

Case Report

## BCG Osteitis of the Distal Tibia: A Case Report

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### ABSTRACT

The authors report the case of a 19-month-old girl with an osteolytic lesion in the distal metaphysis of the left tibia. Based on clinical, radiological and histological findings, the authors suspected osteitis following Bacillus Calmette-Guérin (BCG) vaccination. After surgical management and antituberculosis treatment for 12 months, radiological and clinical findings suggest an improvement in the diagnosis. This uncommon case in paediatric practice may be an area of interest to orthopaedic surgeons as well, since the long bones are most frequently affected.

**Key words:** osteitis of tibia, BCG, case report

### INTRODUCTION

The BCG vaccine contains a live attenuated strain of Mycobacterium bovis, which effectively protects against severe infant tuberculosis, including tuberculosis meningitis. <sup>(1)</sup> This vaccine is recognized as one of the most reliable vaccines against tuberculosis available today. <sup>(2,3)</sup> Although considered a safe procedure, local and systemic complications may occur, including osteitis of long bones. <sup>(4-7)</sup> Mycobacterium reaches a bone through lymphatic and haematogenous dissemination, while clinical manifestations occur in 1-6 % of cases. <sup>(8)</sup> Complications occur as a consequence of the side effects of the BCG vaccine, or due to the presence of both the BCG vaccine and a lack of immunobiological resistance, especially cellular immunity. <sup>(9)</sup> Osteitis, following BCG vaccination, is extremely rare with an incidence of 0.39/1,000,000, depending of the bacillus used. <sup>(10)</sup> The lesions are

localized to the metaphysis or epiphysis of long bones. <sup>(11)</sup> In countries such as Finland, Sweden, the Czech Republic and Slovakia, the incidence of osteitis following BCG vaccination varies, depending on the strain used for vaccination. <sup>(12)</sup> The lesion site on the bone is not necessarily associated with the injection site. <sup>(13)</sup> Osteitis after BCG vaccination is a poorly understood disease, with slow progression and mild symptoms, making diagnosis difficult. Although clinical manifestations usually occur 18 months after vaccination, this interval may range from several months to five years. The initial symptoms are sensitivity, pain and limited movement in the affected region, when the present fever is low and does not affect the patient's general status. <sup>(10,14)</sup>

### CASE REPORT

A 19-month-old girl was referred to an orthopaedic examination because of

limping on the left leg for four days. At the time of the examination, the girl had daily episodes of fever of 38°C and inflammation of the middle ear while a blood test revealed the following: leukocyte 12.2, SE 42 mm/h. An orthopaedic surgeon observed a normal general status of the patient on examination. The girl walked with slight limping on her left leg, with the passive range of motion in her lower extremities rated as normal and without pain on palpation. The girl was hospitalized at the orthopaedic clinic to be further examined for suspected coxitis transitoria of the left hip. The RTG and ultrasound examinations of her hips were normal. A further blood test (ESR 30 mm/hour, CRP 3.6 mg/L, leukocyte 12.7, antistreptolysin O antibodies (ASTO)<55.3, rheumatoid factor (RF)<8.0) and a throat swab culture showed the presence of the klebsiella pneumoniae bacteria, which were treated with antibiotics. A paediatrician and an ENT specialist also examined the patient. Five days later, the girl was referred to the clinic for children's diseases. A re-evaluation of the tests was done within the following five days. An increase in ESR and leukocyte was observed (ESR 60 mm/h, leukocyte 21.15, CRP 5.30 mg/L), while a chest X-ray examination showed an initial infiltration on the right side. Neither fever nor limping was reported; and, after consulting the ENT specialist, the girl was discharged from hospital on the seventh day for home care treatment and regular follow-ups with a paediatrician. Four weeks after the initial onset of symptoms, the child's

mother noticed a smaller oedema without redness above the inside-left ankle area. Daily episodes of fever were not reported, while the last throat swab culture was negative and a chest X-ray was without signs of infiltration. The girl was again referred to an orthopaedic surgeon, who performed an X-ray examination of the left lower extremity. The X-ray showed an osteolytic lesion in the distal tibia metaphysis with oedema of the soft tissue (Figure 1).



Figure 1: AP and lateral X-ray, showing an osteolytic lesion in the distal tibia metaphysis with oedema of the soft tissue

The repeated laboratory tests showed no significant changes (ESR62mm/h, CRP3.1mg/L). A surgery procedure was performed by removing granulation tissue and a smaller sequestrum of the bone from the distal tibia metaphysic lesion. Seven days after the surgical treatment, a radiological examination showed a decrease in oedema of the soft tissue (Figure 2).



Figure 2: AP and lateral X-ray, seven days after surgical treatment, showing a significant decrease in oedema of the soft tissue

Pathohistologic analysis showed chronic caseous inflammation of the bone, indicating BCG osteomyelitis. Anamnesis data revealed that the child had received a BCG vaccine in the neonatal period and that there had been no contact with people with chronic cough or pulmonary tuberculosis. The parents' chest X-rays were normal. The child was again referred to the clinic for children's diseases, where antituberculosis therapy was administered (rifampicin, isoniazid, pyrazinamide). Routine blood tests and a functional evaluation of the liver and kidneys were also performed. The chest X-ray showed regression of the previously described infiltration. The Quanti FERON test was negative ( $<0.35$  IU/ml). Scintigraphy of the bones confirmed a pathologic finding on the distal tibia. Immunoglobulin levels were within the

reference values, while the flow cytometry-cellular immunity test was normal. The HIV and brucellosis tests were negative. MRI of the endocranium was normal. Six gastric lavage analyses were performed, all of which were TB negative. The initial antituberculosis treatment included a combination of three drugs (isoniazid, rifampicin and pyrazinamide) for three months, followed by a further nine months of rifampicin and isoniazid. This antituberculosis treatment lasted 12 months in total. At the last examination, the girl had no complications, such as limping, deformities or shortening of the extremity. The last X-ray of the left lower leg showed the replacement of the osteolytic lesion on the tibia with the restoration of the cortical contours (Figure 3).



Figure 3: AP and lateral X-ray, 12 months after the treatment, showing the replacement of the osteolytic lesion with the restoration of the cortical contours

## DISCUSSION

The 19-month-old girl with BCG osteitis in the distal tibia metaphysis responded well to the surgical treatment and antituberculostatic therapy, administered over 12 months. To the best of our knowledge, this is the first case report on osteitis of tibiae following BCG vaccination from Bosnia and Herzegovina. According to the literature, the age at which the onset of osteitis occurs significantly varies. For instance, a study of 222 children from Finland suggested that the age varies from 0.25 to 5.7 years.<sup>(10)</sup> In our case study, the

diagnosis was made in accordance with the criteria suggested by Foucard and Hjelmstedt in 1971, i.e., vaccination in the neonatal period, a period of less than four years between vaccination and the onset of symptoms, no contact between the child and any adult with tuberculosis, a consistent clinical profile, and a histopathology suggestive of tuberculosis.<sup>(15)</sup> The girl received antibiotic therapy from the beginning, yet did not respond to it, while mild clinical signs and laboratory tests justified a suspicion of BCG osteitis. Similar to this case, the long-term

development in most patients is favourable. (5,6,10) The prognosis of this disease is good and sequelae of the bone or growth deficit are described in only 3% of cases. (10)

## CONCLUSION

BCG osteitis is a very rare complication of the BCG vaccination. It is difficult to make a diagnosis and, with initial symptoms, rarely recognized. Therefore, we should be extremely cautious during the examination of small children with atypical symptoms in extremities, especially if they do not respond to initial treatment. To avoid possible further complications, early BCG osteitis diagnosis, treatment with antituberculostatics and surgical intervention are of great importance.

## Declarations

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### Funding

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### Availability of data and materials

Data and materials supporting this report are available in the records of the hospital where this patient was treated and can be requested directly from the corresponding author to some extent, without revealing a patient's identity.

### Authors' contributions

SC, MJ, AP and FK interpreted the patient data regarding the disease, designed the case report, and contributed in writing the manuscript. SS reported the X-ray images and contributed in writing the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

The author obtained from the child's parents the written permission to report this case and images.

### Competing interests

The authors declare that have no competing interest

## Abbreviations

BCG: Bacillus Calmette-Guerin

CRP: C-reactive protein

CXR: Chest X-ray

L: leukocytes

ESR: Erythrocyte sedimentation rate

RF: reuma factor

ASTO: antistreptolysin test

ENT: ear, nose, and throat

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