CASE REPORT

Dissesminated BCG Infection in Immunocompromised Child: A Case Report

Chandrashekar H[1], Basavaraja Gangasamudra Veerappa[2], Nijaguna Nangundappa[3], Prahalad Kumar Appadorai[4], Sanjay K Shivappa[5]

Abstract

Bacillus Calmette-Guérin (BCG) is a live bacterial vaccine of *Mycobacterium bovis* to prevent tuberculosis (TB). It is given at birth or as early as possible according to the national immunization schedule. Usually, BCG is well tolerated. Severe adverse events following BCG vaccinations include local abscess, ulceration, and suppurative abscess. Disseminated BCGosis is the most devastating adverse event with a high fatality rate. It is seen most commonly in infants with primary immunodeficiencies or infants born with human immunodeficiency virus (HIV) infection.

Here we present a 7-month female child who presented initially with BCG adenitis and was later diagnosed with disseminated mycobacterial infection; hence investigated, and the diagnosis was confirmed as severe combined immunodeficiency (SCID).

Keywords: BCG adenitis, BCG vaccine, Primary immunodeficiency, Severe combined immunodeficiency (SCID).

Pediatric Infectious Disease (2022): 10.5005/jp-journals-10081-1368

Introduction

Bacillus Calmette-Guérin is a live bacterial vaccine containing a Danish 1331 strain of *M. bovis* used in India. The vaccine contains about 0.1–0.4-million live viable bacilli per dose. An amount of 0.05 mL of reconstituted vaccine is given in the lateral aspect of the upper arm intradermally.[1]

The vaccine is well tolerated. About 95% of BCG vaccine recipients experience a reaction at the injection site with a papule which may progress to become an ulcer, with healing after 2–5 months, leaving a superficial scar. This is considered a normal reaction. Severe adverse events reported include local site, abscess, severe ulceration, fistula, local suppurative lymphadenitis, ostitis, and osteomyelitis.

Disseminated BCGosis is a serious complication reported after the BCG vaccine, usually seen in infants born with primary immunodeficiencies and infants born with HIV seen in around 0.19–1.56 per million cases with a high fatality rate.[2]

Case Description

A 7-month-old female child presented with a history of redness and swelling in the left axillary region for 2 months. The child was fourth born to a non-consanguineously married couple with two previous sibling death in infancy. The first sibling was a male child who succumbed at the age of 6 months due to severe pneumonia. The third child died at the age of 3 months due to pneumonia.

On examination, the child had multiple matted lymph nodes in the right axilla, the largest measuring 3 × 3 cm (Fig.1). Fine needle aspiration cytology examination and Ziehl–Neelsen staining showed acid-fast bacilli. The specimen was also positive for cartridge-based nucleic acid amplification test (CB-NAAT) for *Mycobacterium*.

Gastric lavage specimen of the child was done for CB-NAAT analysis, and it was positive for *Mycobacterium*. The child was started on category-1 antitubercular therapy.

Primary immunodeficiency was suspected as the child had BCG lymphadenitis and considering the family history of previous sibling deaths. The child was worked up for primary immunodeficiency. The child had CD4 count of 11 cells/μL (0.6%) with gross reduction in immunoglobulins, IgG- <149 mg/dL (reference for age: 500–1200 mg/dL), IgM <20 mg/dL (reference for age: 43–239 mg/dL), suggestive of SCID. Clinical exome sequencing of the child was positive for a homozygous mutation of the recombination activating gene 1 (RAG1) gene, and the diagnosis

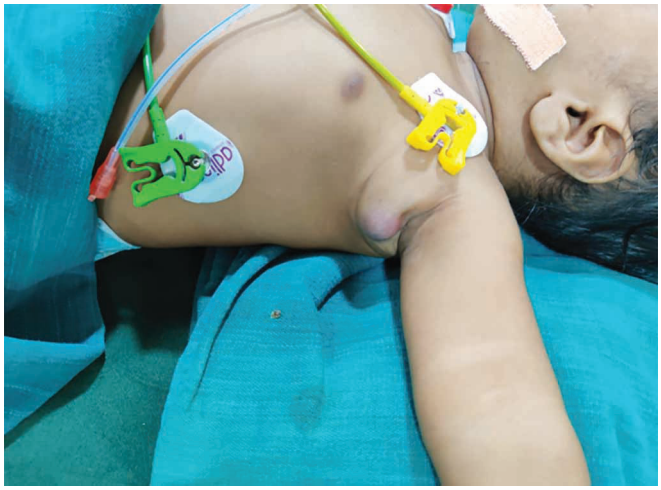

Fig. 1: Right axillary lymphadenopathy

[1–5]Department of Pediatric, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

Corresponding Author: Chandrashekar H, Department of Pediatric, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India, Phone: +91 8147438277, e-mail: chandra2.shekar2@gmail.com

How to cite this article: H C, Veerappa BG, Nangundappa N, *et al.* Dissesminated BCG Infection in Immunocompromised Child: A Case Report. Pediatr Inf Dis 2022;xx(xx):1–2.

Source of support: Nil

Conflict of interest: None

of SCID was confirmed. The child was planned for hematopoietic stem cell transplantation.

Discussion

Bacillus Calmette-Guérin vaccine is a live bacterial vaccine covered in the national immunization schedule of India, given at birth or as early as possible to prevent severe forms of TB at an early age. Efficacy of the vaccine is variable, with upto 82% protection against pulmonary TB in neonatal vaccination.[1] The vaccine is usually well-tolerated with minor local reactions. Severe complications like BCG adenitis, osteomyelitis, and disseminated BCGosis are almost always encountered in immunodeficient recipients. Hence evaluation of immunodeficiency should always be considered in severe adverse events following BCG vaccination. Most commonly associated immunodeficiencies are SCID, chronic granulomatous disease, Mendelian susceptibility to mycobacterium diseases (MSMD), and infants born to HIV positive mothers.[3,6]

Bacillus Calmette-Guérin adenitis of a local lymph node in the immunization site is managed conservatively, but suppuration should be aspirated to prevent sinus formation. Surgical excision, but not incision, is recommended if needle aspiration fails. Other complications, such as chest wall abscess, might necessitate surgical intervention followed by a course of ATT.[4]

Fever (91.1%), skin lesions (88.2%), lymphadenopathy (76.5%), osteomyelitis (58.8%), and hepatosplenomegaly (35.3%) were the most common symptoms of BCGosis.[5] Systemic complications usually occur 6 months after vaccination. Definitive BCGosis is diagnosed by the presence of systemic symptoms (such as fever or subfebrile states, weight loss, or stunted growth), with at least two areas of involvement beyond the site of a BCG vaccination, identification of the *M. bovis* BCG subspecies by culture and/ or PCR, as well as, typical histopathological changes with granulomatous inflammation.[6] Disseminated disease is associated with case fatality rates of 80–83%.[2]

Mycobacterium bovis BCG strains are inherently resistant to pyrazinamide. A three or four drug antimycobacterial treatment, which includes a combination of rifampicin, and ethambutol, together with either an aminoglycoside, fluoroquinolone, and/or isoniazid. European society for immunodeficiencies recommends that antimycobacterial treatment, consisting of a combination of four or more antimycobacterial agents, be given to patients with BCGosis and primary immunodeficiency until full recovery. Usually 12–18 months. After that, a prophylactic regimen with two antimycobacterial agents should be continued until complete immunological reconstitution after a hematopoietic stem cell transplant.[6] Interferon gamma (INF-γ) may be considered an adjuvant immunotherapy in chronic granulomatous disease and MSMD.[6]

Immunodeficiencies were strongly suspected in the index case due to the presence of BCG adenitis. The most typical manifestation of immunodeficiency in children is recurrent sinopulmonary infections. Although infections are common in children in general, an infection exceeding the expected frequency and usually involving multiple sites can suggest immunodeficiency. A single, severe, opportunistic, or unusual infection can also be the presentation of an immunodeficiency.

Various primary immunodeficiencies associated with increased susceptibility to *Mycobacterium* include phagocytic defects like chronic granulomatous disease (CGD), combined immunodeficiencies including SCID, and Mendelian susceptibility to *Mycobacterium*. Although in our index case, complete blood count (CBC) showed normal lymphocyte count in the peripheral blood, functional T cell counts like CD4 and CD8 counts were extremely low, highly suggestive of SCID.

Mendelian susceptibility to mycobacterium diseases is a group of genetic disorders due to inborn errors of INF-γ, interleukin 12B mediated immunity. MSMD is associated with increased susceptibility to TB, other less virulent *Mycobacterium,* and disseminated BCG. Occasionally increased risk of infection to other intracellular pathogens like *salmonella* and candidiasis.[7]

In conclusion, the authors want to reinforce the notion to strongly suspect immunodeficiency disorders when confronted with rare infectious presentations like BCG adenitis in an infant. The authors also wants the bring awareness about the presentation and management of various BCG vaccine-related complications in an infant with known or suspected immunodeficiency.

References

1. Balasubramanian S, Shastri DD, Chatterjee P, et al. IAP Guidebook on Immunization 2018-2019: By advisory committee on vaccines & immunization practices (ACVIP). 3rd Balasubramanian S, Shastri DD, Shah AK, Chatterjee P, Pemde HK, Shivananda S, et al., editors. New Delhi, India: Jaypee Brothers Medical; 2019.
2. Rezai MS, Khotaei G, Mamishi S, et al. Disseminated Bacillus Calmette-Guerin infection after BCG vaccination. J Trop Pediatr 2008;54(6):413–416. DOI: 10.1093/tropej/fmn053
3. Norouzi S, Aghamohammadi A, Mamishi S, et al. Bacillus Calmette-Guérin (BCG) complications associated with primary immunodeficiency diseases. J Infect 2012;64(6):543–554. DOI: 10.1016/j.jinf.2012.03.012
4. Govindarajan KK, Chai FY. BCG adenitis-need for increased awareness. Malays J Med Sci 2011;18(2):66–69. https://pubmed.ncbi.nlm.nih.gov/22135589
5. Shahmohammadi S, Saffar MJ, Rezai MS. BCG-osis after BCG vaccination in immunocompromised children: case series and review. J Pediatr Rev 2014;2(1):47–54. DOI: 10.7508/JPR-V2-N1-62-74
6. Ong RYL, Chan SWB, Chew SJ, et al. Disseminated Bacillus-Calmette-Guérin infections and primary immunodeficiency disorders in Singapore: a single center 15-year retrospective review. Int J Infect Dis 2020;97:117–125. DOI: 10.1016/j.ijid.2020.05.117
7. Bhattad S. Mendelian susceptibility to Mycobacterial disease: a clinical and laboratory approach. Pediatr Inf Dis 2019;1(1):34–36. DOI: 10.5005/jp-journals-10081-1108