maximum daily corticosteroid dose, the cumulative steroid dose, or methylprednisolone pulse therapy.[5,9] The most possible contributing factor to avascular necrosis in this patient was steroid ingestion.

The process of avascular necrosis may appear before the symptoms. It causes pain upon standing, walking, or moving the affected bone and the pain relieved when resting. Due to

severe pain, some people remember the exact day and hour when the pain begin to emerge. Sudden arrival of the pain may occur when there is disruption of the blood supply to the bone. In avascular necrosis of the femoral head, the groin pain may radiate down to one side of the thigh or felt in the buttocks. The gait was antalgic, trying to reduce all motion of the thigh. As the disorder progress, the more likely a hip fracture occurs. The pain somehow increases, the thigh joint becomes stiff and reduces its range of movement.[4,11] This patient complained pain on her right hip accompanied with reduced motion at the hip.

Physical examination may reveal pain and limitation in passive range of motion of the hip, especially forced internal rotation. A distinct limitation of passive abduction may also be noted. Passive internal and external rotation of the extended leg (log roll test) and straight-leg raise against resistance may elicit pain as well.[2] This patient experienced limitation in passive abduction, internal, and external rotation of the leg.

Diagnosis of avascular necrosis can be done trough radiographic imaging. Antero-posterior and frog-leg lateral radiographs should be obtained as part of the work-up; however, early-stage avascular necrosis is not visible on radiographs. MRI should be performed when avascular necrosis of the femoral head is suspected but not obvious on radiographs.[12-13]

The successful treatment of patients with avascular necrosis is related directly to the stage of disease at the time of diagnosis. Staging plays an important role in diagnosis. Ficat and Arlet described the first staging system for avascular necrosis of femoral head in 1960. Hungerford and Lennox modified this staging system when MRI became available, adding stage 0 to the classification. Steinberg et al expanded this staging system, by dividing stage III lesions into femoral heads with or without collapse or hips with or without acetabular involvement. Ohzono et al incorporated the concept of location of the lesion with prognostic value. More recently, a new classification has been completed by The Association Research Circulation Osseus (ARCO), which joins the Ficat and Arlet staging system, the Hungerford-Lennox modification, Steinberg, and Ohzono staging systems.[2,14-16] We report this patient based on Ficat and Arlet staging (table 1).

Table 1 Ficat and Arlet staging of avascular necrosis of femoral head[14-16]

Stage 0	No pain, normal radiographic finding, abnormal findings on MRI or bone scintigraphy
Stage I	Pain, normal x-ray finding, abnormal findings on MRI or bone scintigraphy
Stage II	Pain, cysts and/or sclerosis visible on x-ray, abnormal MRI or bone scintigraphy without subchondral fracture
Stage III	Pain, femoral head collapse visible on x-ray, abnormal MRI or bone scintigraphy, crescent sign (subchondral collapse) and/or slip-off in contour of subchondral bone
Stage IV	Pain, acetabular disease with joint space narrowing and arthritis visible on x-ray, abnormal MRI or bone scintigraphy

MRI, magnetic resonance imaging

MRI is representing the gold-standard of non-invasive diagnostic evaluation of avascular necrosis and become the most sensitive and specific means of diagnosing avascular necrosis. MRI has several advantages such as allows accurate staging by clearly depicting the size of the lesion; detection of asymptomatic lesions that are undetectable on plain radiographs, thus facilitating early treatment and better response; provides multi-planar imaging and excellent soft tissue resolution. Whole-body STIR (short tau inversion recovery) MRI permits the evaluation of the entire skeleton in a single examination that can be completed within a reasonable period of time.[14,17]

Characteristic MRI findings for avascular of the hip include a low signal intensity band (seen on T1 and T2 images) that demarcates a necrotic antero-superior femoral head segment. The extent and location of femoral head necrosis on MRI have been studied as predictors of femoral head collapse. Smaller lesions (less than one fourth the diameter of the femoral head) and more medial lesions (away from primary weight-bearing areas) predict a better outcome. The ability of MRI to detect the early stages of avascular necrosis may allow earlier intervention to ameliorate disease progression and to minimize more severe long-term sequelae.[9,16-17] From patient's pelvic radiography, there were no changes from the femoral head. So, it was decided to order more advance imaging modality of MRI. The MRI revealed collapse of the femoral head. Based on Ficat and Arlet staging, this patient was classified under stage III. Sometimes in stage III, anteroposterior radiograph may appear normal, like in this patient, but frog-leg lateral view often reveals a crescent sign under the subchondral bone.[18] Unfortunately, we did not perform the frog-leg lateral view in this patient.

Management of avascular necrosis consists of non-operative and operative measures. Non-operative management is often used for small, asymptomatic lesions in which subchondral bone collapse is absent. Non-operative measure usually results in an unfavorable prognosis. Most methods of non-operative treatment have involved restricted weight bearing, pharmacologic agents, and various external, biophysical modalities such as electromagnetic stimulation, extracorporeal shock-wave therapy, and hyperbaric oxygen. Restricted weight bearing with use of a cane or crutches has not been shown to affect the natural history of the disease and is useful only in controlling symptoms. Those biophysical modalities only provide symptomatic control without altering the course of the disease. Pharmacological intervention includes statin to lower the lipid level. Pritchett reported that at a mean of 7.5 years avascular necrosis of the femoral head had been developed in only 1% of patients who were taking high doses of steroids as well as various statin drugs.[2,4,15,19]

Table 2 Recommendation of decision-making hierachy for the treatment of patients with avascular necrosis of the femoral head[12,18-21]

Stage	Treatment
0 (asymptomatic, no radiographic changes)	Possible core decompression
I (no radiographic changes)	Core decompression, percutaneous drilling
II (pre-collapse)	Core decompression, percutaneous drilling, bone-grafting, osteotomies
III (cresent sign)	Hemiresurfacing, total tip arthroplasty
IV (joint deformity, acetabular involvement)	Total tip arthroplasty

Operative treatment (see table 2 for recommendation) of avascular necrosis of the femoral head can be categorized as either prophylactic measures (to retard progression) or reconstruction procedures (after femoral head collapse). The most commonly performed prophylactic surgical treatment is core decompression (removal of the inner layer of bone) and bone-grafting (healthy bone from one part of the patient to be transplanted in the diseased area; at present vascularized-grafts are used). Core decompression is usually performed in earlier stage of avascular necrosis. The goal is to decompress the femoral head and thereby reduce the intraosseous pressure in the femoral head, restore normal vascular flow, and subsequently reduce the hip pain. Bone-grafting may be effective, compared with core decompression, for larger lesions just before head collapse.[14,15,18,20-21]

There are some reconstruction procedures for avascular necrosis of femoral head such as total hip arthroplasty, osteotomy, limited femoral resurfacing arthroplasty, and bipolar arthroplasty. Most hips that undergo collapse ultimately require reconstruction. Prosthetic replacement offers the most predictable means of pain relief in advanced avascular necrosis. Total hip arthroplasty is a predictably effective treatment of avascular necrosis of the femoral head when the disease is progressed to Ficat and Arlet's stages III and IV.[14,15,20-21] This patient progressed into stage III based on Ficat and Arlet, so total hip replacement is mandatory in this case.

SUMMARY

We have reported a case of avascular necrosis of the femoral head in female patient with systemic lupus erythematosus. Steroid might contribute as one factor for the development of avascular necrosis. According to the staging, the patient should be treated with total hip replacement, but after establishing the diagnosis the patient was loss to follow-up.

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