Allergy and Immunology

AIMS Allergy and Immunology, 10(3): 184–198.
DOI: 10.3934/Allergy.2026013
Received: 10 July 2026
Revised: 13 September 2026
Accepted: 21 September 2026
Published: 23 September 2026

https://www.aimspress.com/journal/Allergy

Review

Complications related to Bacillus Calmette-Guérin vaccine and management approaches: A review

Sezer Okay*

Department of Vaccine Technology, Vaccine Institute, Hacettepe University, Ankara, Türkiye

* **Correspondence:** Email: sezerokay@gmail.com.

Abstract: Tuberculosis (TB) is an infectious disease, particularly preventable in children using the Bacillus Calmette-Guérin (BCG) attenuated vaccine. Individuals with strong immune systems can safely receive the BCG vaccine; however, certain factors such as age, immune system problems, vaccine dose, and injection route can cause side effects. Mild local reactions and ulceration at the intradermal injection site are common after BCG vaccination. However, in individuals with weakened immune systems, serious complications such as suppurative lymphadenitis, osteitis, or disseminated BCG disease (BCGosis) may develop. Therefore, the BCG vaccine should be carefully considered in individuals infected with human immunodeficiency virus (HIV) and patients with primary immunodeficiency disorder (PID). Treatment methods depend on the severity of the condition. In cases of uncomplicated injection site ulceration and minor, non-suppurative lymphadenopathy, local wound care and observation are conservative treatments. However, management approaches for deep or disseminated disease include surgical interventions and antimycobacterial therapy in addition to immunological evaluation. Furthermore, while hematopoietic stem cell transplantation may be considered in some PID patients, urgent enzyme replacement therapy using polyethylene glycol–modified adenosine deaminase (ADA) is necessary in patients with ADA deficiency. In conclusion, the BCG vaccine is a powerful tool in preventing TB, especially in childhood, and is safe in people with healthy immune systems. However, in individuals with any immune system–related disease, the administration of this attenuated vaccine should be evaluated by specialist physicians, and immediate intervention should be sought in case of serious side effects.

Keywords: adverse event; BCG; BCGosis; vaccination

1. Introduction

Tuberculosis (TB) is an infectious disease caused by various strains of mycobacteria, especially by *Mycobacterium tuberculosis* in humans. According to the World Health Organization (WHO), at least 10 million people contract TB each year, and more than 1 million die from it. Therefore, *M. tuberculosis* is the leading infectious agent causing death by itself, and TB ranks among the top 10 causes of death worldwide [1].

TB is a preventable disease, especially in children. The Bacillus Calmette-Guérin (BCG) vaccine is a live attenuated strain of *Mycobacterium bovis*, developed by Albert Calmette and Camille Guérin between 1908 and 1921, and it is widely used for the prevention of TB in childhood [2,3]. Every year, the BCG vaccine, which is safe for individuals with a competent immune system, is administered to approximately 100 million children. However, factors including the vaccinee's age, immune status, and vaccinator's skills, in addition to the vaccine dose and *M. bovis* strain used, affect the extent of responses to this vaccine. BCG may cause mild local reactions and ulceration of the intradermal injection site [4]. Other adverse events include suppurative lymphadenitis, osteitis, and BCG disease, which can be disseminated (BCGosis) or localized (BCGitis) [5,6]. Huang et al. evaluated 95 children with severe BCG-related complications and reported 33 patients with injection site reactions: 36.4% ulceration, 9.1% lichenoid lesions, 9.1% granulation hyperplasia, and 45.4% deep abscesses (Figure 1). Moreover, 55 patients had lymphadenitis, and 7 children had BCGosis [7].

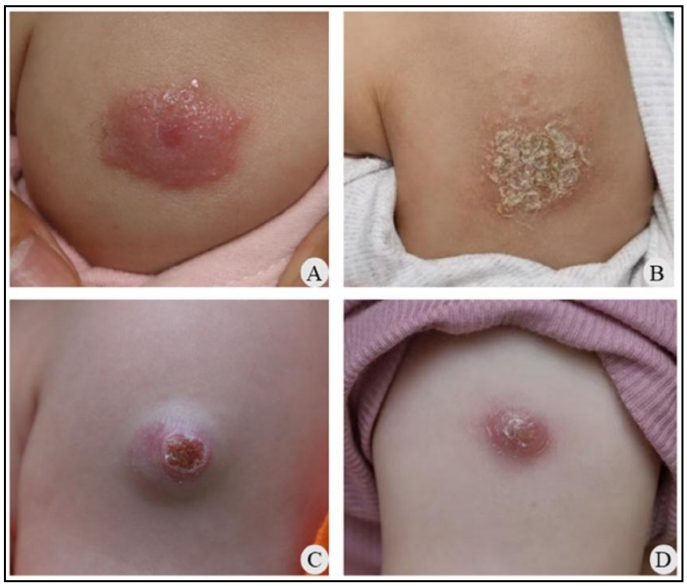


Figure 1. Adverse reactions in the injection site of BCG vaccine: (A) ulceration, (B) lichenoid lesions, (C) granulation hyperplasia, and (D) deep abscesses. The figure was reproduced from [7], licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

The aim of this review is to describe the common, mild, and serious complications of BCG vaccination, as well as the risk factors and groups. Also, the outcomes of overdose and incorrect injection route are evaluated. Moreover, the status and consequences of BCG vaccination in HIV-

infected individuals and patients with primary immunodeficiency disorder (PID) are discussed. Finally, the management of BCG complications is described.

2. Review methodology

A comprehensive literature search was conducted to identify published evidence concerning complications following BCG vaccination. The search was performed in PubMed/MEDLINE, Scopus, Web of Science Core Collection, and Google Scholar using the following core search terms with appropriate database-specific adaptations: ("*BCG vaccine*" OR "*Bacillus Calmette-Guérin*" OR "*Bacille Calmette-Guérin*" OR "*BCG*") AND ("*complication*" OR "*adverse event*" OR "*adverse effect*" OR "*vaccine-associated*" OR "*vaccine-related*") AND ("*management*" OR "*treatment*" OR "*therapy*" OR "*diagnosis*" OR "*outcome*" OR "*risk factors*") AND ("*immunodeficiency*" OR "*HIV*" OR "*PID*" OR "*SCID*" OR "*BCGosis*" OR "*BCGitis*"). In addition, global TB reports and other sources of information reported by the WHO were examined.

No restriction on publication year was initially applied in order to capture early reports describing rare but clinically important BCG complications. Peer-reviewed human studies published in English primarily within the last 10 years and with accessible full-text were selected, without restrictions regarding age, gender, or geographic location. The following articles were excluded: Studies regarding experimental or non-vaccine uses of BCG; animal, in vitro, and purely laboratory-based studies; publications lacking sufficient clinical data and evidence on BCG-related complications; duplicate publications; articles that had not undergone peer review; articles that were published in languages other than English, or for which the full-text was inaccessible.

3. Complications

3.1. Common complications

BCG causes a predictable course of local inflammation in most recipients and a set of commonly reported systemic and cutaneous reactions [8]. These encompass early local ulceration and a range of skin and regional-node findings not threatening life [9]. Erythema, induration [10], ulceration, scarring [11,12], blistering, and keloid formation [13] are typical local findings at the injection site reported as common cutaneous complications.

3.2. Mild complications

3.2.1. BCG lymphadenitis

Lymphadenitis is the most common mild complication of BCG, characterized by the enlargement of the ipsilateral regional lymph node next to the injection site. For the BCG vaccine to be successful, *M. bovis* needs to rapidly multiply at the injection site and move through the lymphatic system to the regional lymph nodes. Therefore, subclinical non-suppurative lymphadenitis is expected within 6–24 months after vaccination and usually regresses spontaneously within weeks without leaving any sequelae. However, a suppurative form of BCG lymphadenitis may develop as the affected lymph nodes progressively enlarge; in this case, swelling, edema, erythema, and

increased pigmentation of the overlying skin may be observed, along with pustule formation. Suppurative glands may recover spontaneously through perforation and sinus formation; later, the sinus is closed by cicatrization. Occasionally, fine-needle aspiration (FNA) can be used to speed up healing. Surgical excision is rarely necessary in cases where FNA fails or in the drainage of BCG nodules [14,15]. The suppurative condition can develop into necrotizing lymphadenitis, which may require surgical intervention [16].

A meta-analysis including 21 studies reported the mean incidence of BCG lymphadenitis to be 4.45% (95% CI: 3.02%–6.15%), which was estimated using the random effect model due to the remarkable heterogeneity of the studies included [17]. In the study of Villanueva et al. involving 1387 participants who received the BCG vaccine, the incidence of injection site abscess and regional lymphadenopathy was reported as 3%, but this rate was found to be higher in revaccinated individuals. Age and gender were associated with BCG lymphadenopathy, but not with injection site abscess [18]. Vaghasiya et al. reported 13 cases under two years of age who developed BCG lymphadenitis after receiving the BCG vaccine in the left arm. Left axillary lymph node enlargement was observed in all cases, and the aspirates were pus-like (46%), mixed with blood (39%), and cheese-like necrotic (15%). Diagnostic categories were defined as necrotizing granulomatous lymphadenitis (46%), necrotizing lymphadenitis (23%), suppurative granulomatous lymphadenitis (8%), non-necrotizing granulomatous lymphadenitis (8%), and suppurative lymphadenitis/abscess (15%) [19]. Another study included 60 children with BCG lymphadenitis, who received an initial anti-TB therapy (ATT) for 1–9 months. However, ATT was ineffective in 52 children with lymph nodes approximately 3 cm in size, and surgical intervention was performed to prevent spontaneous rupture and sinus formation [20].

3.2.2. Rare mild complications

Papulonecrotic tuberculid [21], lupus vulgaris [22], and other granulomatous eruptions [23] have been described as less common and non-serious systemic or immune-mediated skin manifestations, particularly in the context of altered host immunity or BCG immunotherapy exposures. Recently, cases of erythema and inflammation at the site of BCG scars have been reported following the administration of COVID-19 mRNA vaccine (Figure 2a) [24–26]. Additionally, BCG vaccine can induce the formation of childhood-onset keloids (Figure 2b), with the vast majority (92.9%) reported in females in a cohort in Japan [27].

3.3. Serious complications

Severe BCG-related diseases are uncommon but important because they can be protracted or fatal without prompt recognition and treatment. A serious complication is the BCGosis, presenting with multiorgan involvement, which can be life-threatening. BCGosis is classically associated with primary immunodeficiency disorders and requires rapid diagnostic and therapeutic work-up [19].

BCG can also cause bone infections (periostitis/osteomyelitis/osteitis), which may present months after vaccination and can require prolonged treatment [28]. Lin et al. reviewed 34 studies on BCG osteomyelitis/osteitis covering 331 cases, mostly diagnosed by culture and histopathology, while polymerase chain reaction (PCR) was rarely used. Lesions were observed in the lower limbs in 55.6%, in the upper limbs in 15.4%, in the axial skeleton in 26.0%, and in multiple bones in 3.0% of all cases. Surgical intervention was reported in 80 cases; 50 of these were for diagnostic purposes, while the

remainder involved total/partial bone excision, incision/drainage, trepanation, and multiple surgeries. Details of ATT were provided for 64 patients, and almost all cases responded well. In only one case, diagnosed late, a 14-mm developmental delay in the left leg was observed due to damage to the growth plate of the left tibia. Four more cases reported delayed leg development, while one case each presented with arm deformity, scoliosis, and disability involving multiple bones [29].

BCG-related caseating granulomas in draining lymph nodes and conversion to suppurative lymphadenitis or abscess are well described and may need surgical management [30]. Caseating granulomas due to BCG vaccination can also be seen on the glans penis [31]. Moreover, case reports include death from BCGosis in infants with severe combined immunodeficiency (SCID) despite intensive therapy and hematopoietic stem cell transplantation attempts [32,33].



Figure 2. Inflammation of the BCG scar following COVID-19 mRNA vaccine (A), and BCG-induced childhood-onset keloid formation (B). The figure was reproduced from [24] and [27], licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

4. Risk factors and groups

Certain host and programmatic factors consistently associate with more severe or atypical BCG outcomes, and they should guide vaccination policy and post-vaccination vigilance. Early identification of vulnerabilities reduces morbidity and informs management. PID is the strongest risk factor for severe or disseminated BCGosis, including SCID, chronic granulomatous disease (CGD), and Mendelian susceptibility to mycobacterial disease (MSMD) [3]. As to the young age and family history, infants (especially neonates) and those with a family history of immunodeficiency are at elevated risk, prompting recommendations to defer vaccination until PID is ruled out in such contexts [34].

Vaccine strain is another risk factor affecting prevalence and size of the scar, and there may be gender-based differences in the effects on disease rates [35]. More reactogenic strains, incorrect dilution, improper injection technique, or storage/preparation errors can increase local complications

and contribute to variability across settings [36]. Overdose or administration errors have caused unusually severe local disease and require specific management and reporting when they occur [37,38].

5. Overdose and incorrect injection route

The multidose BCG vaccine is mostly provided in amber-colored vials to be protected from light. The lyophilized vaccine is reconstituted using physiological saline. After this process, it should be stored at 2–8 °C (36–46 °F) and should be used within 4–6 h; unused reconstituted vaccine should be discarded. The BCG vaccine is administered intradermally, and the injection site is the upper left arm in many countries. The injection volume is 0.05 mL for infants under one year old, and 0.1 mL for those over one year. Accurate administration creates a small weal or a bleb on the skin, which develops into a papule within 2–3 weeks and reaches a size of 4–8 mm within 5–6 weeks. Finally, the papule ulcerates, and the wound heals within 2–5 months post-vaccination, often leaving a scar at the injection site [39,40].

Some cases of BCG vaccine overdose have been reported. According to the report by Wei et al., a BCG vaccine, mistakenly diluted to 2 instead of 3 mL, was administered as 0.1 mL to 20 healthy infants under one year of age. An ATT was not planned, as the infants initially showed no adverse effects. Later, abscesses formed at the injection sites in three infants, but these healed within six weeks without any treatment, and mature injection site scars occurred without complications [41]. Qureshi et al. reported that 0.05 mL of ONCO-BCG vaccine, normally used in patients with urinary bladder cancer, was accidentally injected into 26 newborns. The administered dose (20 mg) was 80 times higher than the routine BCG vaccine given to infants. An initial ATT was started with 10 mg/kg/day of isoniazid and 15 mg/kg/day of rifampicin for at least three months. Skin lesions at the injection site were observed in 61.5% of infants, and the vast majority resolved within two weeks. One infant developed axillary lymphadenopathy, and another developed intracranial bleeding. None of the babies developed clinical TB. All infants with one year of follow-up survived [42].

In some cases, incorrect injection routes were used for the administration of BCG. Puliyel et al. reported that 857 infants in Manchester were mistakenly given percutaneous BCG vaccine intradermally, and 556 of them sought follow-up at health centers. Axillary lymphadenopathy was observed in 48 infants, papules and ulcers developed in six infants each, and one had an injection site abscess. Additionally, an infant diagnosed with SCID received ATT but died from pulmonary hemorrhage following a bone marrow transplant, with no sign of BCGosis [43].

In one case of BCG vaccine misadministration, a 30-year-old man who had previously received two BCG vaccines at ages 2 and 14 was mistakenly given an intramuscular dose of BCG. The injection site swelled within a week, and pus formed within a month. He was given 300 mg of isoniazid daily for four weeks as ATT. Later, he developed draining sinuses at the injection site and in the previous BCG scar, a palpable lymph node in the left axilla, and muscle atrophy in his left upper arm. Five months following the injection, due to continued ulceration, discharge, and muscle atrophy, only superficial scarring was initiated [44]. In a similar case, a 51-year-old man with bladder cancer inadvertently received the BCG vaccine intramuscularly for four weeks. In addition to frequent adverse reactions (erythema, tenderness, and indurations), a rare complication, gluteal swelling, was also detected. A *M. tuberculosis* complex resistant to pyrazinamide was isolated from the patient. Management included ATT with isoniazid, rifampicin, ciprofloxacin, and ethambutol in addition to incision and drainage of abscess; the patient fully recovered nine months later [45].

According to the national vaccination schedule of the Ministry of Health in Türkiye, all two-month-old infants receive 0.05 mL BCG vaccine intradermally. However, in one case, a healthcare worker accidentally injected 1 mL (20 times higher than the routine dose) of BCG vaccine intramuscularly into a two-month-old infant. The baby was quickly taken to the hospital after the error was discovered, and no complications were found other than mild redness at the injection site. After six days of hospitalization, the baby was discharged with prophylaxis on 10 mg/kg/day of isoniazid, and antibiotic treatment continued for six months. No abnormalities were observed during a one-year follow-up [46].

6. BCG vaccination in individuals with impaired immunity

6.1. BCG vaccination in HIV-infected people

In countries where TB is prevalent, the WHO's recommendation for the BCG vaccine until 2007 was that it should be contraindicated in infants with symptomatic HIV infection. However, in 2007, this recommendation was revised to make it a complete contraindication in children infected with HIV based on the retrospective studies reporting the development of BCGosis in children infected with HIV and the gaps about the protection of BCG against TB in these children [47,48]. Nevertheless, the BCG vaccine is recommended for individuals who are clinically well, immunologically stable, and receiving antiretroviral therapy (ART). Immunological stability is indicated by a CD4% above 25% in children under five years of age, or a CD4 count of at least 200/mm^3 in those over five years of age. Furthermore, undetectable viral load, together with the absence of new opportunistic infections, also indicates a clinically well status. For newborns, if the mother is HIV-positive and the baby's HIV status is unknown, the BCG vaccine should be administered if the baby does not have clinical signs of HIV infection, regardless of the mother's ART status [49].

It is important to note that the vast majority of children infected with HIV live in countries where TB is prevalent. For example, in sub-Saharan Africa, approximately 57% of children receiving ATT are HIV-positive. Therefore, easy access to ART and ATT is essential for widespread administration of the BCG vaccine. In addition, it should be remembered that co-treatment of HIV and TB is complicated due to drug–drug interactions [50]. Furthermore, subunit vaccines such as MVA85A would offer a solution for the complications of live BCG in individuals infected with HIV [51].

Juzi et al. reported BCG-related complications in 18 HIV-positive children under 13 years old. Primary surgical treatment (drainage/biopsy) was preferred for BCG lymphadenitis, but perioperative complications occurred. Therefore, primary surgical treatment is not recommended in HIV-positive patients due to the high rate of fistulization and poor wound healing [52].

6.2. BCG vaccination in PID patients

Since BCG is a live vaccine, its use is contraindicated in individuals with immunodeficiency. PID is a group of inherited diseases resulting from insufficient maturation and/or dysfunction of the immune system. PID has more than 150 types with associated gene defects, and exhibits a variety of clinical manifestations, including elevated susceptibility to infections, autoimmunity, and malignancies [3,53]. MSMD, CGD, combined immune deficiency (CID), and SCID are the most common types of BCG-associated PIDs [54,55]. In a study from Türkiye, of 47 patients diagnosed

with BCGitis (n = 34) and BCGosis (n = 13), 21.2% had MSMD, 12.7% had predominantly antibody deficiency (PAD), 10.6% had SCID, 6.3% had CGD, and 4.2% had CID. The ratio of parental consanguinity was 84% in these patients (55). Another study from the same hospital reported that 104 patients were diagnosed with complications associated with the BCG vaccine, and 46.2% had MSMD, 22.4% had SCID, and 9.5% had CGD. The rate of BCG-related complications was significantly lower in the patients who received ATT [56].

MSMD causes selective predisposition to clinical diseases caused by mycobacteria with low virulence, such as the BCG vaccine. At least 30 different MSMD subtypes have been identified based on allelic heterogeneity, depending on the mode of transmission, the effect of mutations, and the affected function. The most frequently reported genetic defect in MSMD is mutations in *IL12RB1*, followed by *IFNGR1* and *IL12B*, involved in the IFN-γ/IL-12/IL-23 signaling, which is critical for immunity against mycobacteria. However, in approximately 60% of patients who clinically present with MSMD, no identified genetic cause is found [57].

In CGD, a heterogeneous genetic disorder, the production of reactive oxygen species (ROS) is defective due to an error in nicotinamide adenine dinucleotide phosphate (NADPH) oxidase activity. Mutations in the X-linked *CYBB* gene or in *CYBA*, *NCF1*, and *NCF2* genes cause defects in superoxide production, and phagocytic cells cannot kill microorganisms. Recurrent bacterial and fungal infections occur due to the disruption of the ROS-dependent antimicrobial mechanism. Additionally, inflammation is dysregulated, and granuloma formation is increased in CGD patients [3].

In CIDs, T-cell development or function is defective due to various genetic disorders, resulting in immunological deficiencies [58]. T cells play a crucial role in the production of antibodies that recognize pathogens with high specificity. Therefore, in T-cell-mediated immunodeficiencies, at least some degree of impairment in antibody production is inevitable [59]. SCID is a severe form of CID, resulting from complete gene variants and significant T-lymphocyte deficiency. Therefore, SCID patients develop serious impairment of cellular and humoral immune function, causing fatal infectious diseases and growth retardation within the first three to six months of life, and they die in the early stages of life [58,60].

7. Management

Management is tiered to severity. Conservative care includes local wound treatment and observation, which are appropriate for uncomplicated injection-site ulceration and small, non-suppurative lymphadenopathy. Moreover, procedural or surgical interventions for suppurative complications, as well as ATT plus immunological assessment for deep or disseminated disease, can be considered as management approaches [7]. FNA or surgical excision/drainage is commonly used for suppurative nodes and deep abscesses; combining surgical management with ATT was effective in a large series of severe cases [61]. Baek et al. reported the case of a five-month-old male infant who developed a 1.5 cm mass in the left axilla following BCG vaccination and was diagnosed with lymphadenitis. The infant received ATT for four months, but the mass continued to grow. At 13 months of age, the size of the necrotic cystic lesion was enlarged to 5 × 4 cm. Therefore, a surgical intervention was performed, including drainage of the pus from the cyst and removal of the abscess along with its wall. Subsequently, the patient received adjuvant therapy and ATT for three months, and complete remission without complications was achieved [16].

In case of BCGosis or deep organ disease, ATT tailored to *M. bovis*/BCG plus prompt immunological evaluation is recommended [62]. Hematopoietic stem cell transplantation may be required for underlying SCID, but outcomes can be poor if the disease is advanced [63,64]. An increased rate of complications can be observed in adenosine deaminase (ADA)-deficient SCID (ADA-SCID) patients because of the uncontrolled replication of *M. bovis*. In this case, an urgent enzyme replacement therapy (ERT) using polyethylene glycol–modified ADA (PEG-ADA) is recommended [65].

Molecular methods to distinguish BCG from other mycobacteria improve diagnostic accuracy, and controversies remain about the optimal drug regimens and duration for vaccine-derived disease [66]. Recently, a single-center series found that surgery combined with ATT achieved good outcomes for suppurative and deep lesions, and that early immunological work-up identified PID in some disseminated cases [7]. Their management protocol for adverse reactions on the injection site is shown in Figure 3. Studies emphasize screening or delaying BCG in infants with PID risk factors to prevent severe events.

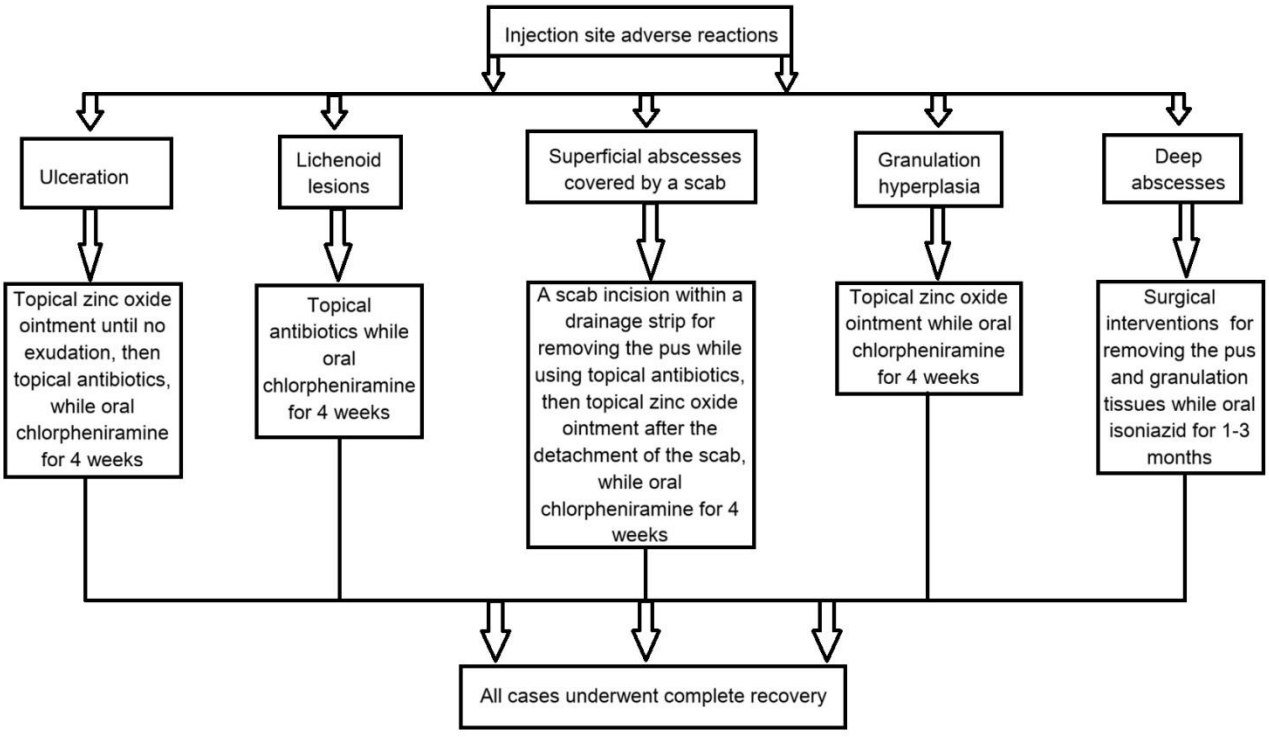


Figure 3. Management protocols of adverse reactions in the BCG injection site in children and their outcomes. The figure was reproduced from [7], licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

In non-muscle invasive bladder cancer (NMIBC), intravesical BCG administration is commonly used for treatment. However, some local or systemic infections can occur with this treatment due to the nature of the BCG vaccine, including live *M. bovis* cells. The treatment involves six weekly induction sessions, followed by a maintenance regimen lasting 1–3 years. However, due to side effects, the planned treatment course cannot be completed in many patients. The incidence of BCGosis in these patients is 3%–7%. Mostly, the disease is disseminated (34.4%), but it can be localized in the

genitourinary organs (23.4%), musculoskeletal system (19.9%), or rarely in vessels (6.7%). The treatment regimens mostly start with isoniazid, rifampicin, ethambutol, and pyrazinamide, followed by levofloxacin and moxifloxacin [67,68].

8. Conclusions

TB is a deadly infectious disease if left untreated and without preventative measures. The most powerful tool in preventing this disease is the BCG vaccine. In individuals with no immune system problems, the BCG vaccine is safe and only causes mild side effects. However, there may be contraindications to administering the live BCG vaccine to individuals with any immune system problems, such as those with HIV infection or PID. The situation of these patients should be evaluated by specialist physicians. Surgical intervention is necessary in cases of suppurative complications. In cases of BCGitis and BCGosis, ATT should be applied. While hematopoietic stem cell transplantation may be beneficial in some cases of SCID, PEG-ADA replacement is necessary in ADA-SCID patients.

Use of AI tools declaration

The author declares that Artificial Intelligence (AI) tools have not been used in the creation of this article.

Conflict of interest

The author has no conflicts of interest to declare.

Ethics approval of research

Ethical approval was not required for this study because it is a review article based exclusively on previously published literature and did not involve human participants, animals, patient data, or clinical specimens.

References

1. World Health Organization (2025) Global tuberculosis report 2025. Available from: https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2025.
2. Ong RYL, Chan SB, Chew SJ, et al. (2020) Disseminated Bacillus-Calmette-Guérin infections and primary immunodeficiency disorders in Singapore: A single center 15-year retrospective review. *Int J Infect Dis* 97: 117–125. https://doi.org/10.1016/j.ijid.2020.05.117
3. Norouzi S, Aghamohammadi A, Mamishi S, et al. (2012) Bacillus Calmette-Guérin (BCG) complications associated with primary immunodeficiency diseases. *J Infect* 64: 543–554. https://doi.org/10.1016/j.jinf.2012.03.012

4. Rezai MS, Khotaei G, Mamishi S, et al. (2008) Disseminated Bacillus Calmette-Guerin infection after BCG vaccination. *J Trop Pediatr* 54: 413–416. https://doi.org/10.1093/tropej/fmn053
5. Elsidig N, Alshahrani D, Alshehri M, et al. (2015) Bacillus Calmette-Guérin vaccine related lymphadenitis in children: Management guidelines endorsed by the Saudi Pediatric Infectious Diseases Society (SPIDS). *Int J Pediatr Adolesc Med* 2: 89–95. https://doi.org/10.1016/j.ijpam.2015.05.003
6. Liu Q, Dai X, Wei S (2025) BCGitis and BCGosis: Clinical spectrum, immunological mechanisms, and risk management. *Vaccines* 13: 1179. https://doi.org/10.3390/vaccines13121179
7. Huang S, Cheng F, Guo H, et al. (2025) Clinical characteristics and outcomes of severe adverse reactions to Bacille Calmette-Guérin (BCG) vaccination in China: A single-center retrospective study. *Sage Open Pediatr* 12. https://doi.org/10.1177/30502225251346345
8. Tural-Kara T, Ozdemir H, Erat T, et al. (2017) Local cutaneous complications after Bacille Calmette-Guerin vaccine: Experience of a single center. *Int J Clin Pediatr* 6: 37–41. https://doi.org/10.14740/ijcp279w
9. Elitok GK (2025) Management of Bacille Calmette-Guérin vaccine adverse event: Case report. *Bagcilar Med Bull* 10: 320–322. https://doi.org/10.4274/BMB.galenos.2025.46220
10. Loh ACE, Kua PHJ, Tan ZL (2019) Erythema and induration of the Bacillus Calmette-Guérin site for diagnosing Kawasaki disease. *Singapore Med J* 60: 89–93. https://doi.org/10.11622/smedj.2018084
11. Villanueva P, Crawford NW, Croda MG, et al. (2023) Factors influencing scar formation following Bacille Calmette-Guérin (BCG) vaccination. *Heliyon* 9: e15241. https://doi.org/10.1016/j.heliyon.2023.e15241
12. Eregie CO (1997) Ulceration of a previously healed BCG scar in suspected disseminated BCG infection. *Ann Trop Paediatr* 17: 135–139. https://doi.org/10.1080/02724936.1997.11747876
13. Ghattaura A, Eley KA, Molenaar E, et al. (2009) A case of extensive ulcerating vasculitis following a BCG vaccination. *J Plast Reconstr Aesthet Surg* 62: e286–e289. https://doi.org/10.1016/j.bjps.2007.11.031
14. Castresana G, Arango CA (2020) BCG vaccine-related lymphadenitis and BCGitis. *Consultant* 60: e8. https://doi.org/10.25270/con.2020.03.00017
15. Goraya JS, Virdi VS (2002) Bacille Calmette-Guérin lymphadenitis. *Postgrad Med J* 78: 327–329. https://doi.org/10.1136/pmj.78.920.327
16. Baek SO, Ko HS, Han HH (2017) BCG vaccination-induced suppurative lymphadenitis: Four signs to pay attention to. *Int Wound J* 14: 1385–1387. https://doi.org/10.1111/iwj.12755
17. Rangesh S, Vaidya PC, Mehra N, et al. (2022) Incidence of lymphadenitis following Bacillus Calmette-Guérin (BCG) vaccination in north Indian children. *Indian J Tuberc* 69: 596–601. https://doi.org/10.1016/j.ijtb.2021.09.008
18. Villanueva P, Wadia U, Crawford N, et al. (2022) Revaccination with Bacille Calmette-Guérin (BCG) is associated with an increased risk of abscess and lymphadenopathy. *NPJ Vaccines* 7: 6. https://doi.org/10.1038/s41541-021-00421-5
19. Vaghasiya VL, Nasit JG, Rupavatiya B, et al. (2024) The spectrum of cytological findings in patients with BCG lymphadenitis: A series of 13 cases. *Ann Diagn Pathol* 69: 152260. https://doi.org/10.1016/j.anndiagpath.2023.152260

20. Nazir Z, Qazi SH (2005) Bacillus Calmette-Guerin (BCG) lymphadenitis-changing trends and management. *J Ayub Med Coll Abbottabad* 17: 16–18.
21. Miyamura T, Egashira S, Yoshino Y, et al. (2019) Papulonecrotic tuberculid after Bacillus Calmette-Guérin (BCG) vaccination with lung infiltration that mimics disseminated BCG infection. *J Dermatol* 46: e267–e268. https://doi.org/10.1111/1346-8138.14819
22. Parmar NV, Al Falasi A, Almualla A (2021) Bacillus Calmette-Guérin vaccine-induced lupus vulgaris in a 3-year-old child. *An Bras Dermatol* 96: 636–638. https://doi.org/10.1016/j.abd.2020.07.022
23. Adalı Ruşen Y, Mungan U, Yörükoğlu K (2025) Exploring the role of granuloma formation in the prognosis of BCG-treated bladder carcinoma. *Bull Urooncol* 24: 75–79. https://doi.org/10.4274/uob.galenos.2025.2025.3.1
24. Hung TK, Leung D, Duque JSR, et al. (2022) Bacillus Calmette-Guérin Scar erythema in a 14-year-old girl post-BNT162b2 vaccination. *Pediatr Int* 64: e15090. https://doi.org/10.1111/ped.15090
25. Lopatynsky-Reyes EZ, Acosta-Lazo H, Ulloa-Gutierrez R, et al. (2021) BCG scar local skin inflammation as a novel reaction following mRNA Covid-19 vaccines in two international healthcare workers. *Cureus* 13: e14453. https://doi.org/10.7759/cureus.14453
26. Günaydın SD, Atakan N (2023) Bacillus Calmette-Guerin (BCG) site reaction after Coronavirus Disease 2019 (COVID-19) mRNA vaccination. *Indian J Dermatol* 68: 355. https://doi.org/10.4103/ijd.ijd_64_22
27. Noishiki C, Hayasaka Y, Yoshida R, et al. (2023) Over 90% of childhood BCG vaccine-induced keloids in Japan occur in women. *Dermatol Ther* 13: 1137–1147. https://doi.org/10.1007/s13555-023-00916-0
28. Han TI, Kim IO, Kim WS, et al. (2000) Disseminated BCG infection in a patient with severe combined immunodeficiency. *Korean J Radiol* 1: 114–117. https://doi.org/10.3348/kjr.2000.1.2.114
29. Lin WL, Chiu NC, Lee PH, et al. (2015) Management of Bacillus Calmette-Guérin osteomyelitis/osteitis in immunocompetent children—A systematic review. *Vaccine* 33: 4391–4397. https://doi.org/10.1016/j.vaccine.2015.07.039
30. Vaisban E, Melamed-Snapir Y, Braester A, et al. (2005) Bone marrow fibrosis and caseating granulomas associated with intravesicular BCG treatment. *Eur J Intern Med* 16: 301–303. https://doi.org/10.1016/j.ejim.2004.11.015
31. French CG, Hickey L, Bell DG (2001) Caseating granulomas on the glans penis as a complication of Bacille Calmette-Guérin intravesical therapy. *Rev Urol* 3: 36–38.
32. Botaro MH, Maria E Silva J, et al. (2025) BCG vaccination in children with severe combined immunodeficiency in a tertiary center: Evaluation of complications and risks. *J Pediatr* 101: 224–230. https://doi.org/10.1016/j.jped.2024.09.008
33. Jafari L, Hamidieh AA, Behfar M, et al. (2023) Effect of early Bacillus Calmette-Guerin vaccination of pediatric severe combined immunodeficiency patients on the outcome of hematopoietic stem cell transplantation using a reduced-intensity conditioning regimen. *Transplant Cell Ther* 29: 188.e1–188.e8. https://doi.org/10.1016/j.jtct.2022.12.007
34. Roxo-Junior P, Silva J, Andrea M, et al. (2013) A family history of serious complications due to BCG vaccination is a tool for the early diagnosis of severe primary immunodeficiency. *Ital J Pediatr* 39: 54. https://doi.org/10.1186/1824-7288-39-54

35. Frankel H, Byberg S, Bjerregaard-Andersen M, et al. (2016) Different effects of BCG strains—A natural experiment evaluating the impact of the Danish and the Russian BCG strains on morbidity and scar formation in Guinea-Bissau. *Vaccine* 34: 4586–4593. https://doi.org/10.1016/j.vaccine.2016.07.022
36. Siroosbakht S, Rezakhaniha B (2019) Complications of Bacillus Calmette-Guérin vaccination at a university hospital in Iranian neonates. *J Compr Ped* 10: e67098. https://doi.org/10.5812/compreped.67098
37. Jamil H, Sama G, Nohri AR, et al. (2025) Medical error in paediatric vaccination: Case report of accidental ONCO-BCG administration in neonates. *J Health Wellness Community Res* 3: e190. https://doi.org/10.61919/w4sn7v08
38. Al-Maqbali AA, Al-Maani AS (2016) The adverse events, signs, and management of neonatal Bacillus Calmette-Guérin vaccine overdose. *Oman Med J* 31: 315–317. https://doi.org/10.5001/omj.2016.61
39. Chetan C, Patra S, Singh SK, et al. (2023) Double BCG vaccination in a neonate: Implications, management and prevention. *BMJ Case Rep* 16: e256766. https://doi.org/10.1136/bcr-2023-256766
40. World Health Organization (2026) WHO TB Knowledge Sharing Platform. Available from: https://tbksp.who.int/en/node/2051.
41. Wei SH, Ho WC, Chen YT, et al. (2018) The management and outcome of Bacillus Calmette-Guérin vaccine overdose. *Pediatr Neonatol* 59: 208–210. https://doi.org/10.1016/j.pedneo.2017.07.004
42. Qureshi S, Ahmad K, Fatima P, et al. (2019) Outcome of inadvertent high dose BCG administration in newborns at a tertiary care hospital, Karachi—Case series. *PLoS One* 14: e0219324. https://doi.org/10.1371/journal.pone.0219324
43. Puliyel JM, Hughes A, Chiswick ML, et al. (1996) Adverse local reactions from accidental BCG overdose in infants. *BMJ* 313: 528–529. https://doi.org/10.1136/bmj.313.7056.528
44. Pasteur MC, Hall DR (2001) The effects of inadvertent intramuscular injection of BCG vaccine. *Scand J Infect Dis* 33: 473–474. https://doi.org/10.1080/00365540152029981
45. Buyukoglan H, Gulmez I, Tutar N, et al. (2011) Gluteal abscess: An unusual complication of Bacille Calmette-Guérin. *Ann Thorac Med* 6: 235–236. https://doi.org/10.4103/1817-1737.84780
46. Yaşöz G, Belet N, Şensoy G (2014) Overdose and intramuscular administration of Bacille Calmette-Guerin vaccine in a 2-month-old infant. *Turk J Pediatr* 56: 669–672.
47. Hesseling AC, Caldwell J, Cotton MF, et al. (2009) BCG vaccination in South African HIV-exposed infants--risks and benefits. *S Afr Med J* 99: 88–91.
48. World Health Organization (2007) Safety of BCG vaccine in HIV-infected children. Available from: https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/bcg-vaccines.
49. World Health Organization (2026) Children living with HIV and neonates. Available from: https://tbksp.who.int/en/node/2050.
50. Rabie H, Frigati L, Hesseling AC, et al. (2015) Tuberculosis: Opportunities and challenges for the 90-90-90 targets in HIV-infected children. *J Int AIDS Soc* 18: 20236. https://doi.org/10.7448/IAS.18.7.20236
51. Dieye TN, Ndiaye BP, Dieng AB, et al. (2013) Two doses of candidate TB vaccine MVA85A in antiretroviral therapy (ART) naïve subjects gives comparable immunogenicity to one dose in ART+ subjects. *PLoS One* 8: e67177. https://doi.org/10.1371/journal.pone.0067177

52. Juzi JT, Sidler D, Moore SW (2008) Surgical management of BCG vaccine-induced regional axillary lymphadenitis in HIV-infected children. *S Afr J Surg* 46: 52–55.
53. McCusker C, Upton J, Warrington R (2018) Primary immunodeficiency. *Allergy Asthma Clin Immunol* 14: 61. https://doi.org/10.1186/s13223-018-0290-5
54. Xia L, Yang Y, Li XY, et al. (2026) Primary immunodeficiency diseases with BCG-induced diseases: A 15-year longitudinal cohort study. *J Clin Immunol* 46: 30. https://doi.org/10.1007/s10875-026-01996-1
55. Soyak Aytekin E, Keskin A, Tan C, et al. (2021) Differential diagnosis of primary immunodeficiency in patients with BCGitis and BCGosis: A single-centre study. *Scand J Immunol* 94: e13084. https://doi.org/10.1111/sji.13084
56. Ozsezen B, Yalçın E, Ademhan Tural D, et al. (2022) Antimycobacterial prophylaxis regarding Bacillus Calmette-Guérin-associated complications in children with primary immunodeficiency. *Respir Med* 200: 106919. https://doi.org/10.1016/j.rmed.2022.106919
57. Xia L, Liu XH, Yuan Y, et al. (2022) An updated review on MSMD research globally and a literature review on the molecular findings, clinical manifestations, and treatment approaches in China. *Front Immunol* 13: 926781. https://doi.org/10.3389/fimmu.2022.926781
58. Aranda CS, Guimarães RR, de Gouveia-Pereira Pimentel M (2021) Combined immunodeficiencies. *J Pediatr* 97: S39–S48. https://doi.org/10.1016/j.jped.2020.10.014
59. Peters NE, Shields AM, Hambleton S, et al. (2025) Learning from inborn errors of immunity and secondary immune deficiencies about vaccine immunogenicity, efficacy, and safety. *Clin Exp Immunol* 219: uxaf059. https://doi.org/10.1093/cei/uxaf059
60. Jiao Y, Li Q, Chen Z, et al. (2025) Severe combined immunodeficiency with BCG-osis by salvage therapy with allogeneic hematopoietic stem cell transplantation: Cases report and literature review. *BMC Pediatr* 25: 768. https://doi.org/10.1186/s12887-025-06127-0
61. Chan WM, Kwan YW, Leung CW (2011) Management of Bacillus Calmette-Guérin lymphadenitis. *HK J Paediatr* 16: 85–94.
62. Mahdaviani SA, Fallahi M, Jamee M, et al. (2022) Effective anti-mycobacterial treatment for BCG disease in patients with Mendelian Susceptibility to Mycobacterial Disease (MSMD): A case series. *Ann Clin Microbiol Antimicrob* 21: 8. https://doi.org/10.1186/s12941-022-00500-y
63. Cocchi N, Jacobsen EM, Hoenig M, et al. (2022) BCG disease in SCID: Three decades of experience in a pediatric transplant center. *J Clin Immunol* 42: 195–198. https://doi.org/10.1007/s10875-021-01143-y
64. Laberko A, Yukhacheva D, Rodina Y, et al. (2020) BCG-related inflammatory syndromes in severe combined immunodeficiency after TCRαβ^{+}/CD19^{+} depleted HSCT. *J Clin Immunol* 40: 625–636. https://doi.org/10.1007/s10875-020-00774-x
65. Canarutto D, Oltolini C, Barzaghi F, et al. (2023) Outcome of BCG vaccination in ADA-SCID patients: A 12-patient series. *Biomedicines* 11: 1809. https://doi.org/10.3390/biomedicines11071809
66. BrzeziŃska SA, Bielecka T, Zabost A, et al. (2020) Molecular methods in diagnostics of post-BCG vaccine adverse events. *Cent Eur J Immunol* 45: 130–135. https://doi.org/10.5114/ceji.2020.97900
67. Martinson T, Hare CB, Kirmaier A, et al. (2025) Disseminated BCGosis after intravesical BCG installation for bladder cancer. *Case Rep Infect Dis* 2025: 9532859. https://doi.org/10.1155/crdi/9532859

68. Inauen J, Geake J, Sawka A, et al. (2025) A clinical case series of BCGosis as a rare complication of intravesical BCG. *Clin Genitourin Cancer* 23: 102271. https://doi.org/10.1016/j.clgc.2024.102271



AIMS Press

© 2026 the Author(s), licensee AIMS Press. This is an open access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0)