

Bacillus Calmette-Guerin induced reactive arthritis: A case report

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Özet

Mesane içine Bacillus Calmette-Guerin uygulanması sonrası gelişen reaktif artrit: Bir olgu sunumu

Bacillus Calmette-Guerin (BCG) uygulaması süperfişiyal mesane karsinomlarında kullanılan etkin bir tedavi metodudur. Bu tedavi sırasında nadiren reaktif olarak artrit ve artraljiler gelişebilmektedir. Burada, mesaneye dördüncü BCG uygulamasından bir hafta sonra oligoartrit kliniği gelişen 65 yaşındaki bir erkek hasta sunulmaktadır. El bileği, diz ve ayak bileği eklemlerinde asimetric artrit ile başvuran hastada HLA-B27 testi negatif idi. Üç ay süreli indometazin ve izoniazid kombinasyonu tedavisi sonrası tüm semptomlar kayboldu, akut faz reaktanları normal değerlere indi. Bir yıl takibi sonrasında bile hasta eklemler açısından asemptomatik idi.

Anahtar Kelimeler: Bacillus Calmette-Guerin (BCG), Reaktif artrit, HLA-B27

Abstract

Intravesical administration of Calmette-Guerin (BCG) bacillus is well known to be effective in the treatment of superficial bladder carcinoma. Arthritis and arthralgia are among the rare side effects of this treatment. Here, we present a 65-year-old male developing oligoarthritis one week after the fourth instillation of BCG. Wrist, knee and ankle joints were involved asymmetrically. He was HLA-B27 negative. He responded well to indomethacin and isoniazide treatment. After 3 months, all symptoms disappeared and laboratory results returned to normal. One year later the patient is still asymptomatic.

Keywords: Bacillus Calmette-Guerin (BCG), Reactive arthritis, HLA-B27

Introduction

In several malignant conditions BCG has been used as an immunostimulating agent (1). It is commonly used intravesically for the superficial bladder cancer, especially in the stage of carcinoma in situ. BCG induced reactive arthritis is a rare entity, with arthralgias occurring in 1 to 5 % and arthritis in 0.5 to 1 % of the BCG administered patients (2,3). The patients are seronegative for RF and ANA. However, the patients developing arthritis following BCG immunotherapy, are frequently HLA-B27 positive (1,4). Clinical course is transient generally and rarely chronic. The arthritis responds well to the treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, anti-tuberculosis drugs and termination of the BCG (4). Here, we report a male HLA-B27 negative patient who developed oligoarthritis during the BCG instillations for the treatment of superficial bladder carcinoma and gave a good response to the combination of indomethacin and isoniazid.

Case Report

A 65-year-old male was admitted with arthritis on his

right wrist, left knee and right ankle joints. He has been on a BCG immunotherapy for the treatment of his superficial bladder carcinoma. One week after the fourth instillation of BCG manifestations of asymmetrical oligoarthritis have begun. Laboratory results revealed an elevated erythrocyte sedimentation rate, and C-reactive protein level (54 mm/h, and 48 mg/l, respectively). Tests for rheumatoid factor (RF), anti-nuclear antibody (ANA), and HLA-B27 were all negative. Fungal and bacterial cultures including mycobacteria from blood, synovial fluid and urine specimens were all negative. He had no history of a recent infection. In microscopic examination of the synovial fluid, polymorphonuclear leukocytes were observed dominantly. There was no evidence of a crystal arthropathy. Radiographs of the chest, knees, ankles and wrists did not reveal any pathology. He was administered indomethacin 75 mg and isoniazid 300 mg daily in a single dose for three months. Intravesical BCG treatment was also terminated. After 3 months, all symptoms disappeared and the laboratory findings returned to normal. One year later, the patient was still asymptomatic.

Discussion

BCG is a *Mycobacterium bovis* that is attenuated by successive subcultures. *Mycobacteria* (*Mycobacterium tuberculosis*, *Mycobacterium*

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avium-intracellulare and BCG) can cause reactive arthritis. It is accepted to be reactive arthritis because it is observed after administration of BCG and occurs predominantly in patients with a genetic predisposition (HLA-B27); live organisms have not been found in joint fluid; it can resolve with nonsteroidal anti-inflammatory drugs (NSAIDs) without need of antibiotics; and it can recur after a new BCG administration (5,6,7).

A possible pathogenetic explanation to the development of mycobacteria related reactive arthritis is cross-reactivity between mycobacterial antigens and cartilage proteoglycans (8). A second mechanism has been postulated that mycobacterial antigens might disseminate to the joints and stimulate local cell-mediated immune responses (9). The second mechanism is also supported by the demonstration of *Mycobacterium bovis* BCG DNA in the synovial fluid of patients with intravesical BCG induced reactive arthritis (10).

The route of the BCG injection and HLA subtypes effect the presentation of arthritis (5,11). The individuals who develop rheumatoid arthritis(RA)-like symmetrical polyarthritis are generally HLA-DR3 positive and they are subcutaneously BCG injected patients. HLA-DR3 and HLA-DR4 positive patients are reported to be hyper-responsive to mycobacterial antigens (1). The patients who develop asymmetrical oligoarthritis in the large joints are generally HLA-B27 positive, and intravesical route is the common way of treatment (5,11). Our patient had asymmetrical oligoarthritis and he was negative for HLA-B27. HLA-B27 positivity among arthritis patients following BCG therapy was reported as 44% (12). A patient of BCG induced reactive arthritis with HLA-B7 positivity was also reported (5). However, HLA-B7, HLA-DR3 and HLA-DR4 assays were not possible for our patient.

Joint involvement may be as symmetrical polyarthritis, oligoarthritis and rarely monoarthritis. Wrists, knees and proximal digits are involved generally (4). Ankles, sacroiliac joints, toes, metatarsophalangeal and temporomandibular joint involvements were also reported (1,4-6,11,13). The arthritis may occur after any instillation but generally develops in the first month of the treatment (4). Stiffness is usually the first sign of the arthritis and is followed by acute inflammatory signs at the affected joints (1). A sterile inflammation is present at the involved joints. It commonly responds well to the NSAIDs, corticosteroids and anti-tuberculosis drugs (1,6). Even rare, protracted and high dose corticosteroid requiring cases are also reported (4). Our case had an asymmetrical oligoarthritis and responded well to the combination

of indomethacin and isoniazid treatment. Now, one year after the treatment the patient remains asymptomatic.

In conclusion, the possibility of BCG induced reactive arthritis should be considered in patients treated with intravesical BCG immunotherapy. The arthritis may also develop in HLA-B27 negative patients. The articular involvement may differ from asymmetrical mono-oligoarticular to symmetrical polyarticular.

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