Avascular Necrosis of Bone in Patients with Systemic Lupus Erythematosus

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Abstract

Background: Avascular necrosis of bone (AVN) is a well-recognized complication in patients with systemic lupus erythematosus (SLE). The aim of our study was to assess the prevalence of AVN in SLE patients and its correlation with other SLE manifestations.

Methods: We retrospectively reviewed the medical records of our patients with SLE who were complicated by osteonecrosis at the Department of Rheumatology of Imam Reza Hospital, Mashhad, Iran. We extracted data related to the patients, including demographic characteristics, clinical features, laboratory findings, images and type of treatment from files. We divided the patients into 2 groups: patients with AVN as cases, and patients without AVN as controls.

Results: The prevalence of AVN in our patients was 6.9%. The mean disease duration (from diagnosis of SLE to the development of AVN) was 29.00±17.10 months. All patients with AVN had received corticosteroids. The mean total cumulative steroid dose (from diagnosis of SLE to the development of AVN) was 5470±3992.66 mg. The most common involved site was hip joint (96.6%). Hip joint involvement in 25% of cases was unilateral and in 75% was bilateral. Knee and shoulder joints were both involved in 6.8% of cases. There was significant difference between the 2 groups, only in the prevalence of nephritis and thrombocytopenia.

Conclusion: All of our patients with AVN had received corticosteroids. In our study only nephritis and thrombocytopenia had positive association with AVN.

Keywords: SLE, Lupus, systemic lupus erythematosus, AVN, Avascular necrosis of bone, osteonecrosis

I. Introduction

Avascular necrosis (aseptic necrosis, osteonecrosis, ischemic bone necrosis) is a disorder that happens when there is an interruption of blood supply to the bone. AVN is an important cause of morbidity and change in the quality of life in systemic lupus erythematosus (SLE) patients. Dubois and Cozen in 1960 reported AVN in SLE patients for the first time. The prevalence of AVN in SLE patients had been reported from 2.8% to 40%. Osteonecrosis mainly affects femoral head and condyles, humeral head and distal end of the tibia. The main risk factor associated with the development of AVN is the use of corticosteroid at high doses. On the other hand, AVN has also been seen in SLE patients who had not taken steroid. This shows that additional factors related to SLE itself may be responsible for AVN. Osteonecrosis may be asymptomatic or may present with a gradual onset of mild or vague pain that may worsen by movement and then progress to severe pain when bone collapse occurs; in some cases osteonecrosis may present with a sudden onset of joint pain that at first is induced by movement and later is also present at rest.

The aim of this study was to assess the prevalence of AVN in patients with SLE and its association with other SLE manifestations.

II. Patients and methods

We retrospectively reviewed the files of our SLE patients who were complicated by osteonecrosis at the Department of Rheumatology of Imam Reza Hospital, Mashhad, Iran. We extracted data regarding the patients, including demographic features, clinical, laboratory findings, images and type of treatment from files. All patients had SLE, according to the Systemic Lupus International Collaborating Clinics classification (SLICC) criteria for SLE. The diagnosis of AVN was confirmed by clinical and imaging (plain radiographs or MRI) assessments. We divided the patients into 2 groups: patients with AVN as cases, and patients without AVN as controls.

III. Statistical analysis

Data were analyzed by SPSS software (version 20). The numerical variables were described by mean and standard deviation. The clinical and laboratory findings were compared between the 2 groups by the Fisher exact test for the qualitative variables and Student’s t-test or the Mann–Whitney U test for the quantitative variables (according to the nature or distribution of the variables). The level of significance was a P < 0.05.
IV. Results

Among the 487 studied SLE patients, there were 449 females (92.19%) and 38 males (7.81%), with a female to male ratio of 11.81:1. The mean age of patients at the onset of the SLE was 25.5±6.6 years. There were 29 patients (6.90%) with symptomatic AVN. The clinical and laboratory findings of patients with and without AVN are compared in Table 1.

The mean disease duration (from diagnosis of SLE to the development of AVN) was 29.00±17.10 months (minimum 5.00 months and maximum 65 months).

All patients with AVN had received corticosteroid. The mean total cumulative steroid dose (from diagnosis of SLE to the development of AVN) was 5470±3992.66 mg (minimum 5000 mg and maximum 12000 mg).

Fifty-three joints in 29 patients developed AVN. In 8 (27.5%) patients, only one joint was involved. In 21 (72.5%) patients more than 1 joint was involved (2 joints in 18 patients, 3 joints in 3 patients). The most common involved site was hip joint (96.6%). Hip joint involvement in 75% of cases was bilateral and in 25% of cases was unilateral. Knee joint (distal part of femur) was involved in 2 (6.89%) cases (in 1 case only knee and in 1 case knee+hip). Shoulder joint (humeral head) was involved in 2 (6.89%) cases (in both cases hip joint was also involved). All SLE patients with AVN were symptomatic at the diagnosis of their AVN. There were significant differences between the 2 groups (with and without AVN) only in nephritis and thrombocytopenia. Twelve (41.37%) patients have needed total hip replacement surgery (in 19 joints) and 10 (34.48%) patients had received decompression surgery (in 16 joints).

Table 1 Comparisons between Systemic Lupus Erythematosus patients with and without avascular necrosis (AVN).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-AVN group (n=458)</th>
<th>AVN group (n=29)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, N(%)</td>
<td>418 (91.2)</td>
<td>27 (93.10)</td>
<td>0.37</td>
</tr>
<tr>
<td>Mean age at diagnosis (years)</td>
<td>28.10</td>
<td>25.12</td>
<td>0.08</td>
</tr>
<tr>
<td>Constitutional symptoms, N(%)</td>
<td>137 (37.77)</td>
<td>18 (62.06)</td>
<td>0.10</td>
</tr>
<tr>
<td>Arthritis, N(%)</td>
<td>320 (69.86)</td>
<td>21 (72.41)</td>
<td>0.81</td>
</tr>
<tr>
<td>Malar rash, N(%)</td>
<td>154 (33.62)</td>
<td>15 (51.72)</td>
<td>0.47</td>
</tr>
<tr>
<td>CNS, N(%)</td>
<td>101 (22.05)</td>
<td>10 (34.48)</td>
<td>0.14</td>
</tr>
<tr>
<td>Myositis, N(%)</td>
<td>25 (5.45)</td>
<td>1 (3.44)</td>
<td>0.63</td>
</tr>
<tr>
<td>Serositis, N(%)</td>
<td>35 (7.64)</td>
<td>3 (11.11)</td>
<td>0.57</td>
</tr>
<tr>
<td>APS, N(%)</td>
<td>44 (9.60)</td>
<td>4 (13.79)</td>
<td>0.46</td>
</tr>
<tr>
<td>Raynaud, N(%)</td>
<td>38 (8.29)</td>
<td>4 (13.79)</td>
<td>0.30</td>
</tr>
<tr>
<td>Nephritis, N(%)</td>
<td>130 (28.32)</td>
<td>15 (51.72)</td>
<td>0.00</td>
</tr>
<tr>
<td>On dialysis, N(%)</td>
<td>13 (2.88)</td>
<td>3 (10.34)</td>
<td>0.63</td>
</tr>
<tr>
<td>Vasculitis, N(%)</td>
<td>45 (9.82)</td>
<td>5 (17.24)</td>
<td>0.20</td>
</tr>
<tr>
<td>ESR at diagnosis (mm/1st hour)</td>
<td>236 (51.52)</td>
<td>18 (62.06)</td>
<td>0.59</td>
</tr>
<tr>
<td>Anemia, N(%)</td>
<td>224 (48.90)</td>
<td>16 (55.17)</td>
<td>0.51</td>
</tr>
<tr>
<td>Leukopenia, N(%)</td>
<td>170 (37.11)</td>
<td>15 (51.72)</td>
<td>0.11</td>
</tr>
<tr>
<td>Thrombocytopenia, N(%)</td>
<td>74 (16.15)</td>
<td>9 (31.03)</td>
<td>0.04</td>
</tr>
<tr>
<td>High Anti-DNA, N(%)</td>
<td>321 (70.08)</td>
<td>24 (82.75)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

N the number of patients, CNS Central nervous system, APS Antiphospholipid antibody syndrome, Anemia Hb<12 mg/dl

Figure 1 Involved sites of AVN in 29 patients with SLE
AVN is a well-known complication of SLE. The diagnosis of AVN should be considered in any patients with SLE who has pain in one or a few joints (especially hips) if the disease is not active in other systems. The prevalence of AVN in SLE varies extensively from 2.5% to 44.44%.

**Discussion**

AVN is a well-known complication of SLE. The diagnosis of AVN should be considered in any patients with SLE who has pain in one or a few joints (especially hips) if the disease is not active in other systems. The prevalence of AVN in SLE varies extensively from 2.5% to 44.44%. The mean age of SLE onset in AVN group was 6.9%. The mean association of AVN and the duration of disease (from diagnosis of SLE to diagnosis of AVN) was 2.41±1.4 years that was much lower than Mok's study.

In SLE, AVN tends to occur at multiple sites. At the NIH, 90% of 31 cases were polyarticular, and 84% were symmetric. In 72.5% of our cases, AVN was developed in more than one site. The hip joint is the most common site of involvement, but AVN can occur in other joints. In 96.5% of our patient's ship was involved. It is generally accepted that AVN in SLE patients has an association with steroid therapy. However, AVN in SLE is more common than other clinical conditions requiring steroid therapy. Moreover, some AVN patients had no history of corticosteroid usage. SLE also has additional unique features that might predispose a patient to the development of AVN. In our study all patients with AVN had received corticosteroids. The mean total cumulative steroid dose (from diagnosis of SLE to the development of AVN) was 5470±3992.66 mg (minimum 5000mg and maximum 12000mg) that was lower than Mok's study and Faazi's study.

It has been suggested that high doses of steroids (particularly in the first year) and the duration of steroid therapy are associated with a greater risk of AVN in SLE patients. Steroid pulse therapy was not similarly associated with osteonecrosis. These dose-time relationships were confirmed in a meta-analysis (most patients without SLE) by Felson and Anderson, although this confirmation has been challenged. Some studies have shown that risk factors like butterfly malar rash, vasculitis, and Raynaud's phenomenon have a positive association with AVN in SLE patients. However, these results are controversial. Patients with these manifestations were more likely to take higher doses of steroid. In our study only nephritis and thrombocytopenia were associated with AVN. There was no significant difference between cases and controls in the other clinical manifestations. We did not find any relationship between AVN and the following conditions: Raynaud's phenomenon, malar rash, arthritis, vasculitis, central nervous system (CNS) lupus, myositis, peripheral neuropathy and DVT.

**Conclusion**

All our patients with AVN had received corticosteroids. In our study only nephritis and thrombocytopenia were associated with AVN.

**References**


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