

CASE REPORT

BCG-Induced cold abscess as a complication of inadvertent vaccine injection: A case series

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Abstract

We report a four-month-old girl with a right thigh swelling, an eight-month-old girl with a left thigh swelling, and a five-month-old boy with a left thigh swelling with the final diagnosis of BCG-induced cold abscess as a result of erroneous injection of BCG vaccine into the infants' thigh muscle.

KEYWORDS

BCG vaccine, cold abscess, vaccines adverse effect

1 | INTRODUCTION

The Bacille Calmette-Guérin (BCG) vaccine, as the only available vaccine against Mycobacterium Tuberculosis, is recommended by the World Health Organization (WHO) in numerous countries.^{1,2} According to the expanded program of immunization (EPI) in Iran, all children receive BCG (strain: BCG/Pasteur 1173P2) vaccination at birth. BCG is derived from live attenuated Mycobacterium Bovis and there are possible local, regional, or systemic complications following the vaccine injection.^{2,3} The strain of the BCG vaccine, the child's immune response, and injection technique especially dosage and administration route are considerable factors for the development of the possible complications.^{4,5} Mycobacterial infection is the most common culprit for cold abscess, known as an abscess without

severe inflammation. The abscess also can be a result of incorrect intramuscular BCG vaccine injection.^{6,7} Here, we report three cases of BCG-induced cold abscess as a result of erroneous injection of vaccine into the infant's thigh muscle.

2 | CASE PRESENTATION

2.1 | Case 1

A four-month-old girl was presented to our hospital due to a right thigh swelling since four days ago. The parents did not report any fever, poor feeding, or irritability. On physical examination, vital signs were stable. There was a 5*7 cm fluctuating mass with sharp borders at the anterior

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surface of her right thigh (Figure 1). No erythema, deformity, discharge, or tenderness was detected. Both hips and knees had a normal range of motion. The general physical examinations including lung and heart auscultation, abdominal examination, and the examination of lymph nodes were normal. There was no history of insect bite or trauma. The patient had an appropriate growth and developmental history with no prenatal or perinatal difficulties. She had received the routine vaccination for Iranian children that included BCG, the first dose of hepatitis B, the first dose of OPV (Oral Polio Vaccine), and the first dose of DPT (Diphtheria, Pertussis, and Tetanus). The laboratory results were as follows: white blood cell (WBC): 11500/ μ l (polymorphonuclear leukocyte (PMN): 29% and lymphocyte: 66%), hemoglobin: 9.6 gr/dl, platelet: 519000/ μ l, and erythrocyte sedimentation rate (ESR): 50 mm/h. blood urea nitrogen (BUN), creatinine (Cr), blood sugar (BS), and electrolytes were normal. Ultrasound results demonstrated a large collection of thick fluid (49*29*32 mm) with debris and septations in the depth of the anterior thigh muscle. X-ray imaging was otherwise normal. On the first day of admission, needle aspiration of the lesion was done and 5 milliliters of green purulent fluid were drained and sent for gram staining, acid-fast staining, and culture. Gram staining and routine culture were negative. The patient received intravenous Cloxacillin without significant improvement, and so, open surgical drainage was done and light yellow cheesy material was drained and sent for acid-fast staining. Both samples sent for acid-fast staining showed more than 10 acid-fast bacilli per



FIGURE 1 Swelling with sharp borders at the anterior surface of infant's right thigh (case 1)

field. On Loewenstein Jensen culture media, light yellow slow-growing colonies were reported. The patient had no abnormal findings on chest computed tomography (CT) scan and immunological screening tests. The patient received Isoniazid, Rifampin, and Ethambutol with diagnosis of mycobacterial cold abscess, and there was no improvement after three weeks. Clarithromycin was added and the patient improved significantly after two weeks. These medications were continued for four months and Isoniazid and Rifampin for further two months. The patient had good growth and development with no further re-accumulation of pus or any other remarkable health problem during the one-year follow-up.

2.2 | Case 2

An eight-month-old girl was presented to our hospital due to left thigh swelling since birth. There was erythema on the site for the first 40 days after birth, and then, it healed spontaneously but the swelling remained for eight months and was exacerbated in the last three days before referral. The patient's past medical history was unremarkable except for pneumonia when she was one-month-old. At the time of admission, the patient had an appropriate general condition; there was no fever, and other vital signs were stable. On general physical examination, there was no abnormal finding including no lymphadenopathy. There was a swelling mass sized 7*7 (cm) on the lateral side of the left thigh. There was no erythema or inflammation on the site, and it was not tender on palpation. Laboratory findings showed WBC: 19900/ μ l (PMN: 20% and lymphocyte: 80%), hemoglobin: 12.3 mg/dl, platelet: 335000/ μ l, and ESR: 5 mm/h. BUN, Cr, and liver function tests were within normal ranges. The ultrasound examination of thigh soft tissue and X-ray of left femoral bone were requested. Ultrasound results demonstrated an echo-free zone with a thick wall (41*65*39 mm, approximately 57 ml, 6 mm under the skin) containing faint debris in the depth of the left thigh muscle. The X-ray was normal. The patient underwent surgical drainage and debridement of the lesion. Before the surgery, needle aspiration of the lesion was done and samples were sent for gram staining, acid-fast staining, culture, and PCR examination of various mycobacterium types. Gram staining and routine culture were negative. Acid-fast staining and culture on Loewenstein Jensen culture media were both positive for *Mycobacterium Tuberculosis*. The PCR test result was positive for *Mycobacterium Bovis* (the subtype of *Mycobacterium* in the BCG vaccine). Moreover, tuberculin skin test (TST) was done and the result showed 0 mm induration. The patient received Clindamycin after admission to cover possible causes of the abscess. After a

TABLE 1 Comparison of patients' clinical characteristics

Clinical Features	Case 1	Case 2	Case 3
Patient sex	Girl	Girl	Boy
Patient age at presentation	4 months	8 months	5 months
Affected limb	Right thigh	Left thigh	Left thigh
Mass size (ultrasound results)	49*29*32 mm	41*65*39 mm	46*37*47 mm
Drainage route	Needle aspiration	Needle aspiration and surgical drainage	Surgical drainage (2 times)
Treatment regimen	Isoniazid, Rifampin, Ethambutol, Clarithromycin	Isoniazid, Rifampin	Isoniazid and Rifampin
Total duration of treatment	6 months	6 months	6 months

confirmed diagnosis of tubercular cold abscess, clindamycin was discontinued, and Isoniazid and Rifampin were started and continued for the next six months. The patient had good growth and development with no further re-accumulation of pus or any other remarkable health problem during the follow-up.

2.3 | Case 3

A five-month-old boy was presented to the pediatric department as his parents had noticed a progressive swelling and erythema on the left thigh from one month ago. On physical examination, vital signs were stable. There was a swelling sized 4*4 cm on the left thigh and the site was warm. No deformity, discharge, or tenderness was detected. The general physical examinations including lung and heart auscultation, abdominal examination, and the examination of lymph nodes were normal. He had received oral Metronidazole and Amoxicillin-Clavulanic acid for one week without any improvement. The patient had an appropriate growth and developmental history with no prenatal or perinatal difficulties and he had received the routine vaccination for Iranian children. The laboratory results were as follows: WBC: 39000/ μ l, hemoglobin: 9.8 gr/dl, platelet: 510000, and ESR: 21 mm/h. BUN and Cr were normal. Ultrasound results demonstrated a hypo-echoic lesion with internal septations (46*37*47 mm, approximately 42 ml, 10 mm under the skin). X-ray imaging was otherwise normal. Open surgical drainage was done and samples were sent for gram staining, acid-fast staining, culture, and PCR examination of various mycobacterium types. Clindamycin was administered after admission to cover possible causes of abscess and due to inappropriate response, it was changed to Vancomycin and Cefotaxime. Gram staining and routine culture were negative. Acid-fast staining and culture on Loewenstein Jensen culture media were both positive for mycobacterium. The PCR test result was positive for

Mycobacterium Bovis. TST was done and showed 0 mm induration. Isoniazid and Rifampin were administered after the diagnosis of the mycobacterial cold abscess was confirmed. During the next two weeks, regarding the thigh swelling and possible pus re-accumulation, ultrasound examination of thigh soft tissue was repeated and showed an abscess (approximately 9 ml, 19 mm under the skin); so, the patient underwent surgical drainage and debridement of the lesion for the second time. Isoniazid and Rifampin were continued for the next six months. The patient had good growth and development with no further re-accumulation of pus or any other remarkable health problem during the follow-up.

3 | DISCUSSION AND CONCLUSION

Thigh swelling is a clinical sign of various infectious or noninfectious underlying causes (Table 1). Regarding the patients' physical examination, cold abscess was the most probable diagnosis since patients did not have considerable warmth, erythema, and other signs of inflammation at presentation. Mycobacterial infection is the most common cause of cold abscess⁶; so, acid-fast staining was done along with routine culture and was positive. Furthermore, a PCR test was done for the confirmation of diagnosis which was positive for Mycobacterium Bovis.

BCG is derived from live attenuated Mycobacterium Bovis and according to the expanded program of immunization (EPI) in Iran, all children receive BCG vaccination after birth.⁸ BCG is routinely injected intradermally over the deltoid muscle. The abscess location in all patients was in the anterior thigh muscle, the exact site of vitamin K and Hepatitis B vaccine injection at birth. The positive PCR test for BCG Mycobacterium Bovis and the abscess location raised the possibility of erroneous injection of BCG vaccine into the infants' thigh muscle. We checked the hospitals where case 2 and case 3 were born and found

out that vitamin K is injected by the midwife after that, BCG and hepatitis B vaccine is injected by the vaccinator so the most probable situation is the injection of 0.5 ml of BCG intramuscularly to the left thigh instead of hepatitis B vaccine (Hepatitis B vaccine is routinely injected to the left thigh). In case 1, regarding the presence of swelling in the right thigh, probably 0.5 ml of BCG is injected intramuscularly instead of vitamin K at birth (vitamin K is routinely injected to the right thigh). The injection of a high dosage of BCG, 0.5 cc instead of 0.05 ml, and intramuscular injection instead of intradermal are both factors for BCG-related abscess which is observed in these cases. Injection of a high dosage of BCG vaccine, any injection route other than intradermal injection, and immunodeficiency are major risk factors for the development of BCG-induced abscess. Similar cases of BCG-induced cold abscesses are reported in Saudi Arabia and India. Verma et al.⁹ reported a four-month-old girl from India. The patient presented with a swelling on the anterolateral side of her left thigh since receiving an intramuscular Diphtheria, whole-cell Pertussis, and Tetanus (DwPT) vaccine injection at the age of six weeks. Fine needle aspiration of the lesion showed caseating granuloma and staining for acid-fast bacilli was positive. The most probable cause of the abscess, in this case, is thought to be following erroneous BCG injection instead of DwPT vaccine, and the diagnosis is not confirmed since the PCR test for BCG *Mycobacterium Bovis* was not done. This type of error is not considered for our cases because the BCG vaccine is not available in vaccination centers in Iran and the error can only occur in hospital settings while vaccine injection at birth. The article has mentioned that the swelling was completely healed in six months without any anti-mycobacterial therapy. But, we preferred to start treatment to speed up healing and to prevent further complications. Moreover, Namshan et al.⁶ reported five similar cases of BCG-induced cold abscess from Saudi Arabia. They did not perform a PCR test for BCG *Mycobacterium Bovis* and the diagnosis was based on culture results. Three cases received anti-mycobacterial drugs and finally, all cases were healed without remarkable problems during a two-year follow-up. The most extensive report is from Saudi Arabia with 25 cases of BCG-induced abscess as a result of technical errors during vaccine injection. The diagnosis was based on a positive smear for acid-fast bacilli for all cases and a positive culture for 17 cases. Nowadays, PCR test can detect the exact organism and help us for an accurate diagnosis. In the later study, the exact source and route of infection was unknown but we tried to find where the error originates from.¹⁰ Our recommendation to prevent this error is to assign separated staff to inject each of the vaccines, injection of BCG, and hepatitis B vaccine in different rooms, and checking the vaccine injection by a second observer. According to the

study by Walid Daoud,¹¹ training of medical staff about correct techniques of vaccine injection has a significant preventive effect on the rate of BCG vaccine complications. In this study, the rate of complications before and after the training program was 36.61 and 6.25 per 1000 vaccinations, respectively. So, preparing training programs for the medical staff, responsible for BCG vaccination, can be helpful as a preventive measure. In addition, WHO has warned that the correct and precise BCG vaccine injection technique by trained staff is important for optimal efficacy and safety of the vaccine.¹

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this article.

AUTHOR CONTRIBUTION

Iraj Sedighi involved in the management of patients. Parinaz Sedighi, Taravat Sadrosadat, Mahsa Movahedi, and Iraj Sedighi contributed for data gathering and preparing the article.

ETHICAL APPROVAL

Written informed consent was obtained from the patient's parent to publish this report in accordance with the journal's patient consent policy. This study was approved by ethics committee at Hamadan University of Medical Sciences. (Approval ID: IR.UMSHA.REC.1400.532).

CONSENT

Written informed consent was obtained from the patient's parent to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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