



“BCG LYMPHADENITIS: CLINICAL INSIGHTS, CYTOLOGICAL FEATURES, AND MANAGEMENT STRATEGIES – A CASE SERIES”

Pathology

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ABSTRACT

Introduction: Tuberculosis is an infectious disease that often requires high level of suspicion for diagnosis, can be challenging to identify and treat, it is caused by a pathogen with tendency for antibiotic resistance and is most importantly the leading cause of infectious death worldwide. BCG is a live attenuated vaccine; it has been used to prevent tuberculosis since 1921. In general BCG is considered a safe vaccine, but it has been associated with local and systemic complications. **Materials And Methods:** A total of 4 cases are included in our study, which were presented to our department in a period of 1 year. Children under 3 years old, who developed left axillary swelling observed by parents at different time intervals after BCG vaccination, were referred to the cytology section in our department for FNAC, as advised by the clinician. FNAC was performed and slides stained with Hematoxylin & Eosin stain, Wright's stain and Ziehl Neelsen stain. **Results:** Four cases were examined, with mean age of 14.75 months, ranging from 8 months to 2 years, and an equal number of male and female cases. All children presented with left axillary swelling without any other associated symptoms. On FNAC of left axillary lymph node 75% of the cases yielded pus aspirate and in 25% of cases it was cheesy material. Microscopy was studied and two cases showed ZN stain positivity. **Conclusion:** It is crucial for parents, paramedical staff and medical practitioners to be aware of BCG-induced lymphadenitis as a potential complication following BCG vaccination. This awareness ensures prompt diagnosis and proper management of such cases.

KEYWORDS

INTRODUCTION:

Tuberculosis is an infectious disease that often requires a high level of suspicion for diagnosis, can be challenging to identify and treat, is caused by a pathogen with a tendency for antibiotic resistance and is most importantly the leading cause of infectious death worldwide.¹ Every year, more than 10 million people develop active TB disease, and almost 2 million die from it.² The World Health Organization (WHO) developed an effective way of preventing TB by creating a vaccine. So far, the only WHO-approved vaccine is the BCG (Bacilli Calmette-Guérin) vaccine, which was introduced in 1921.³

The world health organization (WHO) has recommended BCG Vaccination as a part of the global expanded program for immunization (EPI) in developing countries.² The efficacy of BCG Vaccine against tuberculosis is uncertain, this vaccine is protective against the meningeal/miliary TB in childhood tuberculosis and not for adult tuberculosis.⁴ BCG vaccine induces delayed type of hypersensitivity (DTH) reaction and cell-mediated immunity in the host 4-8 weeks after vaccination.⁵

BCG may offer protection against leprosy.⁶ It has also been used in the treatment of superficial bladder carcinoma.⁷ In general, BCG is considered a safe vaccine, but it has been associated with local and systemic complications.⁸

MATERIALS AND METHODS:

A total of four cases are included in our study, study conducted over a one-year period from March 2023 to February 2024 in the department of Pathology KMCRI, Hubballi. The patients, children aged less than 3 years old who were brought to our department after parents noticed left axillary swelling at different time intervals after BCG vaccination. These children were referred to cytology section for fine needle aspiration cytology (FNAC) as per the clinician's recommendation. FNAC was performed using a 24-gauge needle, and the collected material was smeared on slides. The slides were then stained with hematoxylin and eosin stain, wright's stain and ziehl - Neelsen stain.

The following criteria were used to identify a case of BCG lymphadenitis: enlargement of isolated axillary lymph node, history of BCG vaccination on the ipsilateral arm, and no local or systemic signs of inflammation.

RESULTS:

The study involved a total of four cases with a mean age of presentation

of 14.75 months, ranging from 8 months to 2 years. There was an equal distribution of male and female cases, with a 1:1 ratio. All children presented with left axillary lymph node enlargement without any associated symptoms, and all had a history of axillary lymph node enlargement following BCG vaccination on the same side. Each child had a healed BCG scar with no signs of reaction or inflammation at the vaccination site. Ultrasonography (USG) was performed on three patients, revealing left axillary lymphadenopathy in 2 cases and in one patient USG showed necrotic left axillary and supraclavicular lymph nodes. FNAC of the left axillary lymph nodes was performed, yielding cheesy material in 1 of the case and pus aspirate in the other 3 cases. Microscopic examination showed caseous necrosis, a few epithelioid cell granulomas, scattered lymphocytes, epithelioid cells, and degenerated cells. In 2 cases Ziehl-Neelsen (ZN) staining revealed acid-fast bacilli.

The details of the cases are given in **Table 1**

	CASE 1	CASE 2	CASE 3	CASE 4
AGE	1 year 3 months	2 years	8 months	1 year
SEX	Male	Female	Female	Male
CLINICAL PRESENTATION	Left axillary swelling since 9 months	Left axillary swelling since 6 months	Left axillary swelling since 2 months	Left axillary swelling since 10 months
EXAMINATION	Left axillary swelling, 2x1 cm, firm, mobile, non tender	Left axillary swelling, 3x2 cm, soft to firm in consistency, mobile non tender	Left axillary swelling 2x2 cm soft to firm in consistency, skin pinchable	Left axillary swelling 1.5x1.5cm firm, mobile, non tender.
USG	Enlarged left axillary lymph node	NA	Necrotic - left axillary lymph node and left supraclavicular lymph node	Enlarged left axillary lymph node
ASPIRATION	Cheesy material	Pus aspirate	Pus aspirate	Pus aspirate

MICROSCOPIC FINDINGS	Caseous necrosis, few epithelioid cell granuloma	Necrosis	caseous necrosis, scattered lymphocytes, epithelioid cells	Necrosis, scattered degenerated cells and epithelioid cells
ZN stain	NA	Positive	Negative	Positive
DIAGNOSIS	BCG Lymphadenitis	BCG Lymphadenitis	BCG Lymphadenitis	BCG lymphadenitis

*NA - Not available

FIGURES

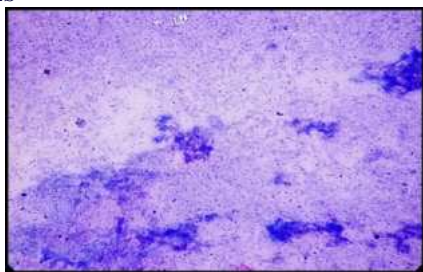


Figure 1: FNAC smear shows caseous necrosis and scattered inflammatory cells (Wright's stain, 100x)

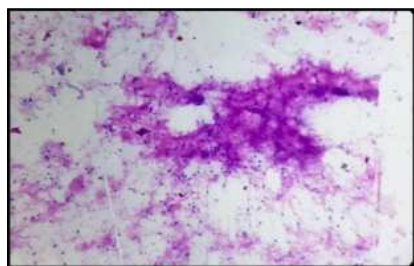


Figure 2: FNAC smear shows caseous necrosis, scattered epithelioid cells, lymphocytes, and degenerated cells (Hematoxylin & Eosin stain, 400x)

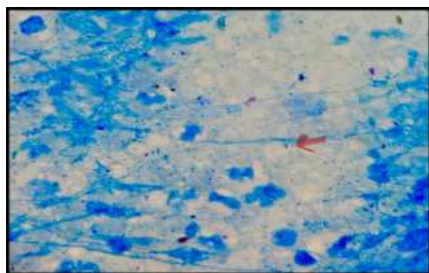


Figure 3: FNAC smear shows acid fast bacilli (red arrow mark) (ZN stain, 1000x)

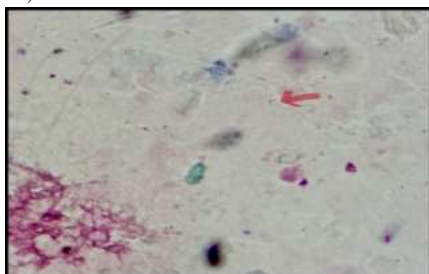


Figure 4: FNAC smear shows acid fast bacilli (red arrow) (ZN stain, 1000x)

DISCUSSION

WHO has classified the adverse events as mild or severe. Mild adverse events include ulceration at the site of injection and ipsilateral axillary lymphadenopathies (less than 1.5cm in size and not adhering to overlying skin); severe adverse events include ipsilateral axillary

lymphadenopathies (adherent to overlying skin), osteitis or osteomyelitis and disseminated disease (BCG-itis).³

A red, tender, and indurated papule usually is seen at the injection site.³ This papule may appear 2 or more weeks after vaccination, it can progress to an ulcer, and then form a crust that falls off after approximately 6 weeks and leaves the commonly known BCG scar.^{3,9}

BCG LYMPHADENITIS

The immunization of newborns with Bacilli Calmette-Guérin (BCG), may result in enlarged lymph nodes, usually the axillary nodes. BCG lymphadenopathies occur in 0.73% to 2.2% of children after a mean interval of 2.5 months and as late as 3 years after vaccination.^{10,11} The iliac lymph nodes may be involved when BCG is used for the intravesical treatment of bladder cancer.¹¹ Children and adults with normal immunity recover spontaneously or after the excision of a tuberculous lymph node. However, in children with congenital immune deficiencies¹² and in patients with HIV infection and AIDS, suppurative lymphadenitis and disseminated, sometimes fatal, tuberculosis develop.¹⁰ Complications of BCG vaccination have been reported both in immunocompetent and immunocompromised individuals.¹³

BCG lymphadenitis occurs in two forms: suppurative and nonsuppurative, with the nonsuppurative type being more common. The nonsuppurative, also known as simple BCG lymphadenitis, usually resolves on its own over a few weeks without causing lasting effects. In contrast, the suppurative form involves the gradual swelling of the affected lymph nodes, accompanied by redness, swelling, darkening of the skin, and the development of pustules.¹⁴

DIAGNOSIS OF BCG LYMPHADENITIS¹⁵

- Isolated axillary (or supraclavicular/cervical) lymph node enlargement.
- History of BCG vaccination on the same side.
- Absence of tenderness and raised temperature over the swelling.
- Absence of fever and other constitutional symptoms.
- Chest radiography, Mantoux reaction, and hematological analysis are not helpful. Fine needle aspiration cytology corroborates the clinical diagnosis in doubtful cases.

MANAGEMENT:¹⁶

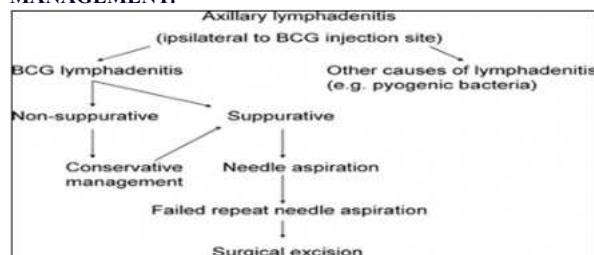


Figure 5: Flow Chart showing management of BCG Lymphadenitis

1. Medical Treatment: Studies have shown that antibiotics and anti-tubercular drugs do not help in managing the condition. Antibiotic therapy is, however, often indicated for treatment of suppurative lymphadenitis proven to be caused by superinfection with pyogenic bacteria
2. Needle Aspiration: This is beneficial for suppurative BCG lymphadenitis, as it helps drain pus, reduces complications from the suppuration, and promotes healing.
3. Surgical Excision: This is considered when needle aspiration fails, or when there are multiloculated or matted lymph nodes and draining sinuses present.

CONCLUSION:

It is crucial for parents, paramedical staff, and medical practitioners to be aware of BCG-induced lymphadenitis as a potential complication following BCG vaccination. This awareness ensures timely diagnosis and proper management of such cases. Non-suppurative BCG lymphadenitis is a harmless condition that resolves on its own without the need for treatment. Suppurative lymph nodes are treated with needle aspiration to prevent the formation of sinuses, ugly scars, and to speed up recovery. Surgical excision is needed when needle aspiration fails.

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