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Case Report

First Reported Case of Bacillus Calmette–Guérin Associated Mastitis in an Immunocompetent Infant: A Rare Complication of Vaccination

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ABSTRACT

Mastitis beyond the neonatal period is an uncommon condition in children, with *Staphylococcus aureus* being the most frequently implicated pathogen. However, mastitis due to *Mycobacterium bovis* Bacillus Calmette-Guérin (BCG) has not been previously reported. Herein, we present the first case of mastitis following a BCG vaccination in a 6-month-old immunocompetent infant.

Keywords: Bacillus Calmette-Guérin, *Mycobacterium bovis*, mastitis

Introduction

The Bacillus Calmette-Guérin (BCG) vaccine, derived from an attenuated strain of *Mycobacterium bovis (M. bovis),* has been in use for over a century (first administered to humans in 1921) and it remains the only widely used vaccine for tuberculosis (TB) prevention (1). It is one of the most broadly administered vaccines globally, with more than 100 million newborns receiving BCG each year as part of infant immunization programs (2). Multiple BCG vaccine strains (e.g., Danish 1331, Tokyo, Moscow) are employed worldwide, all of which are live attenuated *M. bovis* preparations with comparable efficacy (1). In general, BCG has a strong safety profile in immunocompetent infants. Expected local reactions include a small papule at the injection site which may ulcerate and heal with a scar, often accompanied by mild regional lymphadenopathy (1,3). More significant adverse events are rare. Severe or disseminated BCG infections occur in approximately 1 to 15 per 10 million vaccinees, predominantly among individuals with underlying immunodeficiencies (1). Intermediate complications such as osteitis have been reported at rates ranging from 0.01 to 30 per million doses (1). Among immunocompetent children, the most frequently observed complications are localized, including suppurative regional lymphadenitis or, less commonly, cold abscess formation at the vaccination site. Overall, the incidence of BCG-related adverse events remains well below 1% in most published series (1). Nevertheless, isolated case reports have documented that even immunocompetent hosts can occasionally develop atypical, localized infections caused by the attenuated vaccine strain, such as abscesses or granulomatous lesions in tissues distant from the inoculation site (1).

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The breast has not previously been described as a site of BCG-related infection. Mastitis is uncommon in children and, beyond the neonatal period, typically occurs in those aged 8 years or older. Most cases are caused by *Staphylococcus aureus*, and less frequently by other pathogens such as group A *Streptococcus*, and gram-negative bacilli (4). Mycobacterial infection, particularly with an attenuated vaccine strain, has not been recognized as a cause of mastitis in immunocompetent children. We conducted a literature search (PubMed and Google Scholar, up to October 2025) using the terms "BCG vaccine," "*M. bovis* BCG," "mastitis," and "breast abscess," and found no previously published cases of BCG-related mastitis. Herein, we describe what appears to be the first documented case of mastitis caused by *M. bovis* BCG (Moscow strain) following a routine BCG vaccination in an otherwise healthy 6-month-old infant. This rare presentation expands the known spectrum of BCG vaccine complications and highlights the importance of considering atypical mycobacterial infections in unusual pediatric presentations.

Case Report

A previously healthy 6-month-old girl presented with swelling and erythema of the left breast. There was no history of trauma or local skin infection. She had received the BCG vaccine at 2 months of age. A typical local reaction developed with small ulceration and healed spontaneously without lymphadenitis. On physical examination, a fluctuant, erythematous swelling was noted on the left breast (Figure 1), and an erythematous nodule was observed at the BCG vaccination site. No lymphadenopathy was observed. Laboratory tests revealed a white blood cell count of 12×10^9/L with 55% neutrophils, a C-reactive protein level of 10 mg/L, and an erythrocyte sedimentation rate of 18 mm/h. Ultrasonographic evaluation showed features suggestive of a breast abscess. Empirical intravenous ampicillin/sulbactam (200 mg/kg/day) therapy was initiated; however, there was no clinical improvement. Therefore, the patient underwent incision and drainage. Gram stain revealed no microorganisms, and routine bacterial cultures were negative. Despite drainage and antibiotic therapy, swelling persisted, and a draining fistula subsequently developed at the incision site. Consequently, a pus sample was submitted for mycobacterial culture and polymerase chain reaction (PCR) testing. Reverse-transcription PCR detected the *Mycobacterium tuberculosis* complex (MTBC) in two consecutive samples. Deoxyribonucleic acid amplification from the abscess material was performed using a commercial multiplex real-time PCR assay targeting the IS6110, 16S ribosomal ribonucleic acid, and *rpoB* regions specific to the MTBC. In order to further differentiate the strain, RD1 and RD9 deletion analysis was used, confirming *M. bovis* BCG. Spoligotyping subsequently identified the isolate as the Moscow sub-strain. Culture of the drained pus yielded slow-growing acid-fast bacilli on Löwenstein-Jensen medium after four weeks, consistent with BCG. Drug susceptibility testing was not formally performed; however, intrinsic resistance to pyrazinamide was inferred based on the classification of the organism as *M. bovis* BCG. The patient was treated with isoniazid (10 mg/kg/day) and rifampin (15 mg/kg/day) for 6 months as an outpatient and recovered without complications. A summary of the chronological sequence of clinical events is provided in Figure 2. Follow-up immunological evaluations, including lymphocyte subsets, mitogen-induced lymphoproliferation, dihydrorhodamine assay, and flow cytometry for interleukin-12Rβ1 and interferon-gamma-γ (IFN-γ) expression, were all within normal limits. Serologic testing for human immunodeficiency virus was negative.

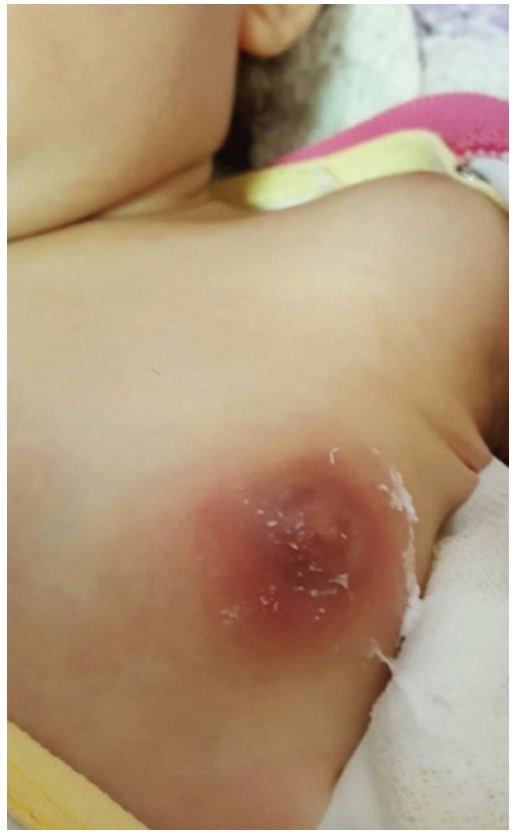

Figure 1. Erythematous, fluctuant swelling on the left breast, consistent with a localized abscess

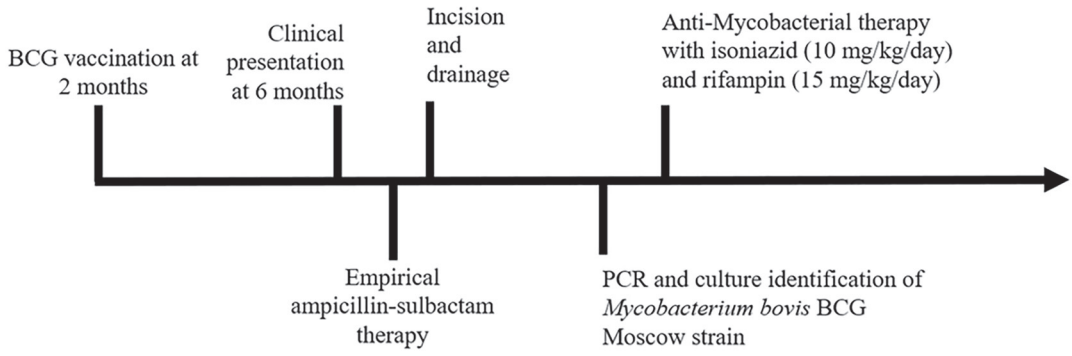

Figure 2. Clinical timeline summarizing the main events in the patient's course
BCG: Bacillus Calmette-Guérin, PCR: Polymerase chain reaction

Discussion

The BCG vaccine remains a cornerstone of TB prevention in infants worldwide, due to its proven efficacy in reducing severe pediatric TB (e.g., miliary TB and TB meningitis) (5). It is generally considered a safe vaccine; in healthy individuals, the vast majority of adverse reactions are limited to mild local effects (1,3). However, as a live attenuated mycobacterium, BCG is capable of causing disease under certain circumstances. Known adverse events range from injection site abscesses and suppurative lymphadenitis to osteomyelitis and disseminated infection (1). The most serious complications, such as disseminated BCGosis, are exceedingly rare and occur almost exclusively in immunocompromised patients with impaired cell-mediated immunity (1).

Severe BCG-related complications are rarely observed in immunocompetent children. Nevertheless, sporadic reports have documented localized infections in otherwise healthy infants, suggesting that even vaccines considered safe can occasionally lead to atypical manifestations. Among these, chest wall and cutaneous abscesses attributable to BCG have been reported in immunocompetent children, occurring at sites distant from the vaccination site (6,7). However, mastitis as a complication of BCG vaccination has not been previously reported.

BCG vaccine complications are most commonly observed within the first six months after vaccination, but cases have been reported as late as 12 months post-vaccination (8). The optimal management of these complications remains uncertain. Disseminated disease occurs only exceptionally and is observed primarily in immunocompromised children (8,9). In our patient, the breast abscess developed approximately 4 months after BCG, which is within the typical timeframe for vaccine complications. In terms of clinical features, the published cases, similar to ours typically involved a localized swelling or abscess with minimal systemic symptoms. For instance, an infant in a Korean case had a tender, erythematous subcutaneous mass on the chest wall but no fever or constitutional signs (10). Similarly, our patient's mastitis manifested as a localized breast abscess without systemic illness. In all such cases, routine bacterial cultures of abscess fluids were negative, prompting further investigation for mycobacterial etiology, as was the case here.

Our patient's presentation aligns with other published reports of distant-site BCG infections in immunocompetent children. For example, Polat and Belen (6) described a cold abscess of the chest wall with rib destruction attributed to hematogenous spread of the BCG strain. Okazaki et al. (7) reported a cutaneous TB granuloma at a distant body site, confirmed by multiplex PCR to be the BCG vaccine strain. Lee et al. (10) also documented a BCG-induced anterior chest wall abscess without dissemination, emerging seven months post-vaccination.

The pathogenesis of BCG-related complications is not completely understood. In our case, direct lymphatic spread from the vaccination site may have contributed to the development of mastitis. Alternatively, local inoculation at a site of minor trauma or microabrasion cannot be entirely excluded. The presence of an erythematous nodule at the vaccination site concomitant with breast involvement suggests a potential link through contiguous or lymphatic spread. Regardless of the exact route, the temporal association between vaccination and breast abscess formation, coupled with the identification of the BCG Moscow strain from the abscess, indicates a causal link.

Management of BCG-related complications remains challenging. While incision and drainage are often performed for abscesses, they may not be sufficient in cases

of mycobacterial infections, and antimicrobial therapy is usually required (8,11). Our patient did not respond to routine antibiotics, which is consistent with the intrinsic resistance of *M. bovis* to several antimicrobial agents, including pyrazinamide. The persistent drainage and lack of clinical improvement prompted further testing, ultimately confirming mycobacterial infection. Once identified, targeted therapy is essential. Anti-tuberculous pharmacotherapy is the cornerstone of treatment. In previous reports, favorable outcomes have been achieved with anti-mycobacterial regimens (11). Our patient responded well to a six-month course of isoniazid and rifampin, mirroring successful treatment protocols in the literature (9,10). Reported cases have generally been managed with a combination of surgical and medical therapy. Surgical intervention (incision and drainage or excisional surgery) is often performed to remove abscess collections or obtain diagnostic material (8); however, surgery alone does not eradicate the infection. When conventional antibiotics fail to resolve presumed pyogenic abscesses, especially in recently vaccinated infants, clinicians should maintain a high index of suspicion for BCG-related disease, even if the child is immunocompetent. The favorable response to a combination of isoniazid and rifampin underlines the importance of early consideration of mycobacterial etiology in non-resolving mastitis cases.

In addition, evaluation for underlying immunodeficiency is critical, since disseminated or unusual manifestations of BCG infection are strongly associated with primary immunodeficiencies affecting the interleukin-12/IFN-γ axis or chronic granulomatous disease (12). In our patient, the comprehensive immunological work-up was normal, supporting the interpretation that this was a sporadic, localized complication in an otherwise healthy infant. This finding parallels other reports in which no immune abnormalities were detected despite the presence of BCG complications (6,7). By contrast, when BCG causes disseminated disease, it is typically in the context of conditions such as severe combined immunodeficiency, chronic granulomatous disease, or genetic defects in IFN-γ signaling. The absence of any immune disorder in our patient reinforces the interpretation that her mastitis was a chance, localized complication of the BCG vaccination rather than a marker of undiagnosed systemic susceptibility.

To the best of our knowledge, this is the first reported case of BCG-induced mastitis in an otherwise healthy infant. Previous reports have described complications such as lymphadenitis, osteomyelitis, and distant-site abscesses, but none have documented breast involvement (6,13). Our case broadens the understanding of BCG-associated clinical presentations and highlights the capacity of *M. bovis* BCG to infect diverse tissues under specific conditions. Fortunately, similar to other localized BCG infections, mastitis responded well to timely diagnosis and appropriate treatment. For healthcare providers, recognizing the atypical presentations of BCG complications is essential, particularly when standard therapies fail. This case adds breast mastitis as a novel clinical manifestation to the existing spectrum of BCG-related adverse effects.

Conclusion

Our case expands the clinical spectrum of BCG-related complications and highlights mastitis as a rare but potential complication in immunocompetent infants. Clinicians should maintain a high index of suspicion for atypical presentations of BCG infection, particularly in cases of mastitis unresponsive to conventional therapy in order to ensure timely and effective management.

Ethics

Informed Consent: Informed consent has been obtained from parents for incorporating the patient details into the manuscript.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.P., Concept: N.A.Ü., M.P., Design: M.P., Data Collection or Processing: N.A.Ü., M.P., Analysis or Interpretation: N.A.Ü., M.P., Literature Search: N.A.Ü., M.P., Writing: N.A.Ü., M.P.

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