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OSTEOMYELITIS RELATED TO BCG VACCINATION: CASE REPORT*

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A nine-month-old girl with osteomyelitis related to BCG vaccination is presented. The patient did not have any clinical evidence of immunodeficiency. Her X-ray examination showed a lytic lesion of the right tibia and of the left ulna. Histopathological examination of biopsy material revealed a chronic granulomatous inflammatory reaction. She improved with intermittent short course antituberculosis therapy. *Key words: BCG vaccine, osteomyelitis.*

Although BCG vaccination against tuberculosis is widespread in the world, very few complications have been reported following inoculation with this vaccine[1-3]. The most common adverse reaction to BCG vaccination is enlargement and / or suppuration of the lymph nodes, with drainage at the inoculation site[3-4]. There are also case reports describing subcutaneous abscess and localized osteitis caused by BCG vaccination[5-7]. It is estimated that the incidence of these complications is approximately 1 per 1 million vaccinees, but that the rates are higher in the Scandinavian countries, especially in Finland[5].

The above-mentioned should be considered in the differential diagnosis of bone infections in young children.

We wish to report a rare case of an infant with a lytic lesion in the ulna and in the tibia which improved after intermittent short course antituberculosis therapy.

Case Report

A nine-month-old girl was admitted to the hospital for evaluation of swellings of the right knee and of the left elbow and limitation of movement. She was born in

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the hospital and her birth weight was 3200 g. She was vaccinated with BCG at one week of age. She was breastfed. When two months old, an enlarged left axillary lymph mode was noticed. At six months of age, it suppurated and healed within 15 days. She had no history of recurrent infections, oral moniliasis, diaper rash, or fever and neither was there a record of tuberculosis in her family. She had a 1.5 month history of right knee pain and had difficulty in taking steps. She subsequently developed swellings on her left arm and elbow. Prior to admission, she had received non-specific antibiotic therapy and a cast was applied, but no improvement was noted. Another physician, who suspected tuberculosis, recommended surgical intervention. The patient was noted to have had no weight loss, anorexia or night fever and sweats.

Physical examination revealed an infant in a good general condition. Her body temperature was 36.3 °C, pulse 156 / min, body weight 7300 g (10-25th percentile) and height 74 cm (75-90th percentile). There was slight scar formation in the left axillary area. Her right leg was painful and swollen. The left arm was tender and painful on palpation and there was swelling of the bony areas movement was restricted in both extremities.

Laboratory findings revealed a haemoglobin of 7.50 g / dl, and the white blood cell count was 12.400 / mm^3. The blood smear contained 26% polymorphonuclear leukocytes, 70% lymphocytes 3% monocytes, and 1% eosinophils. The thrombocyte count was normal. The erythrocytes showed hypochromia and microcytosis. Immunoglobulin concentrations were: Ig A:32.3 mg / dl (33.7 ± 12.6), Ig G:802 mg / dl (705.8 ± 168.2) and Ig M:168 mg / dl (104.2 ± 29). The nitroblue tetrazolium test was normal. Tuberculin and other skin tests were positive. Chest X-ray was normal, while X-ray examination of the extremities showed a lytic lesion of the right tibia and periosteal reaction and a lytic lesion of the left ulna.

On the second day of hospitalization, a biopsy was performed on the right proximal tibia. Periosteal thickening was detected. There was a small amount of fragile, lobulated, blood-tinged, white colored, material in the lesion. The Acid-fast bacilli stain did not yield any organisms and no growth was noted on the Lowenstein culture medium. Histopathological examination of the biopsy revealed a chronic granulamatous inflammatory reaction.

Isoniazid (INH) and rifampin (RMP) were each administered in a daily dose of 10 mg / kg for the first fifteen days. This dose was continued twice weekly for a period of nine months. Within the first three months, radiological studies revealed a definite improvement in the patient's condition. She was able to take a step. The local pain and swelling had completely disappeared. At the end of sixths month of treatment, the patient was able to walk without difficulty. Clinical examination revealed no pathological findings. Treatment was discontinued at the end of the ninth month.

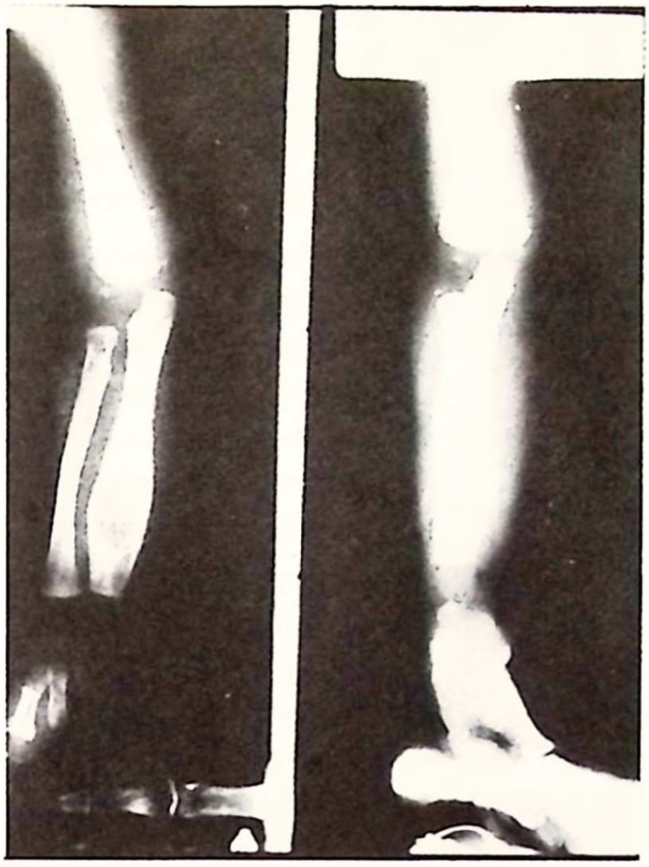

Fig. 1: Anteroposterior and lateral roentgenogram of left forearm. Single lytic lesion and periosteal reaction on ulna.

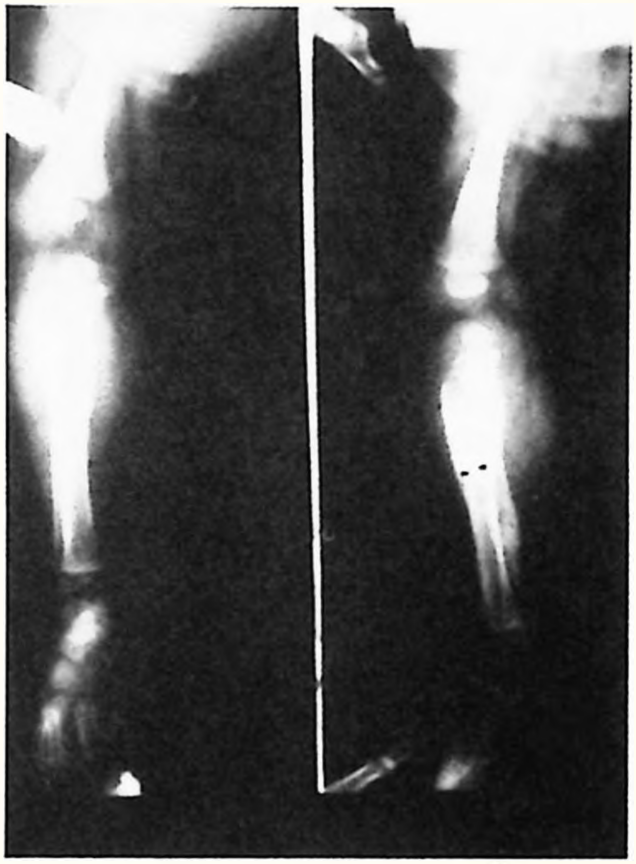

Fig. 2: Anteroposterior roentgenogram of lower extremities. Single lytic lesion on right tibia.

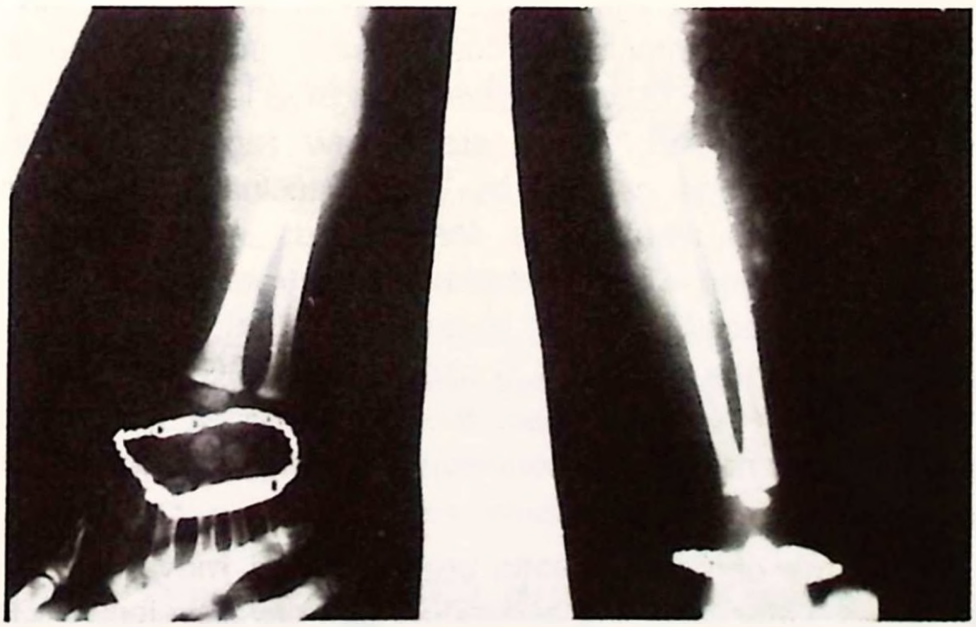

Fig. 3: Anteroposterior and lateral roentgenogram of left forearm (after treatment). There is no lytic lesion or periosteal reaction on ulna.

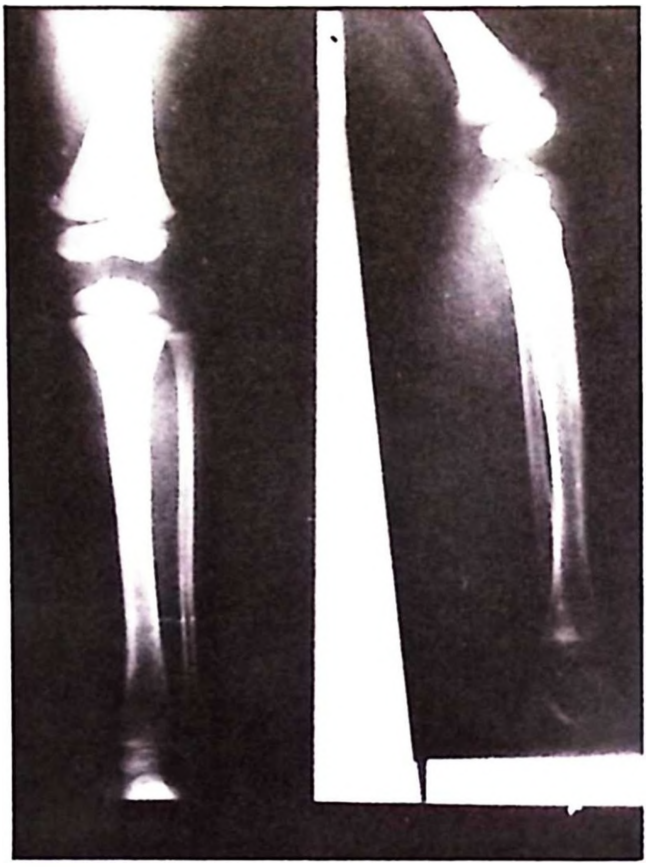

Fig. 4: Anteroposterior and lateral roentgenogram of lower extremities (after treatment). No lytic lesion is present.

Discussion

There are few reports in the literature of severe and disseminated BCG complications, with the exception of thymolymphatic deficiencies with or without hypogammaglobulinemia or agammaglobulinemia, leukocyte and monocyte deficiencies with chronic granulamatous disease and immune deficiencies resulting from other factors[8-10]. Vaccination with BCG is a routine practice in our country as in many others[5]. There are a few reports regarding regional osteomyelitis complications caused by BCG vaccination which have been detected in the sternum, fibula, ulna, femur, talus and vertebrae. The most common site of localization is reported to be the extremities (70%)[1,5-7]. There is no male or female preponderance. It is presumed that in Finland and in other Scandinavian countries the rate of BCG osteitis and BCG arthritis is higher than 1 / 1.000.000 vaccinees[6], while in Spain, this rate is reported to be 1 / 80.000[7]. In young children, lesions may usually develop from several months to three years after vaccination.

The initial symptoms of osteomyelitis are restricted movement and pain on palpation of bones. Later, swelling and induration may develop[6,7,9]. Our patient, like most, did not show signs of thymolymphatic deficiency or hypogammaglobulinemia. However, the possibility of transient immunodeficiency caused either by

a viral, fungal or bacterial infection, should be considered in these types of cases[1]. The clinical findings in BCG-osteomyelitis progress more slowly than in staphylococcal or streptococcal osteomyelitis. In patients with BCG-osteomyelitis, the C-reactive protein value, leukocyte count and erythrocyte sedimentation rate are generally near normal[5-7].

There are no specific roentgenologic characteristics of BCG-osteomyelitis or BCG-arthritis. X-ray findings may resemble those seen in osteosarcoma and osteomyelitis. Radiologically, the typical lesion is a single lytic zone[6], which may have sclerosis or a periosteal reaction[6,7]. However, in our patient two lytic lesions were detected in different bones. The roentgenologic examination should include all extremities, the vertebral column and the lung. It is accepted that radiological improvement after three months of therapy is a common feature in BCG-osteomyelitis[1,5,6], which is consistent with our case. Even though reports in the literature suggest that therapy consisting of three drugs is nearly 100 percent successful[1,5-7], we used intemittent antituberculosis chemotherapy comprising two drugs, and we achieved a successful result. As to our knowledge, this is the first time such a regimen has been reported in the literature. This protocol consisted of a daily dose of INH + RMP for 15 days, which was followed by the same dose twice weekly for a period of nine months.

Despite the fact that the BCG species could not be identified in our case, as in many other cases reported in the literature[6,7], diagnosis was made on the basis of clinical history. There was no record of contact with tuberculosis bacillus, the chest X-ray was normal, and the X-rays of the extremities along with the histopathological examination were abnormal. In addition, the patient had a rapid response to treatment.

In conclusion, this condition should be considered in the differential diagnosis of osteolytic lesions in children vaccinated with BCG less than three years prior to the onset of symptoms.

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