Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report
DOI: 10.6003/jtad.1484c2

Disseminated Mycobacterium Bovis Infection in an Immunodeficient Child: A Case with Cutaneous Lesions

Gökhan Okan,[1] Didem Atay,[2] Nesimi Büyükbabani,[3] Esma Türkmen,[4] Fatih Erbey,[5] Hanife Gülyüz Öztürk[6]

Address: [1]Department of Dermatology, Medical Park Bahcelievler Hospital, [2]Department of Pediatric Hematology and Oncology, Medical Park Bahcelievler Hospital, [3]Department of Pathology, Istanbul University, Istanbul Medical Faculty, [4]Department of Pediatrics, Medical Park Bahcelievler Hospital, [5]Department of Pediatric Hematology and Oncology, Medical Park Bahcelievler Hospital, [6]Department of Pediatric Hematology and Oncology, Istanbul University, Istanbul Medical Faculty, Istanbul, Turkey
E-mail: gokhanokan8@hotmail.com

** Corresponding Author:* Gökhan Okan, MD Medical Park Bahcelievler Hospital, Dermatology Department Istanbul, Turkey.

Published:
J Turk Acad Dermatol 2014; **8 (4)**: 1484c2
This article is available from: http://www.jtad.org/2014/4/jtad1484c2.pdf
Key Words: Mycobacterium bovis, immunodeficiency, cutaneous Bacillus Calmette-Guerin infection

Abstract

Observation: Disseminated bacillus Calmette-Guerin infection is an uncommon condition which is usually associated with primary immunodeficiency. It is characterized by multiple and disseminated cutaneous lesions associated with systemic involvement. Here, we describe a case of disseminated bacillus Calmette-Guerin infection in a patient with severe combined immunodeficiency.

Introduction

Systemic infection associated with bacillus Calmette-Guérin (BCG) vaccine is characterized by multiple and disseminated cutaneous lesions. This is a rare and life threatening adverse event after BCG vaccination, usually related to cellular and severe combined immunodeficiency (SCID) or genetic suspectibility for mycobacterial disease. Family history of severe or fatal reactions to BCG may be a warning sign for early diagnosis of SCID [**1**]. We report a case of disseminated BCG infection in a patient with severe combined immunodeficiency.

Case Report

A 6-month-old Kazakh boy was referred to our hospital for hematopoietic stem cell transplant because of suspected diagnosis of Langerhans cell histiocytosis. He was diagnosed with T-B+NK+ SCID when he was aged 5 months. He had been vaccinated with BCG at the time of birth. He had 1 older brother who was healthy. There was no history of tuberculosis.

Physical examination showed with a 2-month-history of multiple erythematous papular lesions on the trunk, legs, and arms (**Figure 1**). Temperature was 38.5°C, heart rate was 164 beats/min, blood pressure was 144/86 mm Hg, the respiratory rate was 53 breaths/min, and oxygen saturation level was 80%. There was crepitation in both lungs. The liver and spleen were palpable at 2 cm below the costal margins. Chest radiography showed multifocal areas of consolidation in both lungs. Skeletal radiography showed extensive lytic bone lesions in the upper and lower extremities and cranium. Ultrasonography showed hepatosplenomegaly and kidney enlargement. Computed tomography scan of the chest showed diffuse reticulonodular infiltrates in both lungs. Magnetic resonance imaging of the brain showed numerous hypodense lesions in the cerebral hemispheres and brain stem.

A blood test for cell-mediated immune reactivity to *Mycobacterium tuberculosis* (Quantiferon-TB Gold

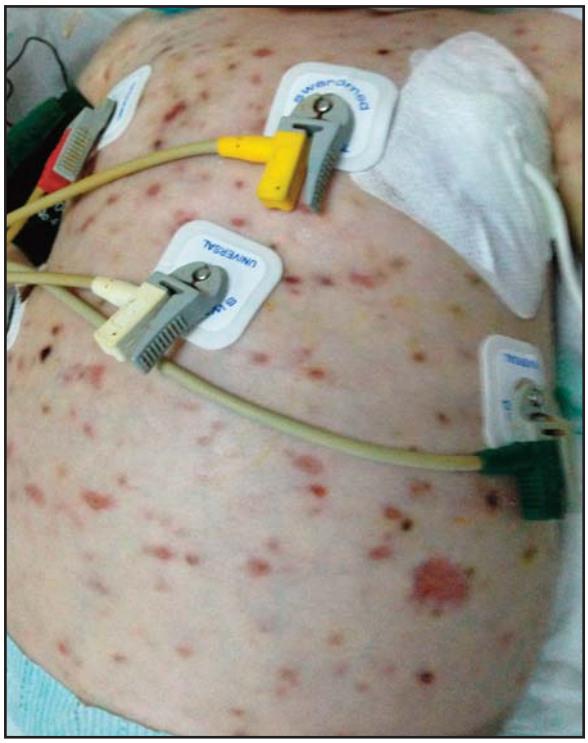

Figure 1. A 6-month-old Kazakh boy who presented with multiple erythematous papular lesions on the trunk, legs, and arms.

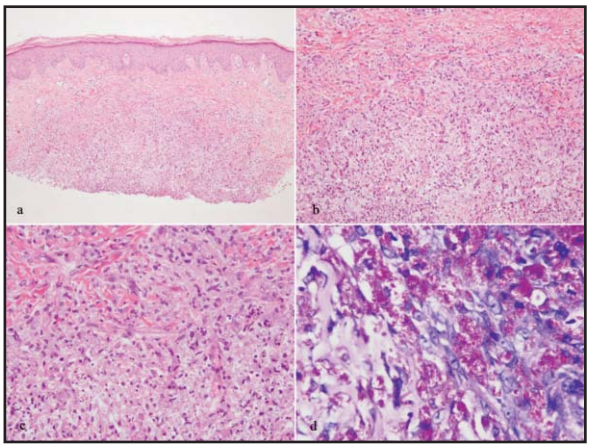

Figure 2. Histology of skin biopsy. (a) Dense inflammatory infiltrate in the mid dermis (hematoxylin-eosin, original magnification ×100). (b) The inflammatory infiltrate contained histiocytes with large, pale granular cytoplasm and few admixed lymphocytes. There was no granuloma formation (hematoxylin-eosin, original magnification ×20). (c) Inflammatory infiltrate with histiocytes and few admixed lymphocytes (hematoxylin-eosin, original magnification ×40). (d) Cytoplasm of histiocytes packed with acid-fast bacilli (Ehrlich-Ziehl-Neelsen, original magnification ×1000).

In-Tube, Qiagen, Hilden, Germany) was negative. Gastric lavage was negative for acid-fast bacilli. Bone marrow and skin biopsy showed stainable acid-fast bacilli but no hemophagocytosis. Histopathologic examination of the skin biopsy specimen showed a dense inflammatory infiltrate including histiocytes with large, pale granular cytoplasm and few admixed lymphocytes; there was no granuloma formation, but the cytoplasm of histocytes was packed with acid-fast bacilli (**Figures 2a, b, c and d**).

Based on the histopathologic and clinical findings, empiric antituberculosis quadruple therapy (isoniazid, rifampin, pyrazinamide, and streptomycin) and immunoglobulin replacement therapy were started, without waiting for culture results. After 3 weeks, there was no response to therapy. He developed respiratory insufficiency and was transferred to the pediatric intensive care unit. Moxifloxacin was added to antituberculosis treatment because of clinical deterioration. He died at 45 days after he was hospitalized; cause of death was acute respiratory distress syndrome and septic shock. Antimicrobial drug susceptibility testing was pending at the time of death. Molecular genotyping showed *Mycobacterium bovis* isolated from the patient after death, and susceptibility testing showed that the mycobacterium was sensitive to isoniazid and rifampin.

Discussion

BCG vaccine is a live-attenuated bacterial vaccine derived from wild-type Mycobacterium bovis. Disseminated BCG infection is life-threatening complication of BCG vaccine. The incidence of disseminated BCG disease ranged from 0.06 to 3.4 cases per million vaccination and the mortality rates remained high in immunocompromised patients [**2**]. Cellular immunodeficiency has been identified as the major risk factor for the disease. Although live-attenuated vaccination is contraindicated in persons with immunologic deficiency, BCG vaccination is usually inoculated prior to diagnosis. The immune response to mycobacterial infection is cell-mediated immunity. Patients who have SCID may be at risk for disseminated *M. bovis* infection [**3**]. Despite quadruple empiric antimycobacterial and immunoglobulin replacement therapy, our case had fatal outcome.

The diagnosis of disseminated BCG disease should be considered in SCID presenting with skin lesions despite of lacking common syste-

mic symptoms. The skin lesions of BGGitis typically include erythematous papules or pustules, with central crusting, disseminated over the trunk, thighs, and limbs, as observed in this patient. Some pustules could evolve into dry or crusted erosions and eventually leave atrophic scar with surrounding brownish post inflammatory halo within 1 to 4 weeks [**4**].

Kazakhstan has a high frequency of tuberculosis and has among the highest frequency of multidrug resistant tuberculosis in the world. Polymorphisms in some genes may be associated with tuberculosis in different ethnic groups. In Kazakhstan, multidrug resistant tuberculosis has been observed in 14% newly diagnosed and 45% treated tuberculosis patients [**5**]. The susceptibility to tuberculosis is controlled genetically in different populations. The DRB1*08:03 allele may be associated with tuberculosis progression and may affect the development of drug resistance and recurrent disease in Kazakhs [**6**]. Although the clinical diagnosis of SCID was the primary reason for the clinical course, genetic factors also may have contributed to the poor prognosis.

There are no clear guidelines about the most suitable appropriate treatment for disseminated *M. bovis* disease [**7**]. The present patient had *M. bovis* that was sensitive to isoniazid and rifampin; *M. bovis* intrinsically is resistant to pyrazinamide, and we do not know whether this organism was resistant to streptomycin.

Talbot et al reported that more than %70 of patients with disseminated BCG infection with SCID died even when they were aggressively managed[**8**]. Possible explanations for poor prognosis of this serious infection include delay in diagnosis or treatment, initial treatment with pyrazinamide to which BCG is resistant and developing of resistance to therapy.

BCG vaccination must be avoided in patients who have cellular immunodeficiency. History taking may help prevent potentially dangerous BCG vaccination, but the present patient had no family history of severe or fatal reactions to BCG vaccine.

In conclusion, disseminated cutaneous BCG infection is usually fatal if not diagnosed promptly. Although it is rare, Mycobacterium Bovis infection should be considered when facing a disseminated eruption in an immunocompromised patient.

References

1. Roxo-Junior P, Silva J, Andrea M, et al. A family history of serious complications due to BCG vaccination is a tool for the early diagnosis of severe primary immunodeficiency. Ital J Pediatr 2013; 39: 54. PMID: 24016734
2. Bernatowska EA, Wolska-Kusnierz B, Pac M, Kurenko-Deptuch M, Zwolska Z, Casonova JL, et al. Disseminated bacillus Calmette-Guerin infection and immunodeficiency. Emerg Infect Dis 2007; 13: 799-801. PMID:18044052
3. Casonova JL, Blanche S, Emile JF, Jouanguy E, Bordigoni P, Lambamedi S, et al. Idiopathic disseminated bacillus Calmette-Guerin infection: A French National retrospective study. Pediatrics 1996; 98: 774-778. PMID: 8885960
4. Barbagallo J, Taper P, Ingleton R, et al. Cutaneous tuberculosis: diagnosis and treatment. Am J Clin Dermatol 2002; 3: 319-328. PMID: 12069638
5. World Health Organization. Global Health Observatory. Country statistics: Kazakhstan. http://www.who.int/gho/countries/kaz/en/. April 17, 2014.
6. Kuranov AB, Kozhamkulov UA, Vavilov MN, et al. HLA-class II alleles in patients with drug-resistant pulmonary tuberculosis in Kazakhstan. Tissue Antigens 2014; 83: 106-112. PMID: 24397488
7. Ikincioğullari A, Doğu F, Çiftci E, et al. An intensive approach to the treatment of disseminated BCG infection in a SCID patient. Bone Marrow Transplant 2002; 30: 45-47. PMID: 12105777
8. Talbot EA, Perkins MD, Silva SFM, et al. Disseminated Bacillus Calmette-Guerin disease after vaccination: case report and review. Clin Infect Dis 1997; 24: 1139-1146. PMID: 9195072