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BCG lymphadenitis: a lesser known entity

Type of manuscript – Case series

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Abstract:
Tuberculosis is a major cause of morbidity and mortality in developing countries including India. The Bacille Calmette-Guerine (BCG) vaccine has been in use for prevention of tuberculosis since 1921. Although BCG is safe, it causes minor adverse reactions such as pain, swelling, redness and rarely suppurative lymphadenitis, BCG osteomyelitis and at times even disseminated disease. The term BCG lymphadenitis applies when lymph nodes have become large enough to be easily palpable and a cause of concern for the parents. Here we report thirteen cases of BCG lymphadenitis with age ranging from 4 month to 2.5 years, eight males and the other five female, all presented with left axillary swelling with no history of constitutional symptoms and without family history of tuberculosis. Routine investigations including chest X-ray were normal. In all the cases, there was history of BCG vaccination prior to appearance of swelling, which did not regress on medical management. Ipsilateral regional lymphadenitis being the most common complication of BCG vaccination a high index of clinical suspicion for BCG adenitis should be kept in mind for patients who are recently vaccinated.

Key words- Granulomatous lymphadenitis, Bacillus Calmette–Guerin, Tuberculosis

Introduction:

The Bacille Calmette-Guerine (BCG) vaccine is a live attenuated vaccine. In India, BCG is routinely administered intradermally in left deltoid region to newborns under National Immunisation Programme.(1) The main role of BCG vaccination is to protect the infants and children against disseminated tuberculosis and tuberculous meningitis.(2) Although BCG is safe, it sometimes causes adverse reactions such as regional lymphadenitis, abscess formation and rarely disseminated infection. Reported incidence of BCG vaccine related complications varies from 0.1% to 17% in different studies worldwide.(3) The lymph nodes draining the site of BCG inoculation are enlarged and the lesion is termed as BCG adenitis, 'BCG-itis' or 'becegitis'.(4) BCG lymphadenitis can be classified as regional BCG lymphadenitis and disseminated BCG infection. Regional BCG lymphadenitis further has two subtypes non suppurative and suppurative lymphadenitis.(5-6)

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Findings –

There are thirteen cases in our study, clinical details are given in the following table.

Table no 1: Clinical details of cases

Sr No	Age	Sex	Clinical presentation	Birth history	BCG Vaccination status
1	6 months	Male	Left axillary swelling since 5 months Gradually increasing in size	Normal vaginal delivery	Given on Day 2 of life
2	6 months	Female	Gradually increasing swelling in left axilla since 4 months	Normal vaginal delivery	Given on Day 1 of life
3	2 years 6 months	Male	Left axillary swelling since 2 years	Caesarean section	Given on Day 20 of life
4	8 months	Male	Left axillary swelling since 6 months	Normal vaginal delivery	Given on Day 1 of life
5	6 months	Male	Abscess in left axilla	Normal vaginal delivery	Given on Day 1 of life
6	1 year	Female	Enlarged left axillary lymph nodes	Caesarean section	Given on Day 2 of life
7	1 year	Male	Gradually increasing left axillary swelling since 8 months	Normal vaginal delivery	Given on Day 1 of life
8	1 year	Female	Left axillary swelling since 1 month	Normal vaginal delivery	BCG given 6 months back
9	10 months	Male	Enlarged left axillary lymph nodes	Normal vaginal delivery	Given on Day 1 of life
10	7 months	Female	Left axillary tender swelling since 5 months	Normal vaginal	Given on Day 1 of life

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				delivery	
11	4 months	Male	Swelling in left axilla since 3 months Pus discharge from it since 10 days	Normal vaginal delivery	Given on Day 2 of life
12	9 months	Female	Left axillary tender swelling	Normal vaginal delivery	Given on Day 2 of life
13	1year and 4 months	Male	Left axillary swelling	Normal vaginal delivery	Given on Day 1 of life

All cases presented with gradually increasing swelling in left axillary region. Two of the cases showed rupture of swelling with draining a pus-like material. There was history of BCG vaccination on the left arm in all the cases. Swelling appeared 3 weeks to 1.5 months after BCG vaccination which increases gradually to the present size. Birth history revealed that most of the children were full term, born by normal vaginal delivery. Developmentally all babies were normal and milestones were appropriate for their age.

There was no history of Kochs contact. On examination BCG scar was present. There was no history of fever, weight loss or any other complaints. Routine haematological investigations and chest X-ray were normal. Ultrasound revealed multiple necrotic lymph nodes. Antibiotics were given but swelling did not regress on medical management. Hence excision was done and sent for histopathological examination.

Gross examination-

We received enlarged matted lymph nodes ranging from 3x2.1x1.5 cm to 6.5x5x3 cm. Two of the specimens were partly covered by skin. The cut surface showed yellowish necrotic areas. (Fig1,2)

Microscopic examination-

Microscopy revealed lymph nodes with multiple granulomas (Fig.3,4) composed of epithelioid cells, Langhan's type of giant cells and lymphocytes.(Fig5) Areas of caseous necrosis were noted. At places foci of necrosis infiltrated by polymorphs forming stellate abscess surrounded by epithelioid cells and lymphocytes were seen. (Fig.6) Periadenitis along with infiltration by inflammatory cells into perinodal adipose tissue was noted in 6 cases. Some of the cases showed sinuses distended with large pale histiocytes. (Fig.7) Many multinucleated giant cells, some showing emperiopolesis were also noted. Overlying skin showed ulceration.

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20% Ziehl –Neelsen (ZN) staining:

ZN staining was performed in all cases. It showed presence of Acid Fast Bacilli (AFB) in eight cases of which four cases showed numerous AFB (Fig.8) Rest 5 cases were negative for AFB.

Considering the clinical scenario, histopathological findings and history of BCG vaccination prior to appearance of swelling - diagnosis of BCG lymphadenitis was given and Phage typing of BCG strain was advice for confirmation.

Discussion:

The history of the BCG vaccine starts with two French scientists Albert Calmette and Camille Guerin who developed a vaccine against tuberculosis. BCG is an abbreviation of Bacillus Calmette–Guerin, meaning the bacilli of Calmette and Guerin.[7]

BCG vaccine is recommended to be given along with Oral Poliovirus Vaccine at first contact of a newborn or as early as possible till one year of age. It is used globally for prevention of serious forms of tuberculosis like tubercular meningitis and disseminated tuberculosis.[8] After intradermal injection, live attenuated strain of BCG gets disseminated to various organs of the body including lymph nodes and causes asymptomatic subclinical lymphadenopathy.[9] Sometimes it will produce symptoms in the form of regional BCG related lymphadenitis which can be suppurative or nonsuppurative type or disseminated BCG infection.

1. Regional BCG related lymphadenitis- is referred when there is a BCG vaccine at one arm with ipsilateral regional lymph node involvement. Features favouring includes BCG vaccination at the ipsilateral arm, child age not more than 2 years, onset between 2 to 6 months after BCG vaccination, absence of systemic manifestations, involvement of axillary lymph node.[5,6,10]

A)Non suppurative lymphadenitis

It typically develops 2 weeks to 6 months post immunization and tends to affect the axillary lymph nodes. Usually it regresses and some may progress to suppuration.[11]

B)Suppurative lymphadenitis

It is characterised by the progressive enlargement of regional lymph nodes with collection of pus and associated with erythema.[5-6] If untreated it frequently ruptures with sinus formation as was seen in two of our cases.

2.Disseminated BCG infection

It is the most serious complication of BCG vaccination. When there is involvement of distant anatomical site beyond BCG administration site and ipsilateral lymph node it is termed as disseminated BCG infection. Synonyms are systemic BCG disease or BCGosis.[12]

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The disseminated BCG infection has been commonly reported in immunocompromised children.[13]

BCG lymphadenitis is a fairly common complication of BCG vaccination, and the incidence differs between the regions but in many of the patients showed spontaneous regression during follow up of first 6 months. If lymph nodes show no signs of regression and remain persistently enlarged for more than 6 to 9 months with a size of 3 cm or more, it needs treatment.[14]

There are different treatment strategies for BCG lymphadenitis, which include watch and see with regular follow-up, anti-tubercular treatment, needle aspiration, incision and drainage or surgical excision of involved lymph nodes. Needle aspiration is an effective measure in cases with suppurative lymphadenitis, but in those with larger size, multiple, matted lymph nodes, needle aspiration usually has no proven efficacy.[14] In our study needle aspiration was tried in two cases but was not effective, so surgical excision was done.

BCG lymphadenitis is often difficult to differentiate from tuberculous lymphadenitis morphologically but is important to differentiate as treatment schemes differ. Isolated axillary lymphadenitis of tuberculous etiology is very rare. Ipsilateral enlargement of regional lymph node with history of BCG vaccination in the absence of any constitutional symptoms is diagnosed as BCG adenitis.[9,15]

Routine investigations such as blood examination, chest X ray, and Mantoux test have no role in the diagnosis. Microbiological separation of BCG is confirmatory, but species identification of acid-fast bacilli often needs phage typing or genetic analysis.[5]

Awareness of BCG lymphadenitis, its various types and differentiation from tuberculosis is important for proper management of this lesser known entity.

Conclusion:

Histopathological evaluation combined with clinical correlation is important in approaching the diagnosis and also in management. A diagnosis of BCG adenitis should always be kept in mind in children presented with lymphadenopathy, who have been recently vaccinated with BCG.

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Figures:

Fig 1: Gross photograph of matted lymph nodes

Fig 2: Gross photograph of lymphadenopathy–cut surface showing yellowish necrotic areas

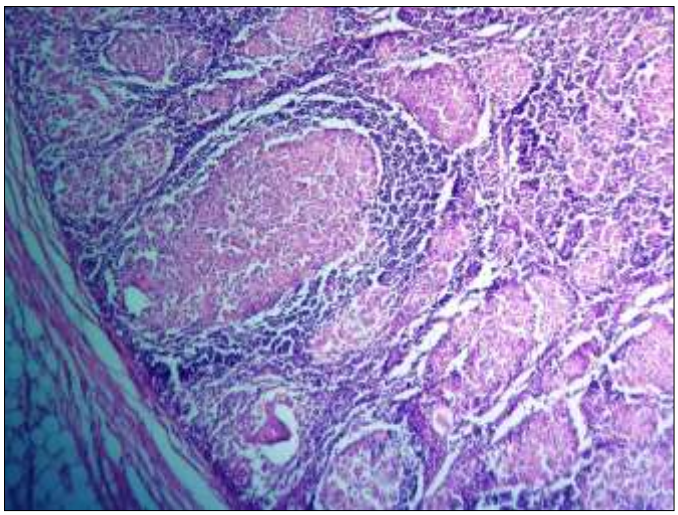

Fig3: Microphotograph showing lymph node with multiple granulomas (H&E100X)

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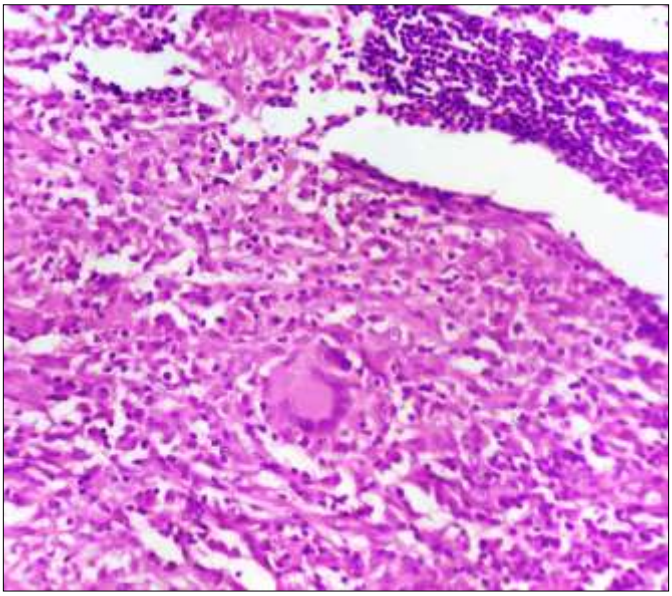

Fig.4: Microphotograph- Lymph node with granuloma (H&E 400X)

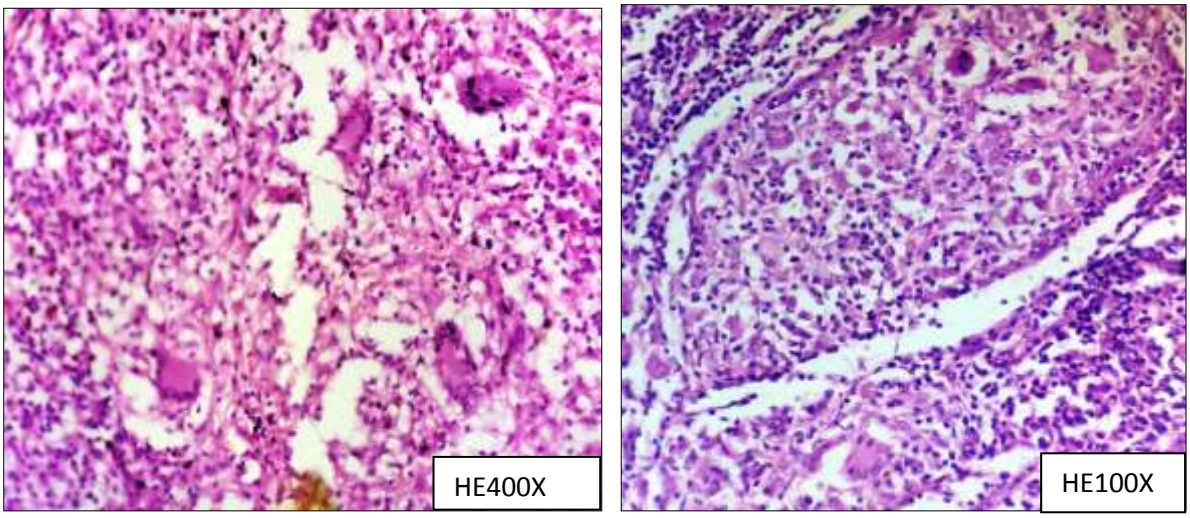

Fig 5: Microphotograph –Granulomas composed of epithelioid cells, lymphocytes and Langhan's giant cell

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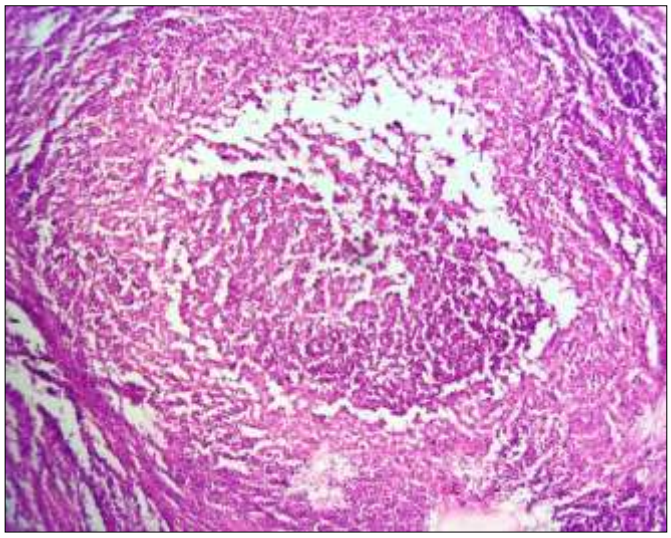

Fig 6: Microphotograph showing stellate abscess(H& E 100X)

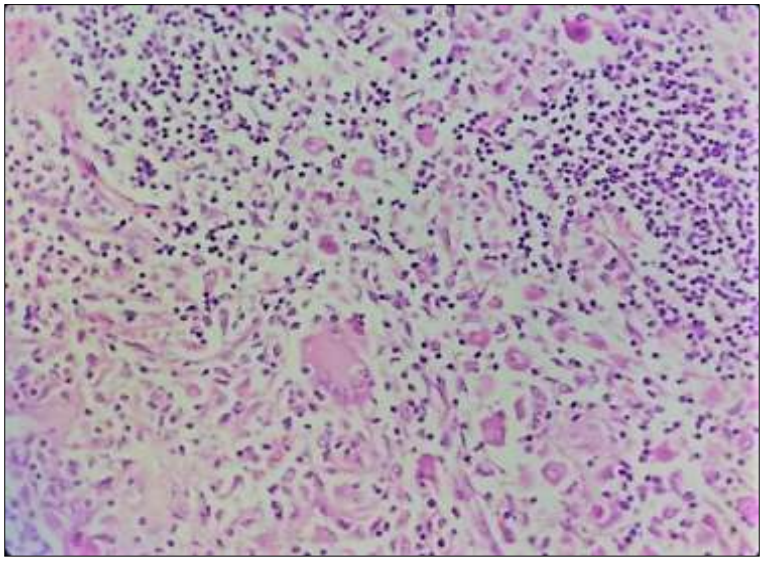

Fig 7. Microphotograph –histiocytic collection (H&E 100X)

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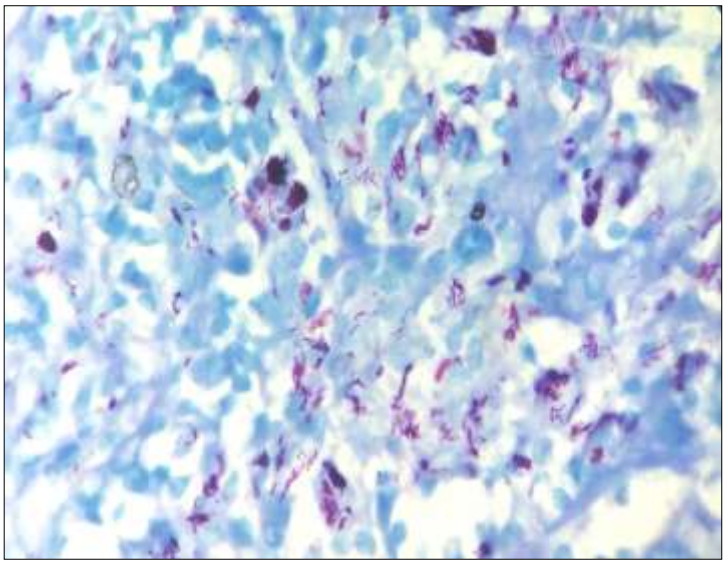

Fig 8: Microphotograph -20% Ziehl –Neelsen staining showing acid fast bacilli in globi