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Coxofemoral Arthritis Caused by Mycobacterium Bovis after Bacillus Calmette-Guérin Therapy

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Abstract

Introduction: Intravesical therapy with bacillus calmette guérin (BCG) has proved to be effective in the treatment of superficial bladder tumors. BCG therapy is generally well tolerated, the osteo-articular adverse effects, occurring in approximately 0, 5 to 1% of patients.

Observation: We report the case of a 58-year-old man who presented with coxo-femoral arthritis after intra vesical BCG therapy performed 8 month earlier. The outcome was favorable following adapted antibiotic course.

Conclusion: Coxo-femoral arthritis is a rare complication of BCG therapy and diagnosis is often difficult to establish. This severe complication must be evoked in front of articular symptoms in patients treated with intra-vesical BCG therapy.

Keywords

BCG therapy, Arthritis, Mycobacterium bovis

Introduction

BCG therapy is the standard treatment for superficial bladder tumors. However, this treatment is not devoid of local and systemic side effects such as flu-like symptoms, liver granulomatosis, damage of both the gastrointestinal and the urinary tracts and bone lesions.

Rheumatological complications such as arthralgia, reactive arthritis and osteoarticular infections, although rare, were reported after BCG therapy [1].

Observation

We report the case of a 58 year-old male patient, heavy smoker (20 packs/year), not vaccinated with BCG, followed for superficial bladder tumor and treated with 6 instillations of BCG.

Eight months after the last instillation, the patient began to complain of pain in the right hip in a context of impaired general condition. This pain was of mechanical type without special radiation, but responsible for lameness. The clinical examination revealed a pelvic asymmetry with unequal legs. The usual blood tests showed normocytic normochromic anemia with a 10 g/dl Hb, normal leukocyte count, 30 mm erythrocyte sedimentation rate (ESR) in the first hour and a 25 mg/l CRP. Renal and hepatic biological assessments were normal. The tuberculin skin test was positive at 10 mm and HIV status was negative. Right hip and pelvis radiographs showed a narrowing coxo-femoral joint space with demineralization and geodes of the femoral head (Figure 1).

Pelvic CT scan showed an asymmetric basin, with the loss of the right femoral head sphericity and ankylosis of the coxo-femoral space with infiltration of the periarticular soft tissue (Figure 2). The search for germs in the joint fluid was negative on direct examination and the histological study of the synovial performed after a CT guided biopsy showed an epitheloid giant cell granuloma with caseous necrosis suggestive of coxo-femoral tuberculosis (Figure 3). Chest X-ray showed no abnormality and Koch bacillus research

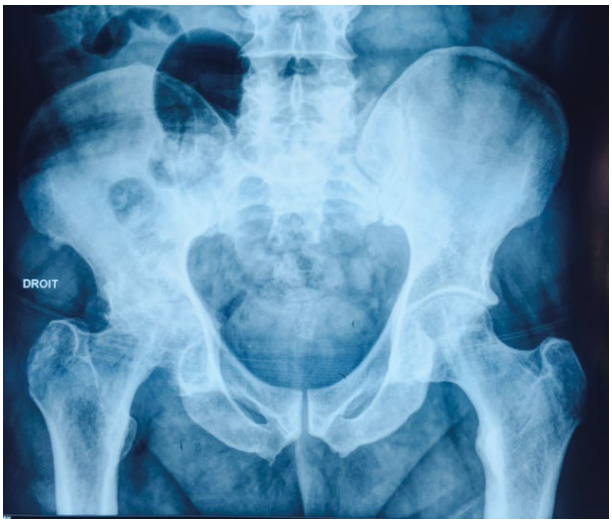

Figure 1: Pelvis radiographs showed a narrowing coxo-femoral joint space with demineralization and geodes of the femoral head.

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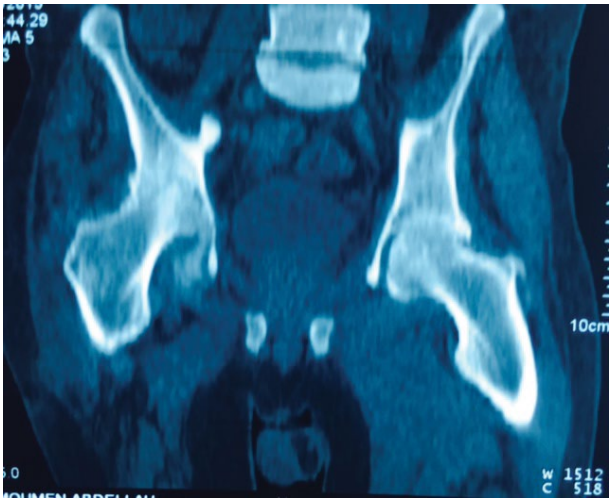

Figure 2: Pelvic CT scan showed an asymmetric basin, with the loss of the right femoral head sphericity and ankylosis of the coxo-femoral space.

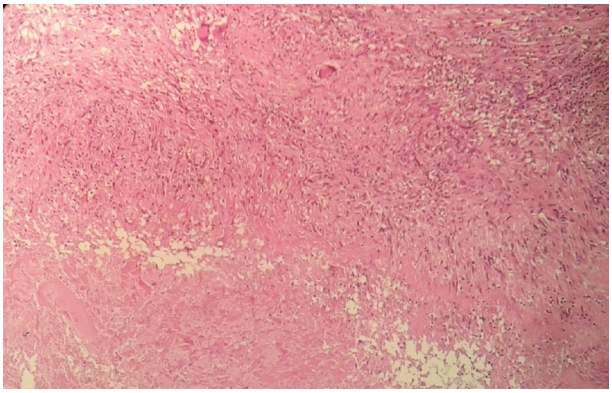

Figure 3: Photomicrograph of specimen showing epitheloid with Langhans giant cells and central caseous acellular necrosis. Hematoxylin-eosin staining × 250.

in sputum and urine was negative on direct examination. Culture of joint fluid showed smooth, whitish, small colonies (1-2 mm) of bacilli resistant to pyrazinamide which is evocative of Mycobacterium bovis. The patient received anti-tuberculous regimen with rifampicin, isoniazid and ethambutol for 2 months, then isoniazid and rifampicin combination for 10 months with good clinical and radiological evolution.

Discussion

The Bacillus Calmette Guerin (BCG) is a mycobacterium (Mycobacterium bovis) attenuated by successive passages on a culture medium. Besides its use as a vaccine for Tuberculosis, the BCG intravesical instillation is the reference treatment of high and intermediate risk superficial bladder cancer [2,3]. However, this treatment is not devoid of local or systemic complications such as flu-like symptoms, liver and lung granulomatosis, lesions of the gastrointestinal tract (ulcerative terminal ileitis and Crohn-like disease), lesions of the genito-urinary tract (prostatitis), bone lesions (osteomyelitis) and joint lesions [4-7]. Mycobacterium bovis infectious complications can be observed after intravesical BCG therapy or intradermal vaccination [1]. Arthritis after intravesical BCG therapy in literature is rare; only eight cases were reported [1]. The pathophysiologic mechanism is not yet well understood, but it seems that the granulomatous infection and systemic manifestations related to infection with BCG involve both direct infection and hypersensitivity reactions.

The positivity of mycobacterium cultures of samples take late after the BCG treatment is very evocative of a spread of the infection [8]. Several factors are involved in the mechanism of blood-borne dissemination of the musculoskeletal Mycobacterium bovis infection: bladder trauma, including recent endoscopic resection, cystitis and repeated instillations [9].

The time between instillations and systemic manifestations varies widely, from days to several years. The early symptoms usually concern lungs, liver, and joints [9]. The musculoskeletal Mycobacterium bovis infection typically affects a single joint, and preferentially the bearing big ones such as hips and knees, as is the case of our patient. After the responsible instillation, infection usually occurs later than aseptic bone and joint complications [1]. It typically achieves a subacute or chronic arthritis, moving towards the gradual worsening in several weeks or months. Pain, swelling, stiffness and functional impairment are the usual signs. General symptoms are inconstant, usually of moderate importance, and combine variably asthenia, anorexia, weight loss, night sweats and low-grade fever.

The blood tests such as ESR and CRP have little diagnostic value. The skin tuberculin test is of little interest. Radiologically, the association of demineralization, bone cysts and joint space narrowing is an evocative triad.

Ultrasound allows diagnosis of joint effusion and guides diagnostic punctures. CT is more sensitive than radiographs to search for small erosions or bone sequesters.

MRI is the gold standard for early diagnosis of bone lesions because it identifies the incipient damage of cartilage and synovium [10]. In the majority of cases, the diagnosis of coxitis is made at a late stage (stage III or IV X-ray).

At a very late stage; we can see a hip dislocation and acetabular protrusion. However, imaging is never pathognomonic and histological and/or bacteriological confirmation remains indispensable. In front of a monoarthritis after intravesical instillation, the differential diagnosis arises with pyogenic germs infections with reactive arthritis.

Before discussing the diagnosis of reactive arthritis-which usually responds to NSAIDs- Mycobacterium bovis septic arthritis should be formally eliminated by joint aspiration [11]. It is essential to clearly distinguish between strains of M. Bovis from those of M. Tuberculosis to make the difference between a BCG reaction and M. Tuberculosis infection. Extra-pulmonary locations of mycobacteria are pauci bacillary and culture remains the reference method in the diagnosis and determination of antibiotic susceptibility of isolates. Colonies of M. Bovis have a 3-6 weeks slow growth on Löwenstein- Jensen solid medium.

They appear flat, small (1 to 2 mm), smooth, white and shiny. The Polymerase Chain Reaction (PCR) new diagnostic methods allows the rapid highlighting of Mycobacterium in an average of 48-72 hours, and quickly identify the different species in the Mycobacterium Tuberculosis complex [12,13]. In our case, the identification of M. Bovis was performed after culture on Löwenstein- Jensen solid medium and phenotypic study.

Bone and joint infections complicating BCG therapy should be treated with rifampicin, isoniazid and ethambutol for two months, followed by rifampicin and isoniazid for ten more months [1]. Pyrazinamide should not be used because all M. Bovis strains are resistant to it. The evolution and articular prognosis is generally favorable in the forms treated early.

The effectiveness of these medical treatments significantly reduced surgical indications. To reduce the risk of spread through blood, it is now recommended not to practice the first BCG instillation sooner than two to three weeks after transurethral bladder resection or biopsy.

Conclusion

Bone and joint infections and hypersensitivity reactions secondary to intravesical BCG therapy are rare, but well recognized. These complications can sometimes occur months or years after completion of treatment. In front of any suspicion of mycobacterial osteoarticular infection, appropriate therapeutic measures must be taken without delay to prevent adverse developments and the occurrence of sequelae.

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