

## **Multifocal Osteonecrosis Induced by Glucocorticoids**

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### **ABSTRACT**

Multifocal osteonecrosis is a rare entity and is defined by the involvement of at least three different territories. It mainly affects young people between the second and fifth decade of life.

We present the clinical case of a patient who presented multifocal osteonecrosis with involvement of both hips, shoulders, knees, right elbow, and neck of the left foot. The main risk factor present in this case is the consumption of glucocorticoids. It required a multidisciplinary approach for both diagnosis and treatment.

### **ARTICLE DETAILS**

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### **INTRODUCTION**

Osteonecrosis (ON), also known as aseptic necrosis or avascular necrosis, is a pathological phenomenon that causes pain and disability in patients who suffer from it.

It mainly affects people between the second and fifth decades of life.

Multifocal osteonecrosis (ONJ) is a rare and highly disabling form of presentation. It affects between 2-3% of patients with ON, and is defined as the involvement of at least 3 different territories (hips, knees, shoulders, elbows, etc.)<sup>1-2</sup>.

Ischemia and subsequent necrosis generate changes in bone architecture such as fragmentation, collapse and collapse<sup>1-2</sup>.

The etiologies can be divided into traumatic, for example the fracture of the femoral neck that causes vascular interruption, decreased blood flow and subsequent necrosis, and those of non-traumatic origin that through intravascular coagulation and adipogenesis generate thrombotic occlusion and extravascular compression. Within this last group, the consumption of glucocorticoids (GC), alcohol, autoimmune diseases, HIV infection, transplants, coagulopathies, among others, stand out.<sup>3-4</sup>

In this work, a case of ONJ in a young patient is presented, where the use of GC is identified as the main risk factor.

### **CASE PRESENTATION**

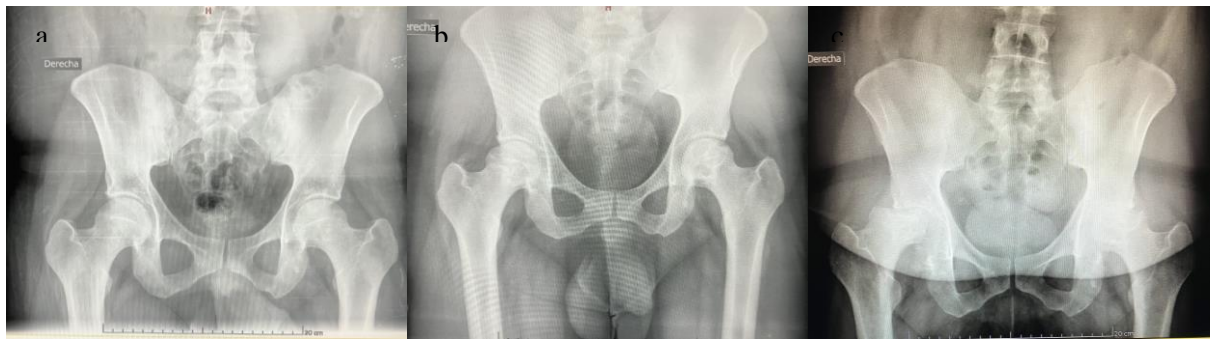
Male patient, 42 years old, nurse. Personal history of overweight, smoker, pack-year index of 5, seasonal allergy

treated with intranasal fluticasone and oral prednisone 20 mg/day as needed. Chronic low back pain due to lumbar disc protrusions and facet osteoarthritis diagnosed in 2013. He received treatment with dexamethasone and prednisone between 20 and 40 mg per day intermittently since the onset of the condition. Epidural blocks on 3 occasions with triamcinolone 1mg/k. History of bilateral coxalgia since 2015, sudden onset, rapidly progressive, mechanical and disabling, VAS (visual analogue scale) 10/10. Difficult to manage pain. During the course, he added pain in both knees, both shoulders, right elbow and left foot neck with similar characteristics.

The general examination revealed Cushing's syndrome, walking with assistance (Canadian canes), hip flexion of 80°, internal rotation 0°, external rotation 20°. At the level of both shoulders elevation of 100°, abduction 80°, external rotation 30° and internal rotation of 0°, not passively improving the range. No neurological or distal vascular involvement.

Pelvic X-rays in 2015 do not show alterations in the bone morphostructure. In 2016, radiolucent images appear surrounded by bilateral epiphyseal sclerotic areas, with loss of normal sphericity of the right hip. Lastly, in 2017, both hips are affected, with epiphyseal subsidence predominating, collapse and alteration of the sphericity of the femoral head as well as loss of joint lumen.

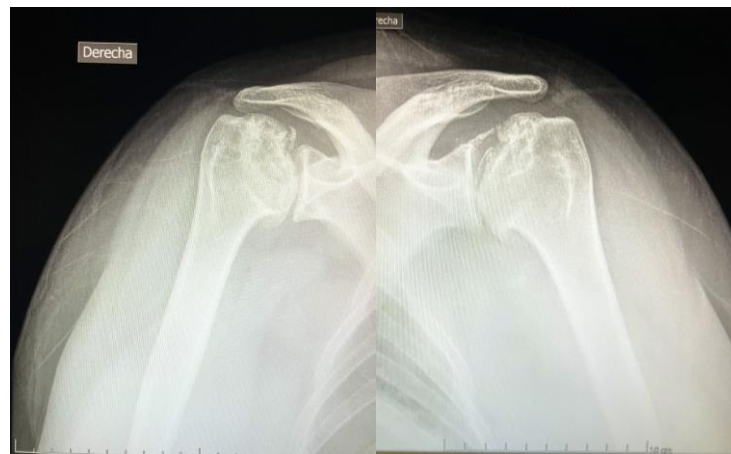
## Multifocal Osteonecrosis Induced by Glucocorticoids



**Figure 1: Anteroposterior radiographs of the pelvis in successive years. a) 2015, b) 2016 and c) 2017.**

You can see the rapid evolution of the disease in the femoral head, going from stage I of the Ficat and Arlet classifications in 2015, to stage II/III in 2016 and ending in stage IV in 2017.

In the shoulder x-rays we observed great fragmentation of both epiphyses with loss of normal morphology and secondary degenerative changes. Figure 2.



**Figure 2. Anteroposterior radiographs of both shoulders.**

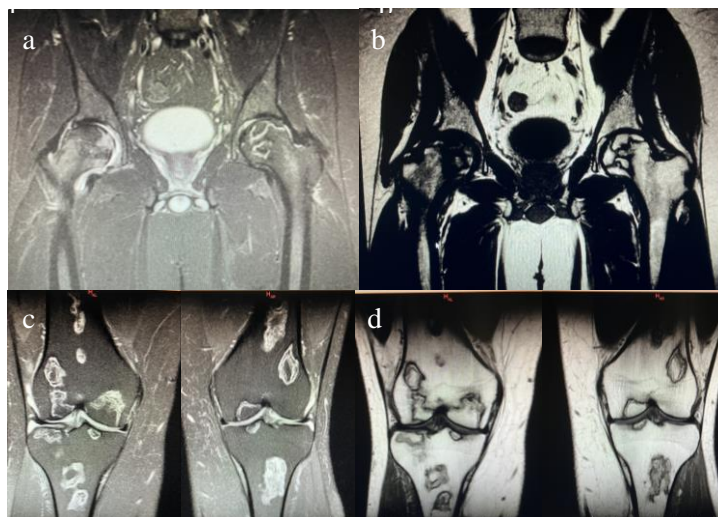
The x-rays of both knees show alterations in the bone structure, where areas of greater radiolucency are evident at the level of both femoral epiphyses surrounded by sclerotic areas. Both at the level of the right elbow and the neck of the left foot, the radiographs obtained showed no alterations. Magnetic resonance imaging (MRI) of the pelvis and both knees shows typical signs of ON. MRI of the pelvis shows at the level of the right hip an area of altered signal intensity of the subchondral bone, with the classic crescent sign with loss of normal sphericity of the femoral head, suggestive of subchondral fracture. At the level of the left hip, areas of loss

of signal intensity of the subchondral bone are also observed, with the double line sign.

At the level of the knees, medullary and subchondral lesions are observed in the distal portion of the femur and proximal portion of the tibia bilaterally as focal, serpiginous images with heterogeneous signal with a halo of high central signal. Images compatible with bone infarcts. Figure 3.

Lesions similar to those found in the knees can be observed at the level of the lower epiphysis of the left tibia and the upper epiphysis of the right radius.

## Multifocal Osteonecrosis Induced by Glucocorticoids



**Figure 3. MRI of the pelvis and knees. Stir coronal pelvis (a), T1 coronal pelvis (b), Stir coronal knees (c) and T1 coronal knees (d).**

Given the clinical characteristics and imaging findings, ONM is proposed. Congenital and acquired prothrombotic factors were requested (antithrombin III, Leiden factor V, protein C and S mutation, and antiphospholipid antibodies), which were negative. ANA negative. Non-reactive HIV serology.

Joint replacement is decided in those joints with greater pain and disability, which cannot be controlled with analgesia. In 2017, a hybrid total hip prosthesis was performed on both hips, improving pain and function. In 2021 anatomical right shoulder prosthesis with identical results.

Corticosteroid treatment was suspended with gradual tapering. In the evolution, good pain control with established surgical treatment, non-steroidal anti-inflammatories and rescue opiates.

### DISCUSSION

ONJ is an aggressive and rare form of presentation of ON, and although there is no exact cause, multiple factors are associated that may be involved.

As can be seen from the clinical history, the main risk factor that we found is the prolonged consumption of GC at high doses and multiple routes of administration. Several authors demonstrated the relationship between GC and ON, especially the appearance of new areas of necrosis in patients with already established disease. There is ample evidence of the relationship between GC consumption and ON, with few cases presenting as ONJ.

Krez et al. (2021)<sup>5</sup> in a prospective study where they evaluated patients who already suffered from ON, were able to conclude that GCs administered orally at maximum cumulative doses are the main risk factor for the appearance of new areas of bone necrosis. They also showed that certain conditions such as systemic lupus erythematosus (SLE) and certain hematological diseases increased the risk of ONJ.

These findings reinforce what was demonstrated by Zhang et al. (2008)<sup>6</sup> and Flouzat-Lachaniette et al. (2015)<sup>7</sup> who had already demonstrated that the main risk factor linked to GCs occurs when they are administered at maximum doses for prolonged periods. As mentioned in the previously analyzed works, we talk about high or maximum doses of GC for prolonged periods of time without defining an exact dose.

LaPorte et al (1998)<sup>8</sup> studied the longest series of patients with ONJ where it was highlighted that 100% had bilateral involvement of the femoral heads, and more than 95% presented bilateral osteonecrosis of the knees and shoulders. Regarding the distribution of ON areas, our patient follows the same pattern as demonstrated by the aforementioned authors, with hips, knees and shoulders being affected bilaterally as well as the left foot neck and right elbow.

As mentioned above, ONJ is an unusual and disabling form of presentation, and in the case of our patient the diagnosis was reached in a period of less than 5 years from the beginning of the symptoms, the evolutionary time coinciding with the aforementioned articles. The main risk factor recognized in our patient is the prolonged consumption of GC, however, as we see in the clinical history, given the extension, other non-traumatic etiologies (systemic autoimmune diseases, coagulopathies, alcohol consumption, HIV infection) were assessed clinically and paraclinically. We consider this fact important since they can often occur isolated or associated with GC consumption.<sup>9-13</sup>

Glucocorticoids are drugs increasingly used in daily medical practice and over-the-counter in our country, whose complications we believe are increasingly frequent and increasing. We are familiar with the most frequent complications such as diabetes mellitus, high blood pressure, Cushing's, infections and even osteoporosis. It seems important to present this case as another less frequent but no less serious complication associated with its consumption,

## Multifocal Osteonecrosis Induced by Glucocorticoids

being a pathology that generates pain and Functional impotence clearly affected the quality of life of patients. Once the diagnosis of ON, probably linked to GC consumption, has been made, it should be suspended and closely monitored for the possible appearance of new lesions or other complications in order to act early. As well as raising awareness in the health system and population about using them in the lowest doses and for the shortest possible time.

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