Unusual Presentation of Bacille Calmette-Guérin (BCG) Osteomyelitis in Immunocompetent Saudi Child: A Case Report

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Abstract*—Osteomyelitis is a rare complication of Bacillus Calmette-Guerin (BCG) vaccine particularly in Immunocompetent children. Recognition and Management of BCG osteomyelitis is challenging. Herein a 7-months-old Saudi girl admitted with right foot swelling, clinical diagnosis of cold abscess was made. MRI imaging revealed osteomyelitis of 1st right tarsal bone, open biopsy tissue culture and PCR were positive for mycobacterium bovis. BCG osteomyelitis is devastating complication of BCG vaccination that should be considered in the appropriate clinical setting.*

Keywords-- BCG vaccine, Osteomyelitis, Immunocompetent

I. INTRODUCTION

BCG Osteomyelitis is a rare complication of BCG vaccination in Immunocompetent hosts, This late complication may occur in children four to 24 months after vaccination. BCG osteomyelitis may occur as a result of direct spread from the vaccine administration site, or less commonly may occur as a result of dissemination of BCG infection. The lesions are usually localized in the metaphysis or epiphysis of long bones.[1,2] The incidence varies between countries, it has been reported in 0.01 per million vaccinees in Japan (multipuncture technique) and 30 per million in Finland (intradermal technique).[1,2] In Saudi Arabia, although all of the newborns are vaccinated with BCG within the first year of life, few cases only were reported with the diagnosis of culture-proven BCG osteomyelitis in immunecompetent children.[3]

Herein, we report culture proven BCG osteomyelitis in immunocompetent infant that was confirmed by real-time polymerase chain reaction (PCR). The aim of this report is to discuss the unusual presentation of BCG osteomyelitis among the immunocompetent patients.

II. METHODOLOGY

A case report is being presented of a rare case of BCG osteomyelitis in immunocompetent infant that was confirmed by real-time polymerase chain reaction (PCR) with the aim to discuss the unusual presentation of BCG osteomyelitis among the immunocompetent patients. This case came in emergency department of with painless swelling in the medial side of the right foot for two weeks duration. After taking written informed consent this was thoroughly investigated and followed. It was found to be a rare case of BCG osteomyelitis. So it was decided to preseent this case as case report.

III. CASE REPORT

A 7-months-old girl presented to the *emergency department* with a complaint of painless swelling in the medial side of the right foot for two weeks duration. A clinical diagnosis of Right foot abscess was made and advice for incision and drainage to be done, but parents refused. Within three weeks, she presented again as swelling is increasing in size. She has no history of fever, previous trauma, recurrent

infections or raw milk ingestion. She received BCG vaccine at birth and the scheduled vaccines at two and four month of age.

On examination, the patient looks well, normal vital signs. She has right foot swelling, at the medial side of the big toe, about (0.78) by (1.1) inches in dimensions, none tender with mild redness on skin overlying. Other systemic examination was unremarkable.

Blood work up was carried out included complete blood count (CBC) and erythrocyte sedimentation rate (ESR) and showed normal parameters, x-ray of the right foot showed soft tissue swelling with multiple lytic lesions in the right 1st metatarsal bone (Figure 1).

Figure1
Plain x ray of right foot

About three weeks of starting symptoms, soft tissue swelling over medial aspect of right foot with multiple lytic areas in the 1st metatarsal bone with cortical breakthrough

Figure 2
Ultrasound of right foot

Ultrasound showing there is a collection measuring around (2,18) cm multiply by (1.2) cm with peripheral increased vascularity is noted

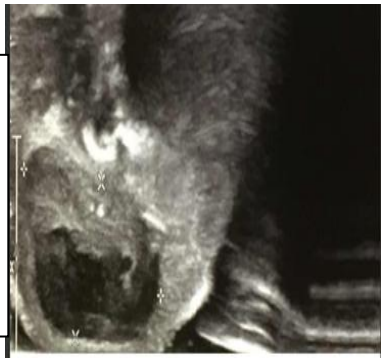
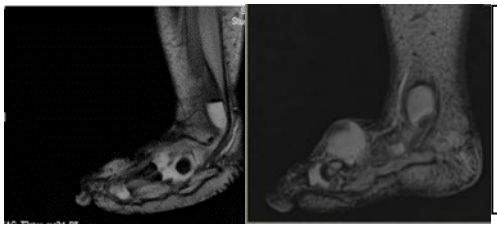


Figure 3
MRI of the right foot



An MRI showed intramedullary expansion of the 1st metatarsal bone with cortical thinning and presence of peristeal reaction. Soft tissue around showing same signal changes with extension dorsomedially that causing bulging

Figure 4
Plain x-ray of right foot

About five months post initiation antituberculosis medication, showing improvements in comparison to the baseline study

Ultrasound of the right foot showed a fluid collection measuring around (2.18) cm by (1.2) cm (**Figure 2**). A magnetic resonance imaging (MRI) of the right foot revealed intramedullary expansion of the 1st metatarsal bone with cortical thinning and presence of periosteal reaction, represent an infectious process (Figure 3). Bone biopsy from the right 1st metatarsal bone was taken and showed granulomatous inflammation with caseation necrosis. Tissue for acid fast bacilli (AFB) and PCR (GeneXpert) was

positive for mycobacterium and after three weeks the culture was positive for mycobacterium bovis most likely BCG strain.

Surgical incision was performed and necrotic tissue excision was done, pus was drained and there was a sinus extending to the 1st metatarsal bone. Anti tuberculous (TB) medications (rifampicin, isoniazid (INH) both given orally at dose (15 mg /kg/day) and Pyrazinamide oraly (20mg/kg/day od) initially planned for two months duration with two weeks of streptomycin (15 mg/kg IM od).

Patient has regular follow up in Pediatric Infectious Disease Clinic where she showed complete clinical resolution. Pyrazinamide was discontinued after culture result and both INH and Rifampicin were continued. Three months after initial presentation, X – Ray of right foot was repeated showing that there was improvement in the radiological appearance in comparison to the previous study (**Figure 4**). Patient still on regular follow up as outpatient and the plan is to continue medication for total one year duration.

IV. DISCUSSION

This study have described a rare case of osteomyelitis involve the 1st metatarsal of the right foot caused by BCG in a seven month immunocompetent girl. For more than 70 years, BCG vaccines have been administered safely to billions of individuals throughout the world.[4] In general, BCG adverse effects including local and systemic complications.

Adverse reaction of BCG depends upon BCG dose, vaccine strain, vaccine administration method, injection technique, and recipient's underlying immune status.[5]

In Saudi Arabia, mainly two different BCG vaccine strains are being used in the country since 2002 namely, Pasteur 1173 P2 and Tokyo 172-1. During 2005, the Danish 1331 strain was introduced for primary use. Interestingly after 2006, two published reports showed a higher rate of BCG related complications in newborns with a highest incidence rate of 3.12 and 10.14 (1.96 before the vaccine change) complications/1000 newborns, respectively and with a predominance of suppurative lymphadenopathy.[6,7]

Generalized BCG infection is extremely rare in immunocompetent patients.[4,7] A few autopsy studies of children who died of unrelated causes have demonstrated granulomas in various organs of vaccinated infants with apparently intact immune systems, suggesting that generalized nonfatal dissemination may occur in normal hosts. [4,8] Through literature review one study showed that of the 38 compensated BCG osteomyelitis/osteitis patients and according to chart review, no patients had immunodeficiency or other underlying conditions.[5]

Because of the subtle nature of the symptoms, the diagnosis is not usually made until it has well advanced. We believe that if there was no history of contact with tuberculosis infected patient, BCG vaccine strain as a source of tuberculous osteomyelitis it seems to be reasonable possibility. In one report four patient labeled as BCG osteomyelitis based on negative history of Tuberculosis contact, with positive history for BCG vaccine and noted histopathological findings, tissue culture for all of them were negative so the only source of tuberculosis is the BCG vaccine.[9]

Our patient presented after about seven months of receiving BCG vaccine. She presented mainly with right foot painless swelling, no movement limitations and good general wellbeing. This is going with the usual presentation for this condition which published through many literatures. In one retrospective study including 38 patients, for 68%, symptoms or signs developed 7–18 months after vaccination,

extremity bones were more commonly involved than axial bones, The tibia was the most common site (9 patients), followed by ankle bones (8 patients), Presentation included a mass 25 [66%] children, tenderness 22 [58%], limping 19 [50%], redness 14 [37%], and heat 7 [18%].[5]

Another case report of three patients from Saudi Arabia was stated that the clinical signs of BCG osteomyelitis generally include limited motion, otherwise, the affected child appears constitutionally and generally well, but may have a low-grade fever and high ESR.[3] Our case doesn't showing fever or even elevated ESR. Same report emphasizing that as serious complications of BCG infection are thought to occur more frequently in patients with immunological deficiencies, they hypothesize that BCG osteomyelitis could occur inimmunocompetent hosts since investigated the immunological status of all reported three patients was normal. Immunological work up studies for our patient not revealed a marker for immunodeficiency status.

Our case showed the normal blood parameters, including normal ESR. Tissue AFB PCR (GeneXpert) was positive and later on after three weeks culture was positive for mycobacterium bovis most likely BCG strain as reported by microbiological laboratory. This was similar to the study of Chiu N-C et al. and his colleague, except that a positive culture which only positive on only four patient from 38 patient had BCG osteomyelitis in one retrospective study where the most of them about 27 patient was detected by a molecular study.[5] This reflect the importance of molecular study and the improvement in laboratory facility contribution in the disease detection.

Beside surgical open biopsy which was included by drainage and evacuation our case was received quadruple therapy initially of antimicrobials including that INH, rifampicin, pyrazinamide and streptomycin. Drug adjustment was done later on, after positive culture result for mycobacterium bovis (BCG) by discontinuation of the pyrazinamide. Surgical treatment following definite diagnosis is controversial. One systematic review was done in immunocompetent patient with BCG osteomyelitis showing that From 34 eligible studies gleaned from a screening of 804 articles, a total of 331 cases were enrolled. Involvement of the lower limbs was present in 55.6%, followed by the axial skeleton (26.0%), the upper limbs (15.4%), and multiple bones (3.0%). Of the 64 patients having records of detailed chemotherapy regimens, 45 patients (70%) received two or fewer drugs.[10] Some of the Literature stated that the Treatment of BCG osteomyelitis usually consists of surgical evacuation plus administration of isoniazid (INH) and rifampin for six to 12 months.[1,2,11] BCG is resistant to pyrazinamide and, unlike treatment of *M. bovis* infection, ethambutol is not generally needed.

V. CONCLUSIONS

Because BCG Osteomyelitis is a rare complication of BCG vaccination , high index of suspicion should be considered in cases of osteomyelitis with clinical, radiological and histopathology presentation suggestive of tuberculosis and negative for usual bacterial culture. Therefore, mycobacterium culture and PCR for BCG should be considered.

ABBREVIATIONS

ESR : Erythrocyte Sedementation Rate, AFB: AcidFast Bacilli, OD: once daily, BCG: Bacillus Calmette-Guerin, Cm: Centimeter, IM: intramuscular, MRI: magnetic resonance imaging, PCR: polymerase chain reaction, PO: per oral.

AUTHOR'S CONTRIBUTION

Alzomor Omar: Dr. Omar conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted

Bukhari Elham: Dr. Elham carried out the initial analyses, reviewed and revised the manuscript and approved the final manuscript as submitted.

Alfeerh A: Prof. Alfeerh A coordinated and supervised and approved the final manuscript as submitted.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

CONFLICT

None declared till date.

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