Management of Adverse Reactions to Bacille Calmette-Guérin Vaccine

J. Mark FitzGerald

Division of Tuberculosis Control, British Columbia Centre for Disease Control Society, Ministry of Health and University of British Columbia, Vancouver, Canada

Published reports appear to underestimate the true rate of adverse reactions to bacille Calmette-Guérin (BCG) vaccine. At a recent national conference on tuberculosis control among aboriginal populations, lack of awareness of what constitutes an adverse reaction was considered a possible contributing factor to underreporting. The following review defines a normal BCG response and discusses the management of complications when they occur.

Adverse reactions to BCG vaccine appear to be grossly underreported. For example, in 1987 there were only 2 adverse reactions to BCG vaccine that were reported in all of Canada [1]. Surprisingly, from 1983 through 1987, 67 such reactions were recorded in British Columbia alone [2]. During the same period, 1456 vaccines were administered, with a prevalence of 0.046% adverse reactions; of the patients with these adverse reactions, 45 had local reactions, 18 had lymphadenopathy, 3 had combined local reactions and adenopathy, and 1 had immunodeficient HIV-uninfected infant died [2].

To estimate the true rate of adverse reactions to BCG vaccine in Canada, clear definitions of normal and adverse reactions are needed. A normal dermatologic reaction to BCG vaccination is a red indurated area measuring 5–15 mm. A crust is formed around this induration, which is soft at the center for 3–4 weeks. At 6–10 weeks, the crust falls off, leaving a flat 3-to 7-mm scar. A 1977 study suggests 10 mm as the cutoff point for the size of a normal reaction [3]. Regional lymphadenopathy in the absence of erythema or vesicle formation should also be considered a normal reaction to the vaccine [4].

An abnormal reaction involves a persistent local abscess and suppurative lymphadenopathy up to 3 months after vaccination. Reactions to BCG vaccine are age and dose dependent. The younger the infant and the larger the dose, the more likely it is that an adverse reaction will occur.

Clinical Studies

Adverse reactions and complications of BCG vaccination include suppurative lymphadenitis, localized abscess (or a combination of both), and, very rarely, disseminated BCG-itis as the most serious adverse reactions to BCG vaccination. As noted earlier, the reported national rate of adverse reactions appears to be lower than the actual rate.

A large European study of infants who received BCG vaccine described 776 adverse reactions in a population of 2.5 million infants aged <1 year and 72 adverse reactions in 2.7 million children aged >1 year [4]. There was significant variation in the adverse reaction reports from the different countries. This variation is thought to be due to a number of factors, including the level of case finding, diagnostic criteria, and the quality, injection technique, and dose of the BCG vaccine used.

A study by Guld et al. [5] that investigated suppurative lymphadenitis after intradermal BCG vaccination in the newborn revealed that the frequency of enlarged glands or local skin ulceration after BCG vaccination was related to the dose. The researchers found that a smaller dose of BCG vaccine was associated with a significantly lower rate of suppurative enlarged glands and ulceration after BCG vaccination. This finding has led to the suggestion of the use of a smaller dose of vaccine (between one-fourth and one-eighth the adult dose) given at least 3 months after birth [6].

In a 1971 study by Belcourt [7], 30 neonates aged 7–21 days were vaccinated with Connaught BCG (0.1 mg) at twice the recommended infant dose. Two infants developed lymphadenitis, and 57% developed suppurative nodules at the injection site. Subsequently, 72 neonates were vaccinated with 0.0125 mg (one-fourth the infant dose). None of the children developed lymphadenitis or suppurative nodules at the injection site, and 89%–91% of the 35 who underwent tuberculin skin testing 8–9 weeks later became PPD reactive.

Experience in British Columbia

Of the ~3000 BCG immunizations completed in British Columbia from 1987 through 1992, 125 (0.24%) were associated with adverse reactions. Because of these reactions, the dose of BCG vaccine for infants was reduced from one-half to one-fourth the adult dose in 1990. Since then, there has been a substantial decline in the number of reported cases of adverse reactions to BCG vaccine; a total of 13 adverse reactions occurred in 1152 infants (0.01%) who were immunized. During the earlier period, all children with reported reactions received specific therapy, whereas during the period with the lower vac-
cine dose, there not only were less adverse reactions but also fewer patients who required specific therapy (6 of 13) [2].

Treatment

Medical therapy for lymphadenopathy is not routinely indicated. However, therapy for suppurative lymphadenitis and abscess formation at the injection site is often recommended. Surgical drainage of suppurative lymphadenitis remains controversial, with no good data to support the use of routine incision and drainage, removal, or simple needle aspiration.

Data supporting the use of isoniazid and erythromycin for the resolution of abscess formation remain inconclusive. Two studies, one comparing isoniazid with erythromycin [8] and the other a controlled placebo study [9], showed no clear benefit from the use of either of these 2 agents for the treatment of suppurative lymphadenopathy.

The 1985 study by Hanley et al. [8] showed no difference in the resolution of local abscess formation in 18 infants, of whom 9 were given isoniazid therapy and 9 were given erythromycin therapy.

In the 1987 study of 120 infants with regional lymphadenitis after BCG vaccination, Cajlayan et al. [9] found no significant differences in suppuration and spontaneous drainage in infants assigned to 4 different treatment groups. In this study, 42 infants received no specific therapy, 36 were treated with erythromycin stearate, 21 were treated with isoniazid, and 21 were treated with a combination of isoniazid and rifampin. The researchers noted that rapid development of lymphadenopathy—within 2 months of immunization—was associated with a higher incidence of suppurative and spontaneous drainage, irrespective of medical therapy. Therefore, early incision was suggested. Treatment recommendations for local abscess formation and suppurative lymphadenitis remain controversial.

On the basis of the above brief review of therapy for adverse reactions to BCG vaccine, the following pragmatic approach has been adopted in our program. In general, the parent and family physician should be reassured about the usual benign course of such reactions. In many cases, such reassurance will be adequate. In our experience, there is often pressure to be “seen doing something,” and in that instance, there may be benefit to giving a short course of cloxacillin or erythromycin syrup if there is evidence that suggests a superimposed bacterial infection. We rarely prescribe isoniazid unless there is clear evidence of a suppurative reaction and associated lymphadenopathy and a strong desire by the parent or primary care physician to initiate such therapy. In our experience, most reactions respond to our conservative approach, and no definitive therapy is required. Rarely, if an enlarged lymph node becomes tense and fluctuant, it may need to be incised and drained.

In summary, adverse reactions to BCG vaccine are dose dependent and usually self-limiting. Reassurance and a conservative therapeutic approach are usually adequate for their management [10].

References