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Review Article

Transient Osteoporosis of the Hip: State of the Art and Review of Literature

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Abstract

Transient osteoporosis of the hip (TOH) is a rare condition that causes sudden pain related to bone marrow edema of the hip. It is a benign disease and usually has a self-limiting course and resolution. Orthopedic literature on this topic is poor and no guidelines or algorithm has been proposed yet. TOH remains a poorly understood topic which happens to be often clinically underestimated. This paper aims to provide an up to date of the current knowledge through a literature revision. Info about TOH from etiology to treatment have been collected in order to guide the orthopedic surgeons among the clinical presentations and the best combination of therapies.

Keywords: Transient osteoporosis; Bone marrow edema; Hip; Femoral head; Osteoporosis; Avascular necrosis

1. Introduction

Transient osteoporosis of the hip (TOH) is generally a benign and self-limiting disorder resulting in bone marrow edema of the hip. It has been described with different names along with the years, but it remains poorly understood and often clinically underestimated. For the first time in 1959, Curtiss and Kincaid reported three cases of unilateral or bilateral hip/thigh pain with radiological signals of hip demineralization in the third trimester of pregnancy with a complete restoration to normal after delivery [1]. In 1988 TOH was first described by Wilson with the term "Transient Marrow Edema Syndrome". Those patients had normal bone or osteopenic values at bone densitometry (DXA) and presented a regional decrease in signal intensity of the bone marrow on T1-weighted scans, and increased signal intensity on T2-weighted scans on MRI [2]. Eventually, in 1993 Solomon introduced the concept of bone marrow edema with or without osteonecrosis explaining how the first one is associated with bone collapse and requires surgery, the second one is transient and self-limiting [3].

Even though the concern about bone marrow edema disorders has progressively increased over the last decade, literature is poor and consists in studies on small groups of patients. In this review, an overview of current knowledge of management and treatment of TOH is presented. Due to the lack of consensus regarding classification, treatments and outcome scores, it is hard to establish applicable guidelines or algorithms. With this work, we aim to provide an up-to-date knowledge that may guide the orthopedic surgeons among the variety of clinical presentations and best combination of therapies. A literature search of PubMed, Embase, and the Cochrane Review system was performed. Search terms were "transient osteoporosis of the hip". A total of 351 studies were obtained in the initial search. Filters were added to restrict the search to studies on humans (305 studies), which were published between January 2003 and June 2019 (151 studies) and whose full text was in one of the following languages: English, Italian, French, Spanish and Portuguese. This reduced the studies' number to 142. The articles were then excluded if they were opinion articles or technique descriptions. Studies focused on other anatomical segments were also excluded. No guidelines were found and almost half of the articles (68) were case reports or small case series. With those criteria, 10 out of 43 reviews and systematic reviews were considered, while all 15 clinical trials were excluded. 10 articles found from other sources were also considered.

2. Epidemiology and Etiology

Transient osteoporosis of the hip has multifactorial etiology and usually has two presentations: it may affect middle-aged men (4^{th} and 5^{th} decade) or it may be present in the last trimester of pregnancy in women [4, 5]. Whether it is normally bilateral in pregnancy, it is most often seen as unilateral in the other presentation. In most cases no triggering events are detected, but theoretically any insult such as previous trauma (including fracture, altered biomechanics, bone edema, subchondral lesions), osteoarthritis, inflammatory diseases (i.e., arthropathies, enthesopathies, gout), vascular lesions (i.e., avascular necrosis, algoneurodystrophy), infective lesions (viral, diabetic foot, osteomyelitis), iatrogen lesions (previous surgery or radiotherapy), neoplastic lesions and other variables (alcoholic consumption, smoking, steroids, hypothyroidism, low testosterone, low vitamin D, osteogenesis imperfecta, pregnancy or breastfeeding) may determine a condition of transient bone edema of the hip [6-10]. Etiology has not clearly been defined so far, but one of the most advocated theories suggested a malfunctioning of the venous drainage of the femoral head as the cause of TOH. This has been supported by angiographic, scintigraphic and Magnetic resonance imaging (MRI) studies that claim an increased perfusion of the affected area as possible cause of ischemic episodes. Whether pathological mechanisms beyond TOH are still unclear, bone specimens from patients going towards core decompression were analyzed: they show diffuse edema of the marrow, angiogenesis and fat cell fragmentation. Moreover, there is no sign of an osteoclastic hyperactivation, but a reduction of hydroxyapatite content in osteoid covering the trabeculae [11-14].

3. Clinical Presentation and Imaging

Clinical presentation is variable, but it is described as a sudden onset of dull pain located in the groin region, buttocks and anterior thigh. The pain may be more severe than osteonecrosis, usually it is worse at night and on weight-bearing. Often a whole range of motion of the hip is preserved. Historically, it follows three steps as

Schapira [15] has described: a sudden onset of pain with antalgic limping that lasts for a month, then a phase of no progression of symptoms that lasts a couple of months and eventually the phase of pain resolution. TOH is usually self-limiting and lasting between 4 and 24 months. Although progression to avascular osteonecrosis (AVN) is a rare occurrence, it has been described in the literature [16-18].

X-rays at onset are often negative and they may only show evidence of this condition after three to six weeks. The radiographic sign is an osteopenia of the femoral head. MRI is the gold standard to diagnose TOH. It may detect areas of bone edema which shows intermediate signal on T1-weighted images and high-signal on T2-weighted and Short-tau inversion recovery (STIR) images. Edema is located at the femoral head and intertrochanteric zone, and it normally has a homogeneous pattern without well-defined borders or focal defects. MRI may also detect possible subchondral fractures, while the absence of subchondral changes on contrasted sequences is crucial for the diagnosis. Some authors report that MRI can detect TOH at 48 hours after the onset of symptoms. In 2004, Malizos et al. demonstrated the absence of correlation between the size of edema and the duration of symptoms. In this study, hips without subchondral bone lesions showed a faster clinical recovery. Nonetheless, MRI also helps ruling out other similar conditions such as AVN, stress fractures, infection and neoplasms [5, 10, 19-23]. A bone scan is usually positive, but has low specificity. Computed tomography (CT) is not indicated as a standard exam.

4. Differential Diagnosis

AVN is the first condition to rule out as it has a similar clinical onset and could be radiographically similar. MRI can distinguish between them: AVN images show subchondral radiolucency (crescent sign), single line sign with edema with on T1 images, double line sign (an outer band of low signal associated with an inner band of high signal) with edema on T2 images and may reveal femoral head deformity. When adding contrast, images may show filling defects, alteration of signal of subchondral areas and focal deformity. However, a study conducted by Hofmann compared patients with TOH with an AVN control group: the first group showed a statistically significant tendency to acetabular retroversion and asphericity of the femoral head-neck junction compared to controls.

Nevertheless, the main edematous lesion seems to be most frequently located in the superior portion of the femoral head [24, 25]. MRI also detects stress fractures and in both AVN and TOH, being the signal of a filling defect and fracture line in the former and an irregular low signal band in TOH [24]. Infections and tumor/tumor-like conditions can be excluded by both clinical and imaging findings. TOH could mimic enchondromas on radiographs, being an area of radiolucency but it lacks central calcification [26]. Even if histology of TOH was previously discussed, a biopsy is not needed.

5. Treatment and Complications

TOH is a self-limiting disease, but the duration of symptoms and the time needed to fully recover are variable. Often, microfractures and bone marrow edema resolve when the primary insult is removed. A symptomatic and supportive treatment is recommended [27]. The aim of the treatment is to suppress bone resorption in order to avoid

further complications, but no consensus has been reached on which type of treatments, on its timing and duration [28-38].

Conservative therapy, including non-weight bearing/minimizing weight-bearing activities, uses of crutches, physiotherapy and non-steroid anti-inflammatory drugs (NSAIDs) is commonly recommended [4, 10, 27]. Medical treatment with bisphosphonate is generally indicated to minimize bone resorption. Emad et al. [33] propose therapy with weekly dose of alendronate 70 mg/week for 6 months and calcium carbonate (600 mg/day) and vitamin D (300 IU/day) supplementation along with conservative treatment. Aledronate is supported by some studies [33, 34], like clodronate [35] and ibandronate [36]. Single dose of zoledronate [28] was also described as effective, recently. However, studies carried out using bisphosphonates are weak and mostly retrospective. Calcitonin does not cross the placenta and appears to be safe during pregnancy: it showed reduction of duration of symptoms in several studies [37, 38]. On the contrary bisphosphonate may lead to fetal skeletal mineralization defects therefore is not recommended. Also 20 μg/day of teriparatide (bioactive portion of the parathyroid hormone) has been proposed for 4 weeks but more evidence is needed to suggest this therapy [32].

In a recent study, extracorporeal shock wave therapy alone was effective in TOH leading to satisfactory clinical results at Harris Hip Score and reduction of mean edema at MRI in a cohort of 22 patients [30]. Other authors proposed pulsated electromagnetic fields (PEMF) as capable of reducing edema and stopping osteonecrosis even in early stage of AVN [39, 40]. Yagishita et al. showed good results in reduction of edema in patients treated with hyperbaric oxygen therapy, but they recommend reserving it for unclear differential diagnosis between AVN and TOH since it does not significantly accelerate recovery in TOH [29]. Even if several authors have proposed core decompression [16, 18, 41], surgical procedures are generally not recommended.

Subchondral, femoral neck and subcapital fractures are rare complications in TOH and they more often occur in patients with osteogenesis imperfecta or during pregnancy due to biomechanical and metabolic changes (including calcium homeostasis and parathyroid hormone regulation) [42, 43]. Even if bone edema raises after osteonecrosis in AVN, several cases of progression from TOH have been described in literature. Thus, it is to be considered another rare complication, but care must be taken to avoid late diagnosis [10].

6. Conclusion

Transient osteoporosis of the hip usually presents with an acute onset of symptoms. An aspecific insulting agent may cause microfractures and vascular alterations that lead to bone marrow edema with separation of bone trabeculae and decreased amount of hydroxyapatite. MRI is essential for the diagnosis, distinguishing TOH from AVN and it is useful for follow-ups. Correct diagnosis reassures the patients and it avoids useless surgical treatments such as core decompression or hip arthroplasty. Treatment is still controversial, but a combined therapy tailored to the patient is most commonly prescribed. Since pregnant women are at risk for fractures, calcitonin should be considered to prevent such complication. Since the actual literature about TOH is poor and weak, further

investigation and randomized clinical trial will be needed to assess the best treatment for symptom relief, quick recovery and minimization of complications.

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