

SHORT COMMUNICATION**Bacille Calmette-Guérin osteomyelitis**

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Abstract

Background: Tuberculosis is an essential problem for healthcare systems especially in developing countries. All newborns are given Bacillus Calmette-Guérin (BCG) vaccine in Iran which is prepared from live bovine tuberculosis bacillus, and is given to protect against tuberculosis. Osteomyelitis secondary to BCG vaccination is rare and usually involves epiphysis of long tubular bones.

Methods: 4 patients, 3 males and a female entered this study and were between 11 to 24 months old. The involved bones were first metatarsi, talus, humerus and tibia bone. The main radiologic finding was lytic lesion with cortical destruction and periosteal reaction.

Results: 3 patients underwent core needle biopsy and the one with the proximal tibia involvement, underwent open surgery. Pathology report suggested granulomatous osteomyelitis and typical caseous necrosis compatible with tuberculosis. Surgical treatment for these patients was curettage and debridement of the bone lesion and involved tissues around. The patients got standard anti TB pharmacotherapy, were completely cured and no short term complication was seen in a one year follow up.

Conclusion: BCG osteomyelitis and cold abscess, should be kept in mind when assessing a child presenting chronic symptoms like pain, limping or local swelling of extremities. The long interval time between BCG vaccination and outbreak of the culture-negative abscess is a major point which emphasizes on pathologic evaluation. Imageguided tissue biopsy and PCR studies confirm diagnosis. Early use of a surgical curettage and debridement along with chemotherapy soon afterwards, enabled these children to enjoy a satisfactory clinical outcome.

Keywords: BCG, Cold abscess, Needle biopsy, Osteomyelitis

Introduction

Tuberculosis (TB) is an important challenge for healthcare systems, especially in developing countries (1). Hence, in Iran in order to prevent its spread all newborns are given Bacillus Calmette-Guérin (BCG) vaccine. It is prepared from a strain of the attenuated live bovine tuberculosis bacillus, mycobacterium bovis, and has been administered to protect against tuberculosis since 1921 (2).

The BCG vaccine is administered intradermally by an injection just under the skin. Complications of the BCG vaccination occur in 3.3% of the population and usually 6-9 months after being inoculated (3). The most common

complications are subcutaneous abscess and local purulent lymphadenopathy (3). However, it may lead to disseminated disease in patients with immunodeficiency disorders (4).

A meta-analysis that investigated 26 past studies about the effect of the BCG vaccination, showed on average a 50% reduction in TB infection risk. This analysis revealed that BCGV is effective both in pulmonary and extra pulmonary tuberculosis (5). Osteomyelitis secondary to BCGV is a rare complication that usually involves epiphysis of long tubular bones (6,7).

Hengster et al. stated that in the first 20-weeks of being vaccinated they had positive cultures in just 46% of cases.

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Therefore, the culture of the BCGV complication lesion is not always positive and this percentage decreases with time (3).

The prevalence of osteomyelitis following BCGV is about 1 in 100000 cases according to different studies (8). How BCGV leads to osteomyelitis is still unknown, but hematogenic dissemination is a probable way due to the long distance between the BCGV location and metaphysics of the long tubular bones. The interval between reported osteomyelitis and vaccination is 3 to 26 months (9). Involved epiphysis or metaphysis of the long tubular bone is seen in 80% of cases and the peripheral skeleton is more involved than the axial skeleton (10).

In order to observe the bacillus in the lesion and to assist in diagnosis Chan et al. performed a CT-guided biopsy in addition to a histopathology evaluation (11). In adults, bone curettage in TB osteomyelitis is known as a treatment accelerator, while other studies suggest just pharmacotherapy following diagnostic biopsy (11, 12). Kroger et al. recommended Isoniazid+Ethambutol+Streptomycin for 3 months, then Isoniazid+ Ethambutol or Rifampin for 4 months continued by Isoniazid for 12 months (13, 14). Other studies suggest four drug treatments for 2 months and then two drug treatments for 7 months (11).

Material and Methods

Four patients (3 males and 1 female) were entered into this study. These patients were selected from children referred to our tumor clinic at Emam Reza hospital, Mashhad, Iran. The girl was 11 months and the boys 17, 18 and 24 months old. The main symptoms in all cases were pain and swelling and in one, the initial symptom was limping. They had no fever or anorexia and, except for one patient, were in good general condition. This one patient presented with proximal humerus involvement and suffered from an immune deficiency disorder. He also had an axillary lymphadenopathy with a cutaneous drainage 6 months previously, which had been reported

secondary to BCGV.

The involved bones were the metaphysis and diaphysis of the first metatarsi on the right foot, the talus, the proximal metaphysis of the humerus, and the proximal epiphysis of the tibia.

Results

In the first patient's radiography there is an ill-defined lytic lesion in metaphysis and diaphysis of the first metatarsi with cortical destruction and periosteal reaction. In his computed tomography scan, an extraosseous component is seen [Figure 1-a,b].

In the second patient's X-Ray there is a lytic lesion in the superior part of the talus body and an uncompleted rim of surrounding sclerosis. In the CT scan cortical destruction is seen. In the MRI, edema around the talus bone and increased ankle joint synovial fluid is seen. MRI involvement is in accordance with X-Ray findings. The other parts of the talus have a normal signal [Figure 2-a,b].

In the third patient's X-ray, there's an ill-defined lytic lesion in the proximal metaphysis of the humerus with epiphysis involvement and periosteal reaction. An uncompleted circumferential bone sclerosis is seen [Figure 3].

In the fourth patient, the proximal epiphysis of the tibia does not seem to be affected based on the X-Ray findings. But in the CT scan, a lytic lesion with posterior cortical destruction and anterior sclerotic border was seen. Furthermore, in the MRI there is a fluid signal out of the bone margin connected to the lesion. No obvious edema or connection to the knee joint synovial cavity was detected [Figure 4-a,b].

Diagnosis & Treatment

Three patients underwent core needle biopsy of their talus, first metatarsi and proximal humerus for pathological evaluation and obtaining cultures. The patient with involved proximal epiphysis of the tibia underwent open surgery because of the connection between the bone cavity and peripheral fluid, which had a similar signal in the MRI imaging, and this finding



Figure 1a. First metatarsus involvement.

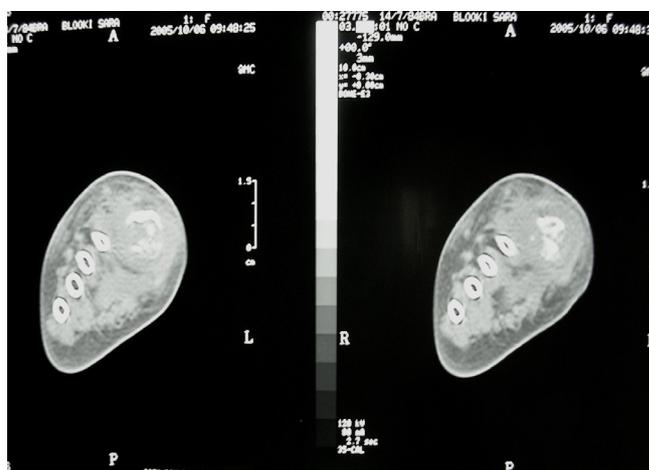


Figure 1b. Axial CT-scan of first metatarsal cortical destruction.

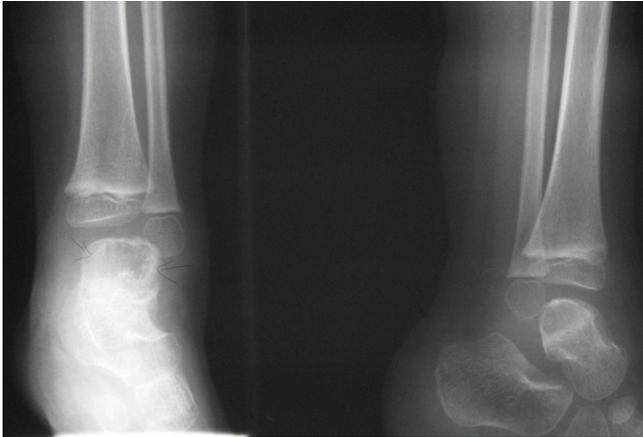


Figure 2a. Talus inbody involvement.



Figure 3. Ill-defined lytic lesion in proximal metaphysis of humerus.

directed the diagnosis toward bone abscess.

In the patients' biochemical lab tests only the Erythrocyte Sedimentation Rate (ESR) was moderately elevated. In the pathology report granulomatous inflammation consisting of epithelioid histiocytes, langerhans type giant cells and typical caseous necrosis was seen - suggestive of chronic necrotising granulomatous osteomyelitis. All microbial cultures including mycobacterium tuberculosis were negative. No metastatic involvement in other organs was detected in our patients. Surgical treatment for these patients was basically curettage and debridement of the bone

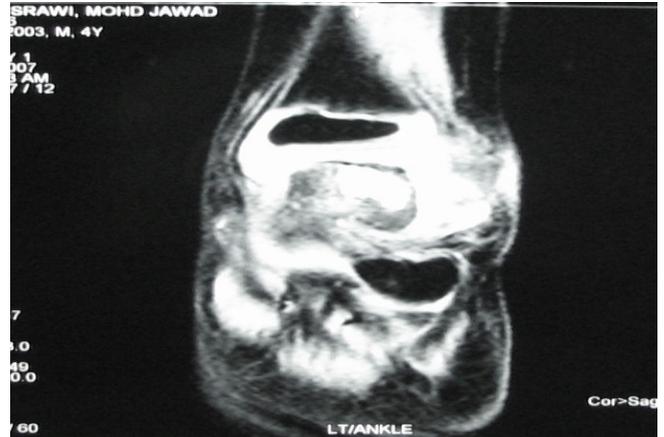


Figure 2b. Edema around talus bone and increased ankle joint synovial fluid in MRI.

lesion and involved surrounding tissues. Another pathology sample was sent for each patient and the report was granulomatous osteomyelitis compatible with tuberculosis, which confirmed the result by the core needle biopsy method. The patients received the standard 9 months of anti-TB pharmacotherapy under the supervision of pediatricist. They were completely cured and no short term complications were seen in their one-year follow up [Figure 5-a,b].

Discussion

TB is an important public health problem. The BCG vaccine is used to protect recipients against severe forms of tuberculosis like TB meningitis (11). Osteitis or osteomyelitis is one of the rare consequences of the BCG vaccination (8).

Because of the subtle nature of the symptoms, the diagnosis is not usually made until it has well advanced (9). Mild pain and swelling of the bone, with slight warmth and tenderness, and overlying swelling of the soft tissues should alert clinicians to the possibility of skeletal tuberculosis. If plain radiographs are normal, more sensitive investigations such as MRI and CT are required to detect and localized lesions.

In this regard, physicians should initially take into consideration that the patients have no clear history of contact with TB patients in their family, so according to histopathological findings the only source of tuberculosis for our patients is the BCGV.

There was no significant advantage observed between the sexes and their age ranged from 11 to 24 months. Due to the long interval between the BCG vaccination at birth and bone abscess symptoms, it is a chronic process in which patients neither have fever nor their general condition is affected by the disease. They all - except for one - were referred to us in a good general condition and only had localized symptoms like pain, swelling and limping. Biochemical laboratory tests showed no acute infection and relatively elevated ESR had more correspondence with a cold abscess.

Lymphadenopathy is the most common acute complication of BCGV, but it did not exist in any of our

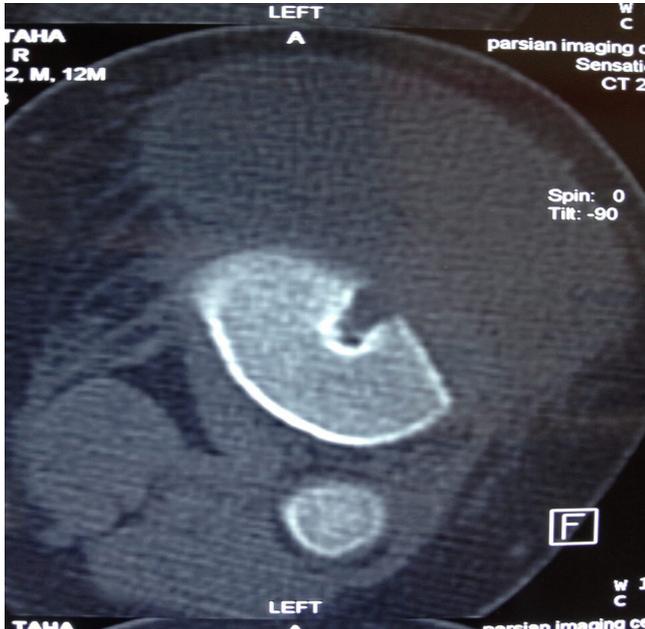


Figure 4a. a lytic lesion with posterior cortical destruction and a sclerotic border.



Figure 4b. there's a fluid signal out of bone margin connected to the lesion in MRI.



Figure 5a. first metatarsus after 1 year.



Figure 5b. talar body complete healing after one year.

patients at the time of diagnosis, except for the one with immune deficiency disease who had a lymph node with cutaneous sinus 6 months previously.

There was negative C Reactive Protein in the biochemical lab test in the patient with talus involvement.

There is was not any specific distribution of involvement in the bones, although it was present everywhere in the metaphysis, epiphysis and short tubular bones.

Conventional radiography located the lesion in three patients. It shows a lytic lesion with some surrounding sclerosis in one case, which puts the chronic abscess at differential diagnosis list. On the other hand, in two cases periosteal reaction and ill-defined lesions suggested tumoral involvement like Ewing sarcoma and

eosinophilic granuloma.

For non-specific symptoms, biochemical lab tests, - especially - the radiologic pattern which arises in tumoral involvement, and biopsy are the only methods to rule out all these probable diagnosis.

The long interval time between BCGV and outbreak of the culture-negative abscess is another major point which emphasizes more on pathologic evaluation.

We adopted the minimally invasive technique: CT guided core needle biopsy for tumoral lesion biopsy. Our technique was done with the least complications and we took TB and other bacterial culture specimens in addition to pathologic samples.

Surgical treatment following definite diagnosis is

controversial. Some writers confine treatment to pharmacotherapy (11). Our approach is the same as a chronic bone abscess including curettage and debridement avoiding any damage to the physis. Our patients took standard pharmacotherapy soon afterward under the supervision of a pediatricist.

Our TB cultures were negative although some other investigations emphasize the PCR technique to confirm tuberculosis osteomyelitis (11).

After one year we saw bone healing without notable residual complications and there were no obvious physeal arrest [Figure 5].

Bacille Calmette-Guérin osteomyelitis and BCG cold abscess, although rare, should be kept in mind when assessing a child presenting with chronic symptoms like pain, limp or local swelling of extremities.

Imaging studies could be suggestive, but using an image guided tissue biopsy and PCR studies confirm diagnosis. Moreover, the BCG vaccine complication should be

considered in such cases even without bacterial isolation.

Early use of a surgical curettage and debridement along with commencement of chemotherapy soon after the histopathological assessment of core needle biopsy samples enabled these children to enjoy a satisfactory clinical outcome.

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