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Surgical management of BCG vaccine-induced regional axillary lymphadenitis in HIV-infected children

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Summary

There are as yet no clear surgical guidelines for the management of BCG vaccine-induced regional axillary lymphadenopathy.

Objectives. The aim of this study was to evaluate the management of the condition and to suggest possible management strategies.

Methods. A retrospective study was undertaken of 23 cases of suspected ipsilateral BCG adenitis following neonatal BCG inoculation (2001 - 2004). Diagnosis of a BCG infection was confirmed by culture and/or gastric washout. The age of the patient and mode of presentation, imaging findings, and results of tuberculin skin testing (Mantoux test) were documented. Because of a change in management policy the first group of patients treated by primary surgery were compared with those treated by fine-needle aspiration (FNA). The influence of HIV status on outcome was assessed. Surgical complications and outcome were analysed.

Results. Twenty-three children under 13 years of age (mean age 8.8 months, male/female ratio 1.9:1) were evaluated. Eighteen patients tested positive for HIV and 5 were HIV-negative. A positive culture for BCG bacillus was identified in 19 cases (83%) – by FNA (*N*=13, 68%), on pus swab (*N*=3, 16%), at surgery (*N*=1, 5%), and by gastric washing (*N*=2, 11%). Three HIV-negative children had granulomas on histological examination without a positive culture.

Forty-five per cent of the 11 patients treated early in the study period by primary surgery (drainage/biopsy) had complications, which included a difficult anaesthetic induction and technical surgical difficulties. The postoperative incidence of wound dehiscence/infection was extremely high in this group and 18.2% developed postoperative cutaneous sinuses. Following a change in management policy, the following 12 patients, with a comparable HIV incidence, treated by initial conservative management, had a much lower incidence of post-procedural complications.

Conclusion. This study confirms a high perioperative complication rate associated with the primary surgical treatment of BCG lymphadenitis in both HIV-positive and negative patients. Primary surgical treatment (incisional drainage or biopsy) is therefore not considered an ideal form of management in BCG lymphadenitis because of the high fistulisation and poor wound healing, especially in the HIV-positive patient. It should be avoided as the initial approach, with needle aspiration being preferred. Surgery should therefore be confined to the unusual event of real doubt about the underlying diagnosis and the treatment of suppurative complications.

Tuberculosis (TB) remains a major threat to health worldwide, with half of the world's population still being exposed to *Mycobacterium tuberculosis*[1] and 10 million new cases of active TB being diagnosed annually.[2] The impact of this disease has not been resolved by antituberculosis drug therapy and no effective vaccine has yet been developed that can entirely prevent the infection.

Despite the wide use of the current vaccine, bacille Calmette-Guérin (BCG), it has been the subject of considerable debate over the years. Although introduced into South Africa as part of a routine programme of immunisation since 1973[3] to induce long-lasting, cell-mediated and humoral immunity against TB, there remain more than 3 million TB-related deaths reported per year, of which 8 - 20% occur in children.[4] This problem is focused in the Western Cape region of South Africa, which has one of the highest TB incidences in the world, and is further complicated by the high rate of HIV disease and the frequent coexistence of the two conditions.[5-7]

The complication rate arising from the use of the current BCG strain is estimated at approximately 36.61 per 1 000 vaccinations.[8] A not-infrequent reason for urgent surgical consultation is BCG-related local reactions and a severe ipsilateral lymphadenitis or even abscess formation as well as the possibility of disseminated BCG disease and osteomyelitis.[7,8] This may be partly strain-specific and associated with

the current Danish-strain BCG, but HIV-positive children appear to be particularly at risk.[6] Similarly, disseminated BCG disease occurs almost exclusively in immunocompromised children and has an extremely high mortality rate.[6,9]

Many surgeons still regard BCG adenitis as a surgical disease requiring drainage but a certain amount of re-assessment is taking place within surgical circles, not least of all because of the reported high complication rate and the added risk of disseminated BCG disease in HIV-infected children.[6,7]

The aim of this study was to retrospectively study the outcomes of BCG lymphadenitis in HIV-positive and negative patients in order to establish surgical guidelines on the best approach to BCG-related local complications.

Material and methods

The study population comprised 23 patients (less than 13 years old) with suspected or confirmed BCG adenitis following neonatal BCG inoculation, referred to the paediatric surgery service at Tygerberg Children's Hospital (2001 - 2004). The diagnosis of a BCG infection was confirmed on fine-needle aspiration (FNA), pus swab and/or gastric washout. All patient charts were reviewed retrospectively to determine patients age and mode of presentation, imaging studies and results of tuberculin skin testing (Mantoux test). The study population in this retrospective study consisted of two groups based on surgical management, viz. those treated early on in the treatment period with an initial surgical approach (both HIV-negative and positive patients) and those treated later using a non-surgical protocol following diagnosis (HIV-positive patients). The surgical complications and outcome were analysed.

Results

Twenty-five children less than 13 years old were admitted to the study group, the mean age being 8.8 months. The male/female ratio was 1.9:1. Eighteen patients tested positive for HIV and 5 were HIV negative. Sixteen presented with axillary lymphadenopathy only (Fig. 1), and 7 with complicated suppurative disease (Table I). Primary surgery performed in the initial stages included drainage/biopsy (*N*=11), with the remainder receiving an initial needle aspiration (NA). Of the 16 non-complicated patients treated, 6 were HIV negative and 10 were HIV positive. Nine of the 16 were managed by initial NA and 7 by primary surgery. Of these, 8 of the 16 (50%) were HIV positive compared with 2 (28%) of the 7 treated by primary surgery. Of the 7 patients presenting with suppurative complications, 5 were HIV positive. Of these, 3 were treated by FNA (2 HIV positive) and 4 by surgery (3 HIV positive) (Table I).

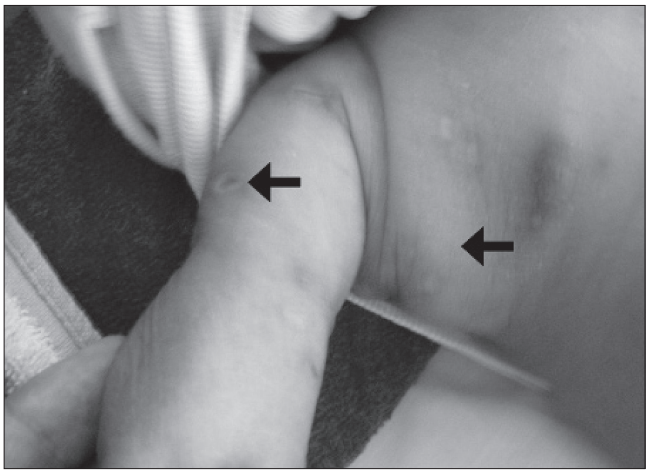

Fig. 1. Arrows mark BCG scar and ipsilateral lymphadenopathy.

A positive culture for the BCG bacillus was identified in 19 patients (83%) with suspected BCG adenitis. BCG infection was established by means of culture of aspirates in 16 of these (NA in 13 (68%), pus swab in 3 (16%)), 1 (5%) from a surgical tissue biopsy and 2 (11%) by means of gastric washings (disseminated BCG infection). Of the remaining 4 patients, 3 HIV-negative patients had a granulomatous lymphadenitis on histological examination, without a mycobacterium being positively identified, and 1 HIV-positive patient had a reactive lymph node. Six were treated with tuberculostatic drugs.

Eleven patients were treated by primary surgery (drainage/biopsy), of whom 8 were HIV positive and 3 negative. The incidence of suppurative lymphadenitis in this group was 5 out of 11 (45%) (Table I). A high incidence of complications was particularly noted in the 8 HIV-positive patients in this group, with 6 experiencing intraoperative problems, including difficult anaesthetic induction. In addition, there were surgical technical difficulties including difficult surgical dissection and an increased bleeding tendency (Table II). The postoperative incidence of wound dehiscence or infection was

TABLE I. PRESENTATION OF BCG LYMPHADENITIS (*N*)

Group	*N*	HIV positive	Needle aspiration	Primary surgery
Uncomplicated	**16**	**10**	**9 (8 HIV+)**	**7 (2 HIV+)**
Suppurative	**7**	**5**	**3 (2 HIV+)**	**4 (3 HIV+)**

TABLE II. COMPLICATIONS OF BCG LYMPHADENITIS (*N*)

Group	*N*	HIV postive	Anaesthesia difficulties	Difficult surgery	Wound dehiscence	Wound sepsis	Postperative sinus
Primary surgery	**11**	**8**	**6**	**5**	**5**	**5**	**2**
FNA determined	**12**	**10**	**N/A**	**N/A**	**1**	**1**	**0**

NA = needle aspiration.

extremely high (45.5%) in this group, with 18.2% developing postoperative cutaneous sinuses that required ongoing care.

The 14 patients treated by an initial conservative approach of aspiration were similar in age and co-existing disease status (11/14 HIV positive), but had a much lower incidence of post-procedural complications (<5%). Three of the 14 patients (22%) had suppurative complications, of whom 2 were HIV positive. A further major advantage in this group was the fact that potentially difficult general anaesthesia was avoided. Only 1 patient developed slight wound sepsis.

Discussion

BCG has been shown to result in marked quantitative changes in the T-cell subpopulations in peripheral blood of young infants[10] and is generally regarded as being a safe and effective (approximately 75%) means of prevention of disseminated TB, and possibly tuberculous meningitis.[11] Complications may occur, however, and in a study of 6 125 infants,[8] 225 BCG-related complications were reported (a complication rate of 36.61 per 1 000 vaccinations). The most frequently reported complications were regional lymphadenitis in 138 (61.33%), local abscess in 48 (21.33%), localised ulcer in 26 (11.56%), and keloid scarring in 12 (5.33%). In addition, a severely immunodeficient infant died from disseminated disease.

The current problem arises from the fact that the relatively high complication rate of BCG vaccination has been compounded by the high rate of HIV infection in areas of high prevalence and carries the greatest risk of disseminated BCG infection. What makes the situation even more complicated is that the vaccine is administered before the HIV status of exposed infants can be determined and few infants show any symptoms. This has posed a problem in surgical decision making as HIV-positive patients carry a risk of underlying pathology. It is clear that the different presentations of BCG lymphadenitis (e.g. lymphadenopathy versus complicated suppurative BCG lymphadenitis) possibly require different types of management.

The problem of the best management of BCG lymphadenitis is by no means solved and may pose particular problems in surgical decision-making. It has been shown that spontaneous healing is possible,[12] and there is a view that uncomplicated BCG lymphadenitis should be treated non-surgically as it usually resolves on its own. A number of studies[12-16] have shown that tuberculostatics are ineffective in cases of local lymphadenitis and do not shorten healing time or complication rate. On the other hand, an initial wait-and-see approach of non-intervention has been shown to be less effective than NA and in the study by Banani and Alborzi[17] aspirated nodes regressed in 58% versus 9% of controls by 2 months (and 95% v. 65% at 6 months).

Our study confirms a high perioperative complication rate associated with primary surgical treatment of BCG lymphadenitis reported in the literature.[17] This resulted in a change in policy in 2003, with satisfying results. Surgical incision or biopsy is therefore not recommended as the primary approach to BCG lymphadenitis because of the risk of persisting sinus formation[18,19] and other complications. It may also carry additional significant anaesthetic risk. NA of BCG abscesses appears to result in a significantly better healing rate, in keeping with other studies,[17] and appears to be the treatment of choice if the clinical presentation is uncomplicated.

Where patients with a suspected BCG-regional axillary lymphadenitis are unaffected by HIV disease, the suggested management protocol should be based on an initial diagnostic NA. We suggest that where lymph nodes are < 3 cm in size, the diagnostic NA should be followed by a wait-and-see policy, thus avoiding the use of ineffective tuberculostatics with the inherent problem of acquired drug resistance as well as avoiding potential surgically related complications. In patients with nodes > 3 cm in size, with a negative culture following aspiration and unresponsive to conventional therapy, other concerns of underlying disease need to be taken into account in evaluating surgical intervention.

HIV-positive patients appear to have a higher complication rate and carry the possibility of generalised BCG systemic infection.[7] This study shows that the incidence of HIV disease was not higher in those treated by primary surgery, excluding any possible bias (Table I). Nor were there more HIV-positive patients in the complicated versus the uncomplicated group. It is clear that needle biopsy avoids many of the complications in the difficult HIV-positive patient group. HIV-positive children with suspected BCG-regional axillary lymphadenitis should have confirmation of the diagnosis of BCG lymphadenitis by culture of NA material, pus swab or gastric washout. The evaluation should include a chest radiograph to exclude the possibility of disseminated mycobacterial disease. If a positive BCG mycobacterium is cultured, initial treatment should be by means of appropriate tuberculostatics and surgery should be avoided and reserved for complicated patients and cases where diagnostic doubt exists.

NA has a number of advantages over primary surgery. Firstly, it facilitates histological examination and confirmation/exclusion of the diagnosis. Secondly, it reduces healing time.[17] Surgical intervention might be indicated when NA has failed and complications ensue. This study shows that this is uncommon if NA is performed out through adjacent normal skin. Secondly, a case can be made for surgery in matted or multiloculated lymph nodes.[17] Thirdly, surgery will be required if a suppurative lymphadenitis has already perforated and resulted in sinus formation.[18,19]

The problem of the best management of BCG lympha denitis is by no means completely solved and a prospective study of HIV-positive children with suspected BCG-regional axillary lymphadenitis is currently being conducted at our institution.

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