Septic arthritis due to *Streptococcus bovis* in a patient with liver cirrhosis due to hepatitis C virus – case report and literature review

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ABSTRACT

Monoarthritis remains a diagnostic challenge in Rheumatology and Orthopedics. The author reports a case of septic arthritis due to *Streptococcus bovis* after several episodes of joint effusion treated with hyaluronic acid (Hylan G-F 20) and methylprednisolone acetate in a 69-year-old patient with liver cirrhosis due to hepatitis C virus. Neither adenoma of the colon nor endocarditis was present. The diagnostic possibilities for this case of monoarthritis, the pathologies related to the microorganism of interest to the rheumatologist, and the possible involvement of joint reaction to hyaluronic acid as a predisposing factor to joint effusion are discussed.

Keywords: septic arthritis, *Streptococcus bovis*, hepatitis C, liver cirrhosis, hyaluronic acid.

INTRODUCTION

Pain accompanied by inflammatory signs and effusion in a single joint usually leads to the practice of arthrocentesis and joint infiltration with no previous definition of the cause of monoarthritis. In addition to causing complications and hindering the treatment, this procedure interferes with the etiological diagnosis.

Despite the advance of diagnostic methods in rheumatology, defining the cause of monoarthritis remains one of the major challenges in the specialty. Diagnostic conclusion almost always depends on the evolution and emergence of other signs and symptoms, especially when the synovial fluid is not adequately assessed.

Septic arthritis should always be considered as a differential diagnosis of monoarthritis, especially when the patient belongs to a predisposing age group, has preexisting joint disease and comorbidities that favor joint contamination.

We report one case of septic arthritis of the knee due to *Streptococcus bovis* (*S. bovis*) with symptomatic degenerative changes, non-responsive to treatment after multiple arthrocenteses and infiltrations with hyaluronic acid and corticosteroids. The patient had cirrhosis secondary to hepatitis C infection.

CASE REPORT

The patient is a 69-year-old male with liver cirrhosis and previous hepatitis C infection acquired after transfusion, with no other comorbidities. He reported pain and swelling of acute onset in the left knee for three months, and was submitted to arthrocentesis, which drained a large amount of clear fluid. Five days after the arthrocentesis, as the swelling recurred, the patient looked for an orthopedist who diagnosed osteoarthritis of the knee and administered hyaluronic acid (Hylan G-F 20). Relative improvement was obtained for a few days. However, after 15 days, the joint effusion recurred, and the patient

Received on 08/03/2010. Approved on 07/01/2011. Author declares no conflicts of interest.
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Figure 1
Knee monoarthritis with inflammatory signs.

underwent the third arthrocentesis with no product administration. Magnetic resonance imaging was performed and showed tricompartmental degenerative changes, insertional tendinosis, and thickening of the anterior cruciate ligament.

After five days, a new joint effusion was observed, and the patient underwent the fourth arthrocentesis and second hyaluronic acid injection. After three weeks and four arthrocenteses, the patient went to another orthopedist who performed another arthrocentesis with depot corticosteroid injection and indicated rheumatological assessment.

Rheumatological assessment occurred three days after corticosteroid injection, and the left knee examination showed increased volume, limitation of 90° flexion, mild inflammatory signs, and a small volume of joint effusion. The complementary exams confirmed mild inflammatory manifestations and laboratory changes compatible with chronic hepatitis.

The findings of digital radiographies of the shoulder, hand, wrist, and knee joints were compatible with osteoarthritis of the hands and knees, with tricompartmental degenerative lesions and no calcifications. On his follow-up visit, the patient reported worsening of the swelling present in the previous visit, but with neither pain nor other clinical manifestation. The patient was then submitted to arthrocentesis, and the synovial fluid drained (30 mL) had an aspect compatible with class II, showing 39,000 cells/mm³ (87% of polymorphonuclear leukocytes, 8% of lymphocytes, and 5% of monocytes) and no crystals. Both bacterioscopy and culture were negative. His full blood count was as follows: hemoglobin, 13.7 g%; hematocrit, 40.6; 3,900 white blood cells (50% of neutrophils, 5.5% of eosinophils, 0.9% of basophils, 36.9% of lymphocytes, 6.7% of monocytes); and 113,000 platelets. The erythrocyte sedimentation rate was 23 mm in the first hour, and C-reactive protein was negative.

The joint effusion recurred 24 hours after arthrocentesis, in a large amount and painfully, accompanied by exuberant inflammatory signs (redness and heat) and 38.4°C fever (Figure 1). The arthrocentesis drained 60 mL of synovial fluid, with a class III aspect, low viscosity, suggesting an infectious process. The clinical diagnosis was septic arthritis. The patient was admitted to the hospital and treated with intravenous antibiotic therapy consisting of ceftriaxone 2 g associated with oxacillin 2.0 g daily. During hospitalization, the patient underwent three other arthrocenteses and one joint lavage with saline solution. The culture of the first sample prior to introduction of antibiotic therapy identified *S. bovis.* Then the patient underwent echocardiography, whose result was within the normal range with no vegetations. Carcinoembryonic antigen (CEA) was 1.6 ng/mL, and digestive tract endoscopy (high and low) showed no changes suggestive of malignant disease or even polyps.

After treating for 10 days, the non-painful joint swelling persisted, and the ultrasound showed increased volume due to the presence of anechoic effusion with thin septations and thick echoic material.

The antibiotics were maintained for two weeks with the patient hospitalized. Because of persistent residual synovitis with no sign of joint effusion, antibiotic therapy was continued for another 10 days at home. Fifteen days after hospital discharge, the patient returned to consultation neither with limitation of motion nor inflammatory signs.

DISCUSSION

In the presence of monoarthritis, it is fundamental to perform a complete anamnesis, comprising patient's habits, cutaneous involvement and history of genitourinary and digestive complaints, and occurrence of comorbidities. Previous history of joint and spine involvement should be detailed. The differential diagnosis of monoarthritis includes the following: psoriatic arthritis, spondyloarthropathies with and without intestinal manifestations, crystal deposition diseases, septic arthritis, and primary or secondary degenerative diseases.

In the elderly, knee inflammation crises with a large collection of joint fluid and radiologic diagnosis of osteoarthritis are typical of patients with pyrophosphate deposition disease. However, to confirm this diagnosis, weakly birefringent

crystals need to be identified in synovial fluid, which is not always easy due to refringence characteristic of this crystal. The fact that no crystal was found in the patient's synovial fluid does not exclude the possibility of pseudogout, although the lack of suggestive radiological signs made this hypothesis less likely. Similarly, considering the peculiarities of gout in the elderly, this diagnosis could have also been considered and would have been confirmed by the finding of monosodium urate crystals in synovial fluid.

The hypothesis of side effects due to hyaluronic acid (Hylan G-F 20) was also considered, especially because joint infiltrations were performed in the presence of joint effusion. Although considered safe, this drug can cause pain and swelling of the affected joint, reactions usually described as mild and that disappear spontaneously or with local therapy. However, such reactions can persist for up to three weeks, often requiring aspiration and corticosteroid infiltration. The differential diagnosis of septic arthritis should always be considered.

The incidence of septic arthritis caused by intra-articular infiltrations is estimated as one case for every 17,000 to 50,000 infiltrations, and can be subacute or insidious, occurring from weeks to three months after the procedure, being more frequent in patients with previous joint disease.

Staphylococcus aureus is the most commonly found bacterium in adult septic arthrites, both in the primary form and in that following trauma or intra-articular injections. Septic arthritis, due to its potential morbidity and mortality estimated as 11%,[1] requires rapid diagnosis and treatment. Thus, antibiotic therapy should be initiated upon clinical suspicion. In the present case, management consisted of prescribing antibiotics that act on that bacterium and on other potential causative agents, such as gram-negative pathogens and opportunistic microorganisms, even before knowing the result of the culture. In addition, our patient had, as an aggravating factor, liver cirrhosis, which is a debilitating disease.

S. bovis is the most frequent enterococcus of group D streptococci, being classified as types I and II. Type I, the most virulent, is more associated with endocarditis (94%) and colon carcinoma (71%), while type II is associated with these complications at the frequencies of 18% and 17%, respectively. Less common infections caused by *S. bovis* include meningitis, neonatal septicemia, spontaneous peritonitis, vertebral osteomyelitis, and septic arthritis with, however, no particular characteristics.

S. bovis is a frequent cause of endocarditis and has been related to intestinal diseases, mainly colon carcinoma,[2,3] although it has also been associated with other neoplasias of the digestive system and even non-malignant diseases, such as cholangitis, polyps, and intestinal inflammatory diseases. The reason for this association has not been well defined, although there are several theories. The microorganism, as well as its 12 protein antigens, has been suggested to be carcinogenic by itself,[4] causing the progression of an existing pre-neoplastic lesion[5] by triggering an inflammatory response, and cell proliferation and transformation.[6] In addition, it is frequently associated with chronic liver disease or cirrhosis.[7,8] The portal of entry for *S. bovis* may be the gastrointestinal, urinary, and biliary tracts, and oropharynx.

Finding *S. bovis* in synovial fluid culture requires excluding the occurrence of other possible comorbidities, such as neoplastic lesions of the digestive tract, and bacterial endocarditis. The association with chronic liver diseases or cirrhosis contributes to increased mortality rate.[9]

Joint infections due to *S. bovis* are rare, and, as in the case here reported, the patients described by Grant,[10] Marín,[11] and Calderón[12] have developed neither endocarditis nor concomitant neoplasias. A fourth case has been described[13] with no endocardial involvement, but associated with sigmoid carcinoma, and two others of late infection following knee arthroplasty associated with ascending colon[14] and sigmoid[15] carcinoma. A fifth case with no endocarditis and/or colon carcinoma has been reported in a 76-year-old patient who underwent knee arthroplasty four months before, and was using prednisone, 50 mg/day, for treating multiple myeloma.[16]

Vertebral osteomyelitis associated with colon polyps and *S. bovis* bacteremia has also been reported.[17] In Brazil, Genta et al.[18] have reported one case of *S. bovis* bacteremia with endocarditis, colon adenocarcinoma, splenic abscess, and spondylodiscitis.

In a review using MEDLINE and the LILACS and SciELO databases, no description of joint involvement by that bacterium was found. This was the first case of septic arthritis of the knee by *S. bovis* with neither endocarditis nor association with intestinal neoplasia reported among us.

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