Original Research Article

BCG Adenitis-Beware of this entity in infants and children after BCG vaccination

M. Anantha Satyanarayana[1*], T. Asha[2]

[1]Associate Professor, Department of Pathology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, India
[2]Professor and HOD, Department of Pathology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, India

Received: 26-06-2020 / Revised: 26-09-2020 / Accepted: 30-09-2020

Abstract

Introduction: Bacillus- Calmette–Guerin (BCG) vaccine containing live-attenuated Mycobacterium bovis was first used in humans in 1921.The minor adverse reactions are local reaction (pain, swelling, redness). Rare vaccine reactions are suppurative lymphadenitis, BCG osteitis and Disseminated BCG infection. **Aim of the study:** To report the cases of BCG lymphadenitis and other complications diagnosed by FNAC after vaccination.**Materials and methods:**All the infants and children (1month to 2 years) who presented with regional lymphadenopathy for FNAC after BCG vaccination and other rare vaccine reactions were included in the study.**Results:**Total of 21 cases of BCG lymphadenitis was found during 3 years period ranging from 2.5 months of age to 2 years. Mean age of presentation was 9.3 months. Male: Female ratio was 1.6:1. Most common site was left axillary lymph nodes (90%) and one case each at left supraclavicular (5%), and left cervicalareas (5%). Most of the cases are diagnosed as suppurative granulomatous lymphadenitis (95%) on FNAC and one case were diagnosed as nonsuppurative granulomatous lymphadenitis (5%). Z-N stain was done in 18 out of 21 cases and it is positive in 13 cases (72.3%) and it was noncontributory in five cases (27.7%).Other rare vaccine reactions encountered are a singlecase of BCG induced abscess at vaccination site,one case each of right and left inguinal lymphadenopathy with disseminated BCG infection. **Conclusion:**A high index of clinical suspicion,FNAC combined with clinical correlation, is useful for diagnosis and management of BCG Lymphadenitis.

Key words: BCG Vaccine, adverse reactions, FNAC.

Introduction

Bacillus-Calmette-Guerin (BCG) vaccine containing live-attenuated Mycobacterium bovis was recomm-ended for infants at birth or as early as possible to till one year of age as per the National Immunisation Schedule for infants, children and pregnant women in India [1]. The main role of BCG vaccination is to protect the infants and children against disseminated tuberculosis and tuberculous meningitis [2]. The freeze dried BCG vaccine was administered intradermally over left upper arm after reconstitution with 1ml of sodium chloride (0.9%w/v).

**Correspondence*

Dr. M. Anantha Satyanarayana

Associate Professor, Department of Pathology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, India.

E- Mail: ananthsvimspath@gmail.com

Dosage used for infants up to 1 month is 0.05 ml and over 1 month is 0.1 ml [2]. The minor adverse reactions are local reaction (pain, swelling, redness). Rare vaccine reactions are prolonged severe ulceration at the site of vaccination, abscess, suppurative lymphadenitis, BCG osteitis, disseminated BCG infection and death [3].

Aim and objectives of the study

- To report the cases of BCG lymphadenitis who are diagnosed by FNAC after vaccination.
- To report the other rare vaccine reactions encountered after BCG vaccination.

Materials and methods

Inclusion criteria

All the infants and children (1month to 2 years) who presented with regional lymphadenopathy for FNAC after BCG vaccination and other rare vaccine reactions were included in the study.

Exclusion criteria: Those who are not willing to give consent were excluded.

Place of the study

Department of pathology, Alluri Sitarama Raju Academy of Medical Sciences (ASRAMS), Eluru.

Duration of the study

Two years (June 2017- June 2019)

Procedure of FNAC

The site of interest was draped with spirit. FNAC was performed by a pathologist involved in the study by using 24 gauge needle connected to 10cc disposable syringe. Material obtained is spread on the slides in the form of smears. Smears are immediately fixed in absolute alcohol and stained with Hematoxylin & Eosin (H&E). For acid fast bacilli (AFB), Ziehl-Nielson staining (Z-N stain) was done. All the stained slides were interpreted by pathologists involved in the study and correlated cytomorphology with the clinical details.

Statistical analysis: Data was compiled by using Microsoft excel sheet 2010 (Microsoft Corporation, Seattle, WA, United States). Simple descriptive statistics was used and data represented in the form of tables.

Results

Total of 21 cases of BCG lymphadenitis were found during 3 years period ranging from 2.5 months of age to 2 years.Mean age of presentation was 9.3months. Male: Female ratio was 1.6:1. Most common site was left axillary lymph nodes (90%), one case of left supraclavicular lymph node (5%), and one case of left cervical lymph node (5%). As shown in Table/Figure 1 most of the cases are diagnosed as suppurative granulomatous lymphadenitis (95%) on FNAC and one case was diagnosed as nonsuppurative granulomatous lymphadenitis(5%).As shown in Table/Figure 2 the other rare vaccine reactions encountered are a single case of BCG induced abscess at vaccination site and one case each of right and left inguinal lymphadenopathy with disseminated BCG infection.Z-N stain was done in 21 out of 24 cases and it is positive in 15 cases (71.4%) and it was noncontributory in six cases (28.5%).

Table 1: Shows the details of infants and children with BCG Adenitis

Case	Age of presentation	Gender	Other C/F	Site of the swelling	Cytology	Z-N Stain
1	2.5 months	M	Swelling over left deltoid region at scar site.	Lt. axilla	SGLA	ND
2	3 months	F	-	Lt. axilla	SGLA	+
3	3 months	M	-	Lt. axilla	SGLA	NC
4	4 months	M	Evening fever	Lt. axilla	SGLA	+
5	5 months	M	Erythema	Lt. axilla	SGLA	+
6	5 months	F	-	Lt. axilla	SGLA	NC
7	5 months	M	-	Lt. axilla	SGLA	+
8	5 months	F	-	Lt. axilla	SGLA	NC
9	5 months	F	Vomiting's	Lt. axilla	NSGLA	ND
10	6 months	F	Fever, not breast feeding	Lt. axilla	SGLA	NC
11	7 months	M	-	Lt.supracla vicular	SGLA	+
12	9 months	F	Fever on &off	Lt. axilla	SGLA	+
13	9 months	M	Erythema with surface excoriation	Lt. axilla	SGLA	+
14	10 months	M	Fever on &off	Lt. axilla	SGLA	+
15	11months	M	Fever & cough	Lt. axilla	SGLA	+
16	11 months	M	-	Lt. axilla	SGLA	ND
17	12 months	F	-	Lt. axilla	SGLA	NC
18	12 months	M	-	Lt. axilla	SGLA	+
19	24 months	M	-	Lt. axilla	SGLA	+
20	24 months	M	Father is retroviral positive but he is not	Lt. axilla	SGLA	+
21	24 months	F	Fever and loss of appetite	Left cervical	SGLA	+

Table 2:Shows the details of infants and children with other complications of BCG Vaccination

Case	Age of presentation	Gender	Other C/F	Site of the swelling	Cytology	Z-N Stain
1	3 months	M	No BCG scar is evident	Lt. deltoid subcutaneous swelling at vaccinated area	BCG induced abscess	+
2	8 months	F	Mantoux positive	Disseminated BCG infection with Lt. inguinal lymphadenopathy	SGLA	+
3	19 days	M	No BCG scar is evident	Disseminated BCG infection with rt. inguinal lymphadenopathy	SGLA	NC

Abbreviations: C/F-clinical findings**,** SGLA- Suppurative granulomatous lymphadenitis, NSGLA-Nonsuppurative granulomatous lymphadenitis, +-Positive, NC-Noncontributory, ND-Not done

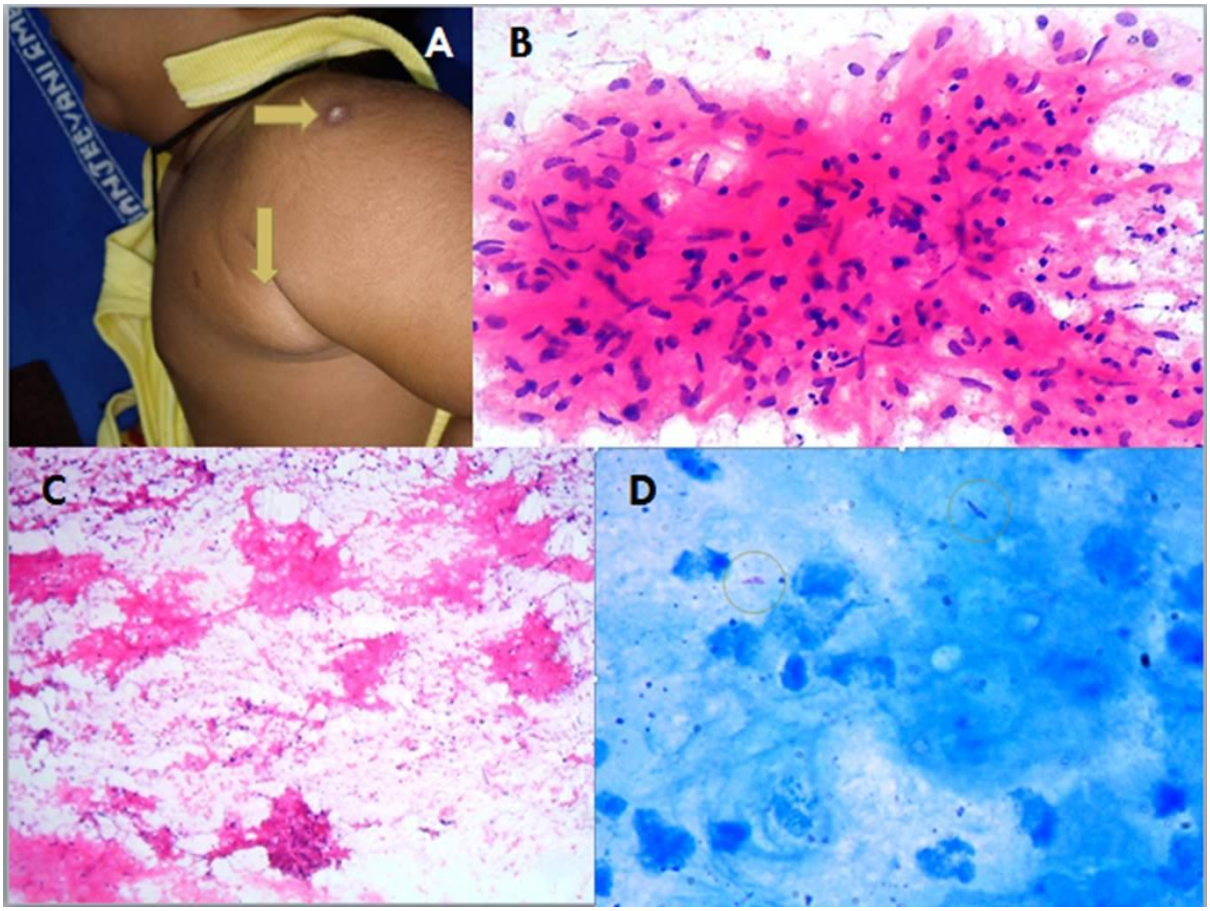

Fig 1: A. 3 month's infant with left axillary lymphadenopathy and induration at BCG scar site. B. FNAC done from left axillary swelling shows epithelioid granuloma. C. Extensive caseous necrosis. D. Z-N Stain shows acid fast bacilli.

Discussion

BCG is the only widely used freeze dried live bacterial vaccine used in India derived from an attenuated bovine strain of tubercle bacilli. The WHO has recommended the "Danish 1331" strain for the production of BCG vaccine. The BCG Laboratory at Guindy, Chennai has been using the "Danish 1331" strain for the production of BCG vaccine and quality control of vaccines is done at the International Reference Centre for BCG quality control at Copenhagen. Adverse reactions such as ulceration and lymphadenitis occur in 1-10 per cent of vaccinations, and disseminated infection occurs in less than one per million vaccinations [4].

A number of host and vaccine related factors are implicated in the pathogenesis which include the age of the child, the technique of vaccination, the BCG strain, the dose, potency, viability and immunogenicity of the vaccine, and prior exposure to mycobacterial antigens [5].

BCG lymphadenitis was clinically defined as ipsilateral regional lymph node enlargement developing within 2 years after BCG vaccination [6]. Two forms have been noticed: nonsuppurative and suppurative lymphadenitis. Nonsuppurative lymphadenitis regresses spontaneously within few weeks and does not need any therapeutic intervention. Suppurative lymphadenitis is diagnosed with the appearance of fluctuation in the lymph node swelling, erythema and edema of the overlying skin[3,5]. Commonest site of lymphadenitis was left axilla (90% of cases) followed by left supraclavicular region (5%) and left cervical region(5%) which is similar to the studies done by Bukhari et al**[7]** and Pal et al**[**8**].**Male infants are more commonly involved than females which are correlating with other studies [7, 8] regarding male preponderance. A single case of BCG induced abscess was encountered with a diameter of 1.6 cm over left deltoid region at vaccination site and a similar case were reported by Riordan [9].A single case of right and left inguinal lymphadenopathy with disseminated BCG infection was seen in our study mostly due to faulty technique as the BCG scar was not evident. Genetic work up has to be done to evaluate underlying immunodeficiency disorder such as severe combined immunodeficiency, complete Di George syndrome and the Mendelian susceptibility to mycobacterial disease[2].

In the present study, most cases came for needle aspiration hence we found suppurative lymphadenitis more common than non-suppurative lymphadenitis which is similar to the study done by Bukhari et al [7]and Suliman et al [10] but in contrast Pal et al [8] reported more number of nonsuppurative adenitis. Z-N stain was positive only in 71.4% of cases of suppurative lymphadenitis in our study which is lower than Pal et al [8] study in which Z-N stain is positive in 91.67% of suppurative lymphadenitis and higher than Suliman et al [10] study in which Z-N stain is positive 66.6% of cases.

Needle aspiration is recommended for all cases of suppurative BCG lymphadenitis as it prevents spontaneous rupture and sinus formation as well as it facilitates rapid regression[2,5,10]. Sometimes repeated aspirations are required for optimal management but latest published guidelines of SPIDS suggest aspiration twice before surgical excision [2].Evidence says that no role for oral antibiotics like Erythromycin and antituberculous drugs as they are ineffective in hastening regression or preventing suppuration in BCG lymphadenitis [5]. Incision and drainage should not be done as it results in poor wound healing [1],irregular scarring and keloid formation [13]. Reassurance and follow up is all that is required in cases of non-suppurative BCG lymphadenitis as it regresses spontaneously over a period of few weeks [5].

Surgical excision may be needed when needle aspiration has failed more than twice as in cases of multiple, matted suppurative lymph nodes [2,5,13]. Fatima et al [11] reported complete resolution of lymphadenopathy was noted in 60 days in cases of aspiration and in cases of surgical excision, resolution was achieved in 7 days. The disseminated BCG infection is usually associated with severe abnormalities of cellular immunity and requires consultation with pediatric immunology and infectious diseases specialists for the optimum management [2].

Various risk factors associated with BCG lymphadenitis are inaccuracy in the injection site and injection method, improper dilution and type of vaccine manufacturer, and a more immunogenic vaccine. Health authorities should reduce the incidence of complications of BCG vaccination with continuous education of the vaccination unit personnel, monitoring the preservation and method of vaccine preparation, change of the vaccine strain and the method of vaccination should be strictly intradermal and no other injection should be given for at least 6 months into the arm which received BCG vaccine [14].

Conclusion

BCG vaccination is a fundamental component of a national tuberculosis programme. BCG administered early in life provides a high level of protection against the disseminated tuberculosis and tuberculous meningitis, particularly in the developing countries of the world. Needle aspiration is recommended for all cases of suppurative BCG lymphadenitis as it prevents spontaneous rupture and sinus formation as well as it facilitates rapid regression. Surgical excision is kept reserved for nonhealing cases of multilocular and matted lymph node abscesses which persist even after repeated needle aspiration.A high index of clinical suspicion,FNA cytology combined with clinical correlation, is useful for diagnosis and management of BCG Lymphadenitis. Education and awareness among health care personnel is essential for prevention, prompt recognition and management of complications of BCG vaccination.

Acknowledgements

I would like to thank Dr. Rashid Hussain and Dr.V.Sundara Rao (Pediatricians) for sending me the cases for fine needle aspiration.

References

1. Ashwin V. Apte, Shruti Sarkar, Dipankar Sarkar. “BCG Adenitis: Action or Inaction?”. Journal of Evolution of Medical and Dental Sciences 2014;3(13): 3446-3454
2. Nagi E, Dayel A, Alshehri M, Alzahrani M, Sami A, Suliman A, et al. Bacillus Calmette Guerin vaccine related lymphadenitis in children: Management guidelines endorsed by the Saudi Pediatric Infectious Diseases Society (SPIDS). Int J PediatrAdolesc Med 2015; 2:89-95.
3. Santosh T, Kothari K, Patil R, Jogi AK. BacilleCalmette–Guerin lymphadenitis in infants: A lesser known entity – Report of two cases. J Med Sci 2018; 38:239-43.
4. Park K. Park’s Text Book of Preventive and Social Medicine: 25th Edition, M/S Banarasidas Bhanol Publisher, India, 2019 pg: 213-15.
5. Goraya JS, Virdi VS. Baccile Calmette-Guerin lymphadenitis. Postgrad Med J. 2002;78(920) :327–329.
6. Kuchukhidze G, Kasradze A, Dolakidze T, et al. Increase in lymphadenitis cases after shift in BCG vaccine strain. Emerg Infect Dis. 2015; 21(9):1677–9.
7. Bukhari E, Alzahrani M, Alsubaie S, Alrabiaah A, Alzamil F. Bacillus Calmette- Guerin lymphadenitis: A 6-year experience in two Saudi hospitals. Indian J PatholMicrobiol 2012; 55:202-5.
8. 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 Physicians 2015; 7:21-5.
9. Riordan A, Cole T, Broomfield C. Fifteen-minute consultation: Bacillus Calmette–Guérin abscess and lymphadenitis. Archives of Disease in Childhood - Education and Practice 2014; 99:87-89.
10. Suliman OM, Ahmed MJ, Bilal JA. Clinical characteristics and needle aspiration management of Bacillus Calmette-Guérin lymphadenitis in children. Saudi Med J. 2015; 36(3):280-285.
11. Naumeri F, Khan MS, Rauf A, Imran S, Tahir M. Role of needle aspiration and surgical excision in management of suppurative Bacillus Calmette Guerin lymphadenitis. J Pak Med Assoc. 2018; 68(7):1120-1123.
12. Satyanarayana S, Mathur AD, Verma Y, Pradhan S, Bhandari MK. Needle aspiration as a diagnostic tool and therapeutic modality in suppurative lymphadenitis following Bacillus Calmette Guerin vaccination. J Assoc Physicians India. 2002;50:788-791.
13. Chan WM, Kwan YW, Leung CW. Management of Bacillus Calmette-Guérin Lymphadenitis. HK J Paediatr 2011; 16:85-94.
14. Siroosbakht S, Rezakhaniha B. Complications of Bacillus Calmette-Guérin Vaccination at a University Hospital in Iranian Neonates, J Compr Ped. 2019 ; 10(1):e67098.

Source of Support:Nil
Conflict of Interest: Nil