Surgical Management of BCG Vaccine - Induced Regional Lymph Nodes Adverse Effects

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Purpose: The objective of this study is to report the increased number of cases presented to paediatric surgical clinic with post BCG vaccine adverse reactions in non immune-compromised children and to evaluate the outcome of our management.

Materials & Methods: In a retrospective study, 156 patients with BCG vaccine complication presented between November 2004 and October 2008. Sixty-three patients were included in our study. Twenty-four patients were treated with needle aspiration and oral Erythromycin (group A). Surgical excision was done in the other thirty-nine patients (group B).

Results: The male to female ratio was 2:1. Sixty Patients presented with axillary lymph node involvement and only 3 patients presented with supraclavicular lymph nodes involvement. Twenty-two out of 24 patients in group A showed complete resolution of lymphadenopathy in 3-6 months of follow up. Two patients did not respond to needle aspiration and Erythromycin, and required surgical excision. Forty-one surgical procedures were done (group B and 2 patients from group A). Thirty-eight patients were cured after surgery. Only 3 patients are still under follow up and on anti-TB treatment for showing signs of disseminated diseases.

Conclusion: successful results with complete resolution in a high percentage of patients were achieved with needle aspiration. Our indications for surgical excision were lymph nodes more than 3 cm in diameter, discharging sinus, fungating axillary mass or residual solid mass after needle aspiration and erythromycin treatment of more than 2 cm.

Index Word: BCG vaccine adverse effects, axillary lymphadenitis, needle aspiration.

INTRODUCTION

Bacille Calmette-Guérin (BCG) is a live attenuated vaccine from a strain of Mycobacterium bovis. It is routinely given to newborn at birth as stated in the guidelines of immunization in Saudi Arabia in order to protect against childhood tuberculosis, tuberculous meningitis and miliary disease, but it does not offer total protection against adult pulmonary tuberculosis. BCG vaccine is the oldest live attenuated vaccine used against human tuberculosis since 1921. The World Health Organization and UNICEF recommend BCG vaccination in developing countries with incidence of tuberculosis infection more than 1%, even though the efficacy of BCG vaccination against tuberculosis is still controversial. BCG vaccine is a single intradermal injection of 0.05ml at the insertion of the deltoid muscle for infants with a birth weight more than 2 kg, and non immuno-compromised or asymptomatic HIV positive infants. Local and systemic adverse effects occur after neonatal BCG vaccine administration in immuno-competent children. The most common complication of
post BCG vaccination is lymphadenopathy or suppurative lymphadenitis, usually in the axilla and rarely in the neck region. This complication occurs about 2 to 8 months after vaccination. Serious disseminated disease develops in less than one in a million of patients with impaired immunity.5,6.

PATIENTS AND METHODS

This is a retrospective study of 156 patients with BCG vaccine complication following neonatal BCG vaccination referred to the pediatric surgical clinic in the Madina Maternity & Children's Hospital, Madina, Saudi Arabia between November 2004 and October 2008. Ninety patients were seen and managed in two of the five paediatric surgical units of the department. Seventy out of the ninety patients were studied. Seven out of the 70 patients are still under treatment, so were excluded from the study. The median age at the time of diagnosis was 5 months (age range 2 – 9 months). All cases received routine BCG vaccination on the left arm within the first two weeks of birth. The most common adverse effects observed were regional lymphadenopathy, suppurative lymphadenitis, supraclavicular and cervical lymphadenopathy. All patients were full-term with birth weight > 2.5 kg. None of them had clinical evidence of immuno-deficiency. Twenty-four patients presented with cystic axillary mass. They had weekly needle aspiration and oral Erythromycin antibiotic for 4-6 weeks with weekly needle aspirations till the mass regressed in size and no puss was further aspirated [Fig. 3]. At the time of presentation, these patients had fluctuant lymph nodes and no sinus formation. Twenty two patients showed complete resolution of lymphadenopathy in 3- 6 months of follow up. Two patients did not respond to this treatment and surgical excision was required. The duration of treatment varied, but all cases were successfully cured.

In Group B, surgical excision was done. This was in 41 patients who had lymphadenopathy more than 3cm in diameter, discharging sinus, fungating axillary mass, or failure of aspiration treatment. The surgical procedure was performed with complete excision of the matted lymph nodes. A pressure dressing was applied for at least 48 hours. All the surgical specimens were divided into two and sent for histopathology and microbiology examination. Histopathological evaluation of excised nodes showed caseous necrosis and granuloma formation, a finding consistent with tuberculosis. Every manipulation or surgical intervention was followed by administration of antibiotic for 2 weeks. Forty-one surgical procedures were done for group B and 2 patients from group A. Thirty-eight patients were cured after surgery. Only 3 patients from group B had serious BCG complication [Table 2]. Two patients developed disseminated infection and one patient had fungating masses in the axilla and neck region and continued on anti-TB treatment [Fig. 4].
Fig. 1: Axillary lymphadenitis post BCG vaccine.

Fig. 2: Supraclavicular lymph node involvement post high BCG vaccine injection.

Fig. 3: Needle aspiration of a cystic axillary mass.

Fig. 4: Post BCG vaccine fungating mass.

Fig. 5: Disseminated disease post BCG vaccine.
Fig. 6: Algorithm for the management of post BCG vaccine adverse effects (solid mass). [*]: (Based on our experience)

- **SOLID MASS**
  - **Cellulitis**
  - **Sinus or fungating mass** [*]
    - Erythromycin 4-6 wks [19,20,*]
    - If not cured
  - **No skin involvement**
    - **Mass < 3 cm**
      - Observation 3-6 mon [24,25,26]
      - If not cured
    - **Mass > 3 cm** [1,15,27,*]
      - Anti – TB [12,21,22]
      - Erythromycin 4-6 wks [16,17,*]
      - If not cured
    - Residual mass > 2 cm or sinus
  - Surgical excision

Fig. 7: Algorithm for the management of post BCG vaccine adverse effects (cystic mass) [*]: (Based on our experience)

- **CYSTIC MASS**
  - **Weekly needle aspiration**
    - **INH & Erythromycin** [18]
    - **Erythromycin 4-6 wks** [1,14,15,*]
    - **Intranodal INH – once** [23]
    - If not cured [*]
    - **Residual mass < 2 cm**
      - Observation
    - **Residual mass > 2 cm or sinus**
      - Surgical excision
### Table 1: Data analysis of sex & clinical presentation of post BCG vaccine

<table>
<thead>
<tr>
<th>Data</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>42 (67%)</td>
</tr>
<tr>
<td>Female</td>
<td>21 (33%)</td>
</tr>
<tr>
<td>Axillary lymph node involvement (normal deltoid injection site)</td>
<td>60 cases</td>
</tr>
<tr>
<td>Supraclavicular lymph node involvement only (high deltoid injection site)</td>
<td>3 cases</td>
</tr>
</tbody>
</table>

### Table 2: Management of post BCG vaccine adverse effects.

<table>
<thead>
<tr>
<th>Management</th>
<th>Total</th>
<th>Cured cases</th>
<th>Failure &amp; Further management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle aspiration &amp; Erythromycin (4-6 wks)</td>
<td>24</td>
<td>22 (92%)</td>
<td>Two had Surgical excision</td>
</tr>
<tr>
<td>Surgical excision</td>
<td>41</td>
<td>38 (93%)</td>
<td>Three on Anti TB – 9 months</td>
</tr>
</tbody>
</table>

(39 + 2 from group A)

**DISCUSSION**

Approximately 100 million children receive BCG vaccine every year. The most common local reaction at the site of injection is in a form of skin induration 5–15 mm wide, and a crust formation occurs from 3 to 4 weeks. When the crust falls off between the 6th and 10th week, a flat scar measuring 3–7 mm remains. The most common complication of BCG vaccination is lymphadenopathy or suppurative lymphadenitis, which occurs in the axilla and rarely in the neck region. The incidence of BCG adverse reaction differs between regions, ranging between 1-10% to 0.1 - 0.5 per 1000 vaccinations. Disseminated infection is a serious complication which occurs at a rate of less than 1 in a million vaccinations, and nearly all reported cases were seen in immuno-compromised patients. Although the lymphadenopathy commonly occurs in the drainage area of the vaccinated site, which is the axilla, the cervical lymph nodes get affected if the vaccine is given in the upper deltoid region.

Suppurative lymphadenitis develops in 30% to 80% of cases. There are variable recommendations for management of post BCG lymphadenopathy and suppurative lymphadenitis. This management ranges from no treatment to treatments such as needle aspiration, drug treatment, surgical drainage, surgical excision, or a combination of two.

Needle aspiration has a major role in the management of post-BCG fluctuant (suppurative) lymphadenitis. The advantage of needle aspiration is prevention of spontaneous perforation and sinus formation. It also facilitates node regression in a relatively short period of time. If properly done, it has no significant complication or morbidity. The effect of needle aspiration was retrospectively studied by the authors on 24 cases. Successful results were achieved with complete resolution in 22 (92%) patients in a period of 3-6 months of follow up. Those patients treated by...
weekly needle aspirations approximately 3-5 times and covered with Erythromycin 30-50 mg/kg for 4-6 weeks. Aglayan et al also obtained satisfactory results in non-drained suppurative adenitis with needle aspiration. One aspiration was found to be effective by some, but repeated aspirations were needed for some patients. Lack of response to needle aspiration may be due to inadequate evacuation. Erythromycin was reported to cure BCG abscess and other troublesome BCG lesions. In one small comparative study of 18 children with local cutaneous complications, responses to one month course of treatment with Isoniazid (6 mg/kg daily to a maximum of 300 mg) and Erythromycin (250 mg four times daily) were similar. Although BCG lymphadenitis is sensitive to Isoniazid, some cases do not respond and the use of Erythromycin proved to have good results. Those whom in favor of using anti-TB drugs (Isoniazid alone or with Rifampicin) applied this method of treatment on non fluctuant lymph nodes and with diameter less than 3 cm.

Other authors advocate a single intranodal injection of Isoniazid after needle aspiration. Local Isoniazid therapy caused significantly earlier resolution of the abscesses (3.9 months) compared with Erythromycin therapy alone (5.2 months; P < 0.001). For adherent or fistulated lymph nodes, the World Health Organization (WHO) suggests drainage and direct instillation of an anti-TB drug into the lesion. Patients with non suppurative and non adherent lymphadenitis were managed in other centers with regular follow up till the lymphadenitis regresses spontaneously over a period of few weeks.

In a series from Japan, lymphadenopathy was detected in 253 (0.79%) of 34,516 vaccinated children. The great majority resolved spontaneously and only eight (0.02%) proceeded to suppuration and discharge.

Total surgical excision has also been advised in certain conditions with rapidly developing adenitis within less than two months after vaccination, because the incidence of spontaneous rupture and sinus formation is significantly higher than in patients with slowly developing lesions. Surgical excision is also advised if the node diameter is greater than 3 cm, and in cases with repeated collection after needle aspiration, especially if the nodes are matted and multicentric, or when suppurative nodes have already drained with sinus formation. Surgery hastens excellent healing and achieves a favorable cosmetic result. Based on our experience and the experience of the others collected from the literature in this field, we propose the policy and guidelines for the management of post-BCG adverse reactions show in Fig. 6 & 7.

CONCLUSION

The optimum treatment for BCG related adverse effects is still debated. There is no clear consensus upon guidelines for the management of BCG vaccine-induced regional axillary lymphadenopathy as yet. Our proposed guidelines for the management of BCG adverse effects in general may still need further evaluation. Successful results were achieved with needle aspiration and complete resolution in a high percentage of patients. Our indications for surgical excision were lymph nodes more than 3cm in diameter, discharging sinus, fungating axillary mass or residual solid mass after needle aspiration and Erythromycin treatment of more than 2 cm.

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