

The Adverse Events, Signs, and Management of Neonatal Bacillus Calmette-Guérin Vaccine Overdose

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ABSTRACT

A two-day-old male neonate was inadvertently immunized with 20-times the recommended dose of Bacillus Calmette-Guérin (BCG) vaccine (1.0 ml instead of 0.05 ml). Examination of the neonate after one day revealed no signs of local reaction at the site of injection or systemic manifestation. However, nine days later, he developed a swelling (4 × 3 cm) at the site of injection without any enlargement of the lymph node, pallor, or jaundice. A needle aspiration of the swelling was done and sent for culture. The culture showed the BCG strain only. The infant was not started on antituberculosis medication, due to the absence of symptoms suggestive of systemic disease. There were no other complications up to the age of 18 months. The case highlights the importance of administering the correct dose and using the appropriate technique of the BCG vaccine, and explains the management options to prevent local and systematic complications that may occur due to overdose.

The Bacillus Calmette-Guérin (BCG) vaccine is the most commonly used vaccine worldwide to protect infants from tuberculosis (TB). It is given to newborns as soon as possible after birth in accordance with the Expanded Program on Immunization, which was implemented by the Ministry of Health (MoH) in the Sultanate of Oman as a routine immunization.

Vaccination is contraindicated in the presence of the following; positive Mantoux test, clinical symptomatic HIV infection, or known immunodeficient pregnant women. The BCG vaccine is given intradermally on the left upper arm (deltoid) with few local adverse events like ulceration and abscess. However, when the technique of administration is incorrect, lymphadenitis can occur.

The BCG vaccine is made from a weakened form of a bacterium closely related to human TB. Because the bacterium is weak, the vaccine does not cause any disease but instead triggers the immune system to produce effective antibodies against *Mycobacterium tuberculosis*. The vaccine is 70–80% effective against the most severe forms of TB, such as TB meningitis in children. It is less effective in preventing respiratory disease, which is the more

common form of the disease in adults. BCG-Connaught vaccine is supplied in powder form in a light protecting vial containing 8–32 × 10⁶ freeze-dried colony forming units (CFUs) per vial, which is reconstituted with the supplied 1.5 ml of diluent. The correct dose is 0.05 ml for children under 12 months of age and 0.1 ml for older children. The MoH recommends the use of the auto disposable syringe (0.05) ml for the vaccine to minimize the risk of an error in the dose.

CASE REPORT

A two-day-old male neonate was inadvertently administered an excessive dose of BCG vaccine using a normal (5 ml) syringe instead of an auto-disposable syringe (0.05 ml) at a rural health center with a limited number of deliveries per year. The whole ampule of the BCG vaccine was injected. Thus, the neonate received 1.0 ml instead of the correct dose, which is 0.05 ml. The injected dose was 20 times the correct dosage. The staff nurse realized the error after one-day and referred the baby to a specialized hospital. On examination, the neonate was afebrile and comfortable with no signs of local or systemic reaction.

At 11-days-old, he developed a palpable non-tender lump on the left deltoid area of the injection site (approximately 4 × 3 cm). There was mild erythema, and fluctuation. There was no sinus and no palpable axillary lymph nodes. No other positive signs were detected.

At one month follow-up, an ultrasound showed a localized abscess within the deltoid muscle of the left arm, measuring 2.2 × 1.5 cm with a volume of 2 ml. The abscess was separated from the bone and joint by infraspinatus muscle with deep extension and no signs of osteomyelitis. Aspiration was done and culture showed BCG resistant to pyrazinamide. At six months follow-up, the infant was not found to have any complication at the injection site and he did not have any sign suggestive of systemic disease.

DISCUSSION

BCG vaccine overdose has been rarely reported in the literature. The severity of overdosing complications is correlated with the dose administered. In some cases, local abscess and necrosis with lymphadenopathy have been reported.^{1,2} Higher doses were reported to cause significantly larger skin lesion and axillary lymphadenopathy.³⁻⁵

A European report documenting all side effects of BCG immunization with more than 10,000 cases, including 398 overdose cases, revealed that the majority of cases develop large, deep ulcers, necrotic lesions or abscesses, and sometimes regional supportive lymphadenitis. Only 8% develop systemic complication including fever, headache, and malaise.⁶ In addition to overdose, incorrect placement of BCG vaccine was associated with an increased risk of local complications, which was related in severity to the type of BCG strain vaccine.⁷ In cases where a 10-fold greater volume has been administered, simultaneous incorrect placement is very likely to have occurred. The specific strain of BCG vaccine used for immunization has also been reported to influence the severity of adverse events.⁸⁻¹¹

None of the published studies have calculated the incidence of BCG overdosing. However, it was estimated by Sanofi Pasteur's Global Pharmacovigilance Department as 2.2 per 1,000,000 doses.¹² There are no consensus guidelines for the management of BCG overdose. There are only recommendations, which includes informing

patients, close follow-up, and use of antituberculosis medication when needed.

To the best of our knowledge, this was the first case report of BCG vaccine overdose with 20 times the correct dose. We did not start the infant on antituberculosis treatment as there was no strong recommendation from other reports. However, we decided to aspirate the lump to test for the strain of BCG, which was positive. The lump was not excised as it developed on day 11, and previous reports only recommended excision immediately after the injection because the vaccine is expected to be present on a small discrete area of subcutaneous tissue. The excision may prevent the development of any immune response that might lead to severe complications like abscess, suppurative lymphadenitis, or necrosis.^{1,13}

Other reports have advised preventive measures to be taken by starting antituberculosis medication (isoniazid) for 60 days to minimize the risk of developing side effects of BCG overdose.¹⁴ However, until the time of publishing this paper, the child (18 months old) was well and had no signs of systematic complications. The child is still scheduled for follow-up with the nearest health institution and the specialized hospital.

CONCLUSION

This case shows the importance of up to date knowledge and training of health care workers on injection technique and dosing of the BCG vaccine. The most common side effect of BCG overdose is a local adverse reaction. The initiation of antituberculosis treatment is individualized according to each case and has been recommended even when the neonate does not develop any systemic complications.

Disclosure

The authors declared no conflicts of interest.

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