International Journal of Community Medicine and Public Health
Singh N et al. Int J Community Med Public Health. 2024 Feb;11(2):870-873
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20240279

Original Research Article

Bacillus Calmette-Guerin lymphadenitis in children: an underdiagnosed entity

Neha Singh*, Prajwala Gupta

Department of Pathology, Atal Bihari Vajpayee institute of medical sciences and Dr. Ram Manohar Lohia Hospital, New Delhi, India

Received: 05 December 2023
Accepted: 20 January 2023

***Correspondence:**
Dr. Neha Singh,
E-mail: drneha_6@rediffmail.com

ABSTRACT

Background: Bacillus Calmette-Guerin (BCG) lymphadenitis is a common complication after BCG vaccination. Fine needle aspiration cytology (FNAC) is a feasible and cost-effective procedure for the diagnosis and management of this entity. Awareness of this entity in cytology is important to avoid misdiagnosis, as the cytomorphologic features are very similar to tuberculosis. The present study described the clinical presentation and detailed cytomorphologic features in patients with BCG lymphadenitis.
Methods: This was a retrospective study from 2018 to 2022 involving a total of 27 patients who presented with isolated left axillary or cervical lymphadenopathy.
Results: Age at presentation ranged from 1 to 24 months. The male- to-female ratio was 2.75:1. Majority of the children had enlargement of the left axillary lymph nodes followed by cervical nodes. Cytomorphology showed the presence of dense acute and chronic inflammatory cells, epithelioid cell granulomas, multinucleated giant cells, histiocytic aggregates, reactive lymphoid cells, lymphohistiocytic clusters and calcification. Necrotic background was present in 25 (92.6%) cases. Ziehl-Neelsen staining for acid-fast bacilli was positive in 17 (62.9%) cases.
Conclusions: A high index of clinical suspicion for BCG lymphadenitis should be kept in mind for children who are recently vaccinated. Diagnosis of this entity is based primarily on clinical grounds. However, cytology and microbiological examination are encountered as part of clinical work up of lymph node swelling. FNAC in conjunction with clinical presentation is useful for diagnosis of BCG lymphadenitis and avoid an unwarranted tubercular treatment.

Keywords: BCG, Cytology, FNAC, Lymphadenitis, Tuberculosis

INTRODUCTION

The Bacillus Calmette-Guerin (BCG) vaccine, which contains live, attenuated *Mycobacterium bovis*, has been used to prevent tuberculosis since 1921 and has been included in the expanded immunization program of the World Health Organization in 1974.[1] BCG vaccination helps avert various complications of tuberculosis (TB) such as meningitis and disseminated TB.[2] Indian subcontinent being an endemic zone for TB, this vaccine is routinely administered to newborns intradermally at the left deltoid region. Intradermal inoculation of the BCG vaccine can result in a skin nodule at the injection site and subclinical involvement of regional lymph nodes that is self-limiting.[3] Although the vaccine is considered safe, both local and systemic complications can occur. Kuchukhidze et al has defined BCG lymphadenitis as "ipsilateral regional lymph node enlargement that develops within two years of vaccination, without fever or other constitutional symptoms".[4] Spontaneous regression is common in BCG lymphadenitis, and rarely it may resolve gradually.[5]

BCG-induced lymphadenitis is the most common complication of BCG vaccination. FNAC is a rapid and minimally invasive technique that aids in the diagnosis as

well as prompting further management of these cases. Patient can be appropriately observed rather than over treatment with antitubercular drugs, which is encountered in many cases.

METHODS

The present study is a cytopathologic review of previously diagnosed cases of lymphadenitis in a specific age group (<2 years) with isolated presentation of left axillary or left cervical lymph node. The patients were labelled as BCG lymphadenitis only if history of BCG immunization was present in the child along with ipsilateral enlarged axillary or cervical lymph node and meeting all the other criteria. The study was conducted in the department of Pathology at a tertiary care hospital in India. This was a retrospective study and included 27 FNAC cases from January 2018 to December 2022. Cases belonging to age range 0-2 years were retrieved from the departmental records and reviewed. Majority of the patients were <1 year of age (Table 1).

In all cases, the site of vaccination was left shoulder over the deltoid muscle. Left axillary lymphadenopathy was the site seen most frequently followed by cervical lymphadenopathy. Based on the history provided by the parents, none of the children had episode of fever or cough. No history of significant weight loss was identified and all the children were taking feeds properly. FNAC of enlarged node was done with 22-23G needle attached with 10 cc disposable syringe. Smears were stained with Papanicolau and May-Grunwald-Giemsa stains in each case. Ziehl-Neelsen (ZN) stain was done in all cases for detection of acid-fast bacilli. All the stained slides were interpreted by cytopathologists involved in the study and cytomorphology of these cases were studied along with clinical details and acid-fast bacilli status following ZN stain.

RESULTS

There was a total of 27 cases over a period of 5 years. Majority of the patients presented in the first 12 months after birth. Mean age at presentation was 9 months (Table 1).

Table 1: Age wise distribution of cases.

Age range	Number of cases
0-6 months	9
7 month-1 year	9
1.1-1.6 year	6
1.7-2 years	3

Male to female ratio was 2:1. The most frequent presentation was left axillary lymphadenopathy in 18/27 cases (66.6%). 9 cases presented with left cervical lymph node enlargement (33.3%). The swellings were present on the ipsilateral side of the BCG scar in all the cases. On FNAC, frank pus was obtained in all except 2 cases (7.4%) where hemorrhagic aspirate was obtained. Smears were stained with Giemsa and Papanicolaou stains. ZN staining was done in all cases. Cytomorphology showed predominantly dense acute and chronic inflammatory cell infiltrate in 17 cases (62.9%), lymphohistiocytic clusters in 5 cases (18.5%) and reactive lymphoid population in 9 cases (33.3%). Few cases (8/27) showed epithelioid cell granulomas (29.6%) (Figure 1A). 6/27 cases showed multinucleated giant cells (22.2%1). The necrotic background (Figure 1B) was consistently present in 25 cases (92.6%). Additional finding of calcification (Figure 1C) was noted in 1 case (3.7%). ZN stain for acid fast bacilli was positive in 17 cases (62.9%) (Figure 1D). One of the cases showed only blood with occasional fibrofatty fragments (Table 2).

Table 2: Cytomorphological features observed in cases.

Cytomorphological features	No. of cases (%)
Necrosis	25 (92.6)
Dense acute and chronic inflammatory infiltrate	17 (62.9)
Epithelioid cell granuloma	8 (29.6)
Multinucleated giant cells	6 (22.2)
Lymphohistiocytic clusters	5 (18.5)
Calcification	1 (3.7)
Reactive lymphoid cells	9 (33.3)

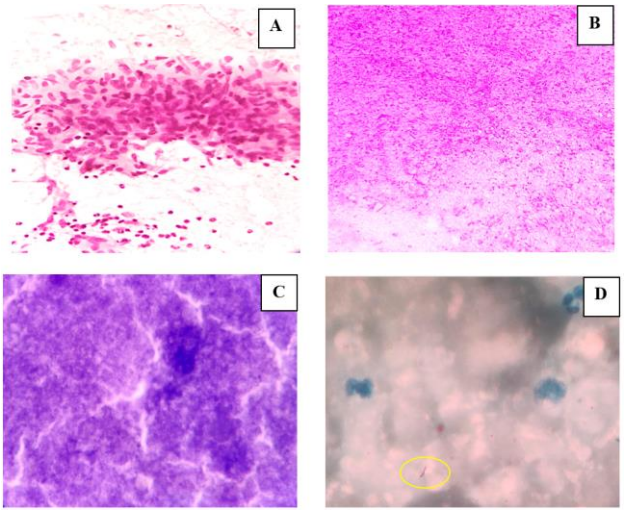

Figure 1: A) Fine needle aspiration cytology showed epithelioid cell granuloma in a background of polymorphs (Papanicolaou, x100); B) thin necrotic background (Giemsa, x200); C) foci of calcification with thick necrosis (Giemsa, x400); D) curved beaded acid-fast bacilli in a background of necrosis (Ziehl Nielsen stain, x1000).

DISCUSSION

Around 120 million doses of BCG vaccine are administered worldwide each year. Most of the BCG

vaccines currently in use are the various strains of *M. bovis* which accounts for about 90% of all BCG vaccines used.[6] After administration of the injection into the left deltoid muscle, the BCG strains begin to divide at the local site and form a hardened nodule, followed by ulceration and healing in the subsequent 10 to 12 weeks. Intradermal BCG vaccine gives rise to classic primary complex that simulates tuberculous infection and consists of a cutaneous nodule at the site of injection along with subclinical involvement of the regional lymph nodes.[7]

The incidence of complications varies from 0.1% to 17%, with lymphadenitis being the most common, which is self-limiting and requires no treatment. Causative factors attributed include early age of the child, immunodeficiency, subcutaneous injection rather than intradermal, higher dose, or strain-related factors.[7,8]

Table 3: Criteria for BCG lymphadenitis.

Clinical features
Age ≤2 years
Site of BCG vaccination at the ipsilateral arm
Onset between 2 weeks to 6 months post vaccination
Absence of systemic manifestations such as fever and weight loss
Absence of tenderness over the lymph node swelling, and
Isolated enlargement of axillary, cervical or supraclavicular lymph node or involvement of any one of these in conjunction with axillary lymphadenopathy proven by ultrasonography or computed tomography scan

Lymphadenitis may be suppurative or non-suppurative. The ipsilateral axillary, cervical, or supraclavicular lymph nodes are most commonly affected. BCG lymphadenitis can present clinically in 2 forms, regional lymphadenitis (Table 3) and disseminated BCG infection.[9]

Non suppurative lymphadenitis is more common and constitute the majority of cases of BCG lymphadenitis. These cases are self-limiting, majority are subclinical and hence go unnoticed.[10] Contrary to this, the present study had cases mostly diagnosed cytologically as suppurative lymphadenitis which is similar to the study done by Bukhari et al and Suliman et al.[11,12] Alfawaz et al also studied 100 cases with more than half of them being of suppurative lymphadenitis.[13]

Suppurative lymphadenitis is characterized by progressive enlargement of lymph node with collection of suppurative material. These cases require management. If untreated, suppurative lymphadenitis can lead to spontaneous perforation and sinus formation. Surgical excision is advisable in cases with failed FNAC attempts and multiloculated/matted lymph nodes/draining sinuses.[10] Inadequacy of the material in 1 case, could be due to very small size of the swelling.

Disseminated BCG infection presents with involvement of distant anatomical site away from BCG administration site along with ipsilateral lymph node enlargement. It is a fatal complication of BCG vaccination. Incidence is 0.06-1.56 cases per million doses. Disseminated BCG is commonly seen in patients with primary immunodeficiency such as Di George syndrome, severe combined immunodeficiency and chronic granulomatous diseases.[14]

Most of the cases of BCG lymphadenitis develop within 1.5 months of vaccination.[3] In the present study, 33.3% (9/27) cases presented within 0 to 6 months of life as compared to 83.3% (25/30) of cases in the study by Pal et al.[15] Bukhari et al studied 145 patients and most of them presented within 3-4 months.[11]

Diagnosis of BCG lymphadenitis depends on clinical history and examination. Ipsilateral enlargement of regional lymph node at the BCG vaccination site in the absence of any constitutional symptoms and when no other obvious cause for the lymphadenitis is present.[3] Mantoux test is not helpful in diagnosing BCG lymphadenitis. The test is expected to be positive after recent BCG vaccination in an immunocompetent host.

BCG lymphadenitis is often difficult to differentiate from tubercular lymphadenitis. Isolated axillary lymphadenitis without constitutional symptoms is a rare finding in TB patients. Routine investigations such as complete blood count and chest x-ray are not of much utility in rendering a diagnosis of BCG lymphadenitis. Microbiologic separation of BCG is confirmatory, but identification of the species of acid-fast bacilli requires phage typing or genetic analysis.[2]

Antibiotics are not recommended for management as it cannot prevent pus formation or shorten healing time. Repeated aspirations are required with use of larger bore needles to facilitate removal of thick inflammatory material. Needle aspiration is considered a safer option compared with surgical excision, which might require general anesthesia in young children.[6] Banani and Alborzi concluded that surgical excision is recommended in non healing cases after three aspiration attempts.[16] Incision and drainage should be avoided in purulent BCG lymphadenitis because of the risk of a persistently draining wound, delayed wound healing, and scarring.

CONCLUSION

BCG lymphadenitis is the most common complication of BCG vaccination and suppurative lymphadenitis may impose diagnostic challenge in young children.

It is challenging to distinguish tubercular lymphadenitis from suppurative lymphadenitis. Cytomorphologic patterns are almost similar in BCG and tuberculous lymphadenitis, these entities should be differentiated

because their treatment differs. However, subtle presenting symptoms like involvement of a single axillary lymph node indicates more in favour of suppurative lymphadenitis. Fine needle aspiration cytology findings with the clinical presentation and history is a rapid, safe, and cost-effective method for early diagnosis. This prompts for further management of BCG lymphadenitis and differentiates it from tuberculosis. Awareness of this lesser-known entity as a possible complication following BCG vaccination is necessary among medical practitioners, paramedical staff and parents to prevent misdiagnosis, overtreatment with antitubercular drugs and ensuring an effective management in all such cases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Goraya JS, Virdi VS. Bacille calmette-guérin lymphadenitis. Postgrad Med J. 2002;78(920):327-9.
2. Pendharkar D, Hassan MJ, Khan S, Khetrapal S, Ahmad N, Jetley S. Cytological diagnosis and management of Bacille-Calmette-Guerin (BCG) induced lymphadenitis in infants. Indian J Pathol Oncol. 2019;6(1):63-6.
3. Gupta N, Kumar V, Nijhawan R, Srinivasan R, Rajwanshi A. FNAC of Bacillus-Calmette-Guerin lymphadenitis masquerading as Langerhans cell histiocytosis. Cytojournal. 2004;1(1).
4. Kuchukhidze G, Kasradze A, Dolakidze T, Baliashvili D, Merabishvili T, Blumberg HM, et al. Increase in lymphadenitis cases after shift in BCG vaccine strain. Emerg Infect Dis. 2015;21(9):1677.
5. Gupta K, Singh N, Bhatia A, Arora VK, Singh UR, Singh B. Cytomorphologic patterns in Calmette Guerin bacillus lymphadenitis. Acta Cytol. 1997;41(2):348-50.
6. Kavuncuoglu A, Ozogul E, Üner A. Bacille Calmette-Guerin (BCG) lymphadenitis in two cases. VIRCHOWS ARCHIV. 2018;473.
7. Jain A, Gupta S, Gupta P, Rohilla M, Gupta N, Srinivasan R, et al. Fine-needle aspiration cytology of Bacille Calmette-Guerin adenitis: a perplexing distinct clinical entity. Diagn Cytopathol. 2021;49(2):226-31.
8. López F, Rodrigo JP, Silver CE, Haigentz Jr M, Bishop JA, Strojan P, et al. Cervical lymph node metastases from remote primary tumor sites. Head Neck. 2016;38(S1):E2374-85.
9. Santosh T, Kothari K, Patil R, Jogi A. Bacille Calmette-Guerin lymphadenitis in infants: A lesser known entity-Report of two cases. J Med Sci. 2018;38(5):239-43.
10. Sonawane DD. Suppurative BCG lymphadenitis in an infant. J Med Sci Clin Res. 2017;05:17440-4.
11. Bukhari E, Alzahrani M, Alsubaie S, Alrabiaah A, Alzamil F. Bacillus Calmette-Guerin lymphadenitis: A 6-year experience in two Saudi hospitals. Indian J Pathol Microbiol. 2012;55(2):202-5.
12. Suliman OM, Ahmed MJ, Bilal JA. Clinical characteristics and needle aspiration management of Bacillus Calmette-Guérin lymphadenitis in children. Saudi Med J. 2015;36:280-5.
13. Alfawaz TS, Alshehri M, Alshahrani D. BCG related complications: a single center, prospective observational study. Int J Pediatr Adolesc Med. 2015;2:75-8.
14. Satyanarayana MA, Asha T. BCG adenitis- beware of this entity in infants and children after BCG vaccination. Int J Health Clin Res. 2020;3:237-41.
15. Pal S, Chakarabarti S, Phukan JP, Biswas S, Sinha A, Sinha R. Role of needle aspiration in diagnosis and management of suppurative Bacille Calmette-Guerin adenitis: an institutional study of 30 cases. J Lab Phys. 2015;7(01):021-5.
16. Banani SA, Alborzi A. Needle aspiration for suppurative post-BCG Adenitis. Arch Dis Childhood. 1994;71:446-7.

Cite this article as: Singh N, Gupta P. Bacillus Calmette-Guerin lymphadenitis in children: an underdiagnosed entity. Int J Community Med Public Health 2024;11:870-3.