

Quiz Case

Granulomas on cervical Pap smear: “Forget me not”

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A 62-year-old female presented with the complaints of heaviness in the lower abdomen for 1 year. She was post-menopausal from the past 15 years. No prior history of fever or cough was present. On gynecological examination, her uterus was anteverted and cervix showed mild erosion. Routine Papanicolaou test was done and stained smears showed features as shown in Figure 1.

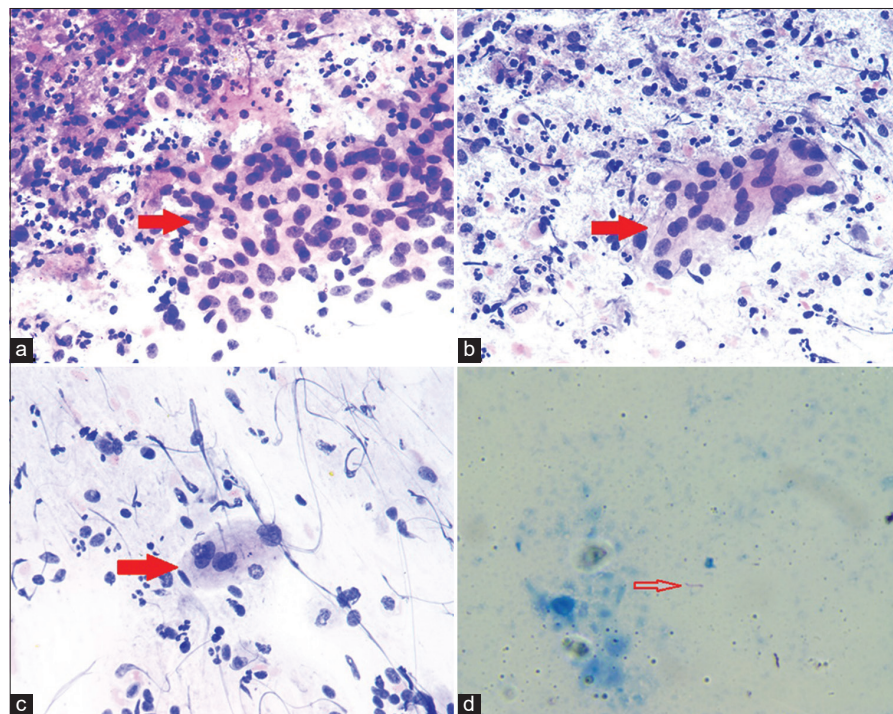


Figure 1: (a and b) Smears show well-formed collection of epithelioid cells forming granulomas (red arrow). The adjacent area shows parabasal cells and inflammation comprising of neutrophils and lymphocytes. ($\times 100$, Papanicolaou [PAP] stain); (c) Smear shows a multinucleated giant cell (red arrow) ($\times 100$, PAP stain); (d) Smear shows a beaded rod-shaped acid-fast bacillus (red arrow) ($\times 1000$ oil immersion, Ziehl Neelson stain).

1. What is your probable diagnosis?
 - a) Sarcoidosis
 - b) Granuloma Inguinale
 - c) Tuberculosis
 - d) Syphilis.

Answer to Question 1: (c)

The granulomas [Figure 1a and b] and multinucleated giant cell [Figure 1c] can be seen in all of the above conditions; however, positive acid-fast bacilli on Ziehl Neelson stain (ZN) are a characteristic feature of *Mycobacterium tuberculosis*.

Tuberculous bacilli are seen as a pink rod shaped slender bacilli on ZN stain [Figure 1d].

2. What is the mode of spread for cervical tuberculosis?
 - a) Hematogenous spread
 - b) Lymphatic spread
 - c) Primary infection
 - d) All of the above.

Answer to Question 2: (d)

Cervical tuberculosis (TB) can spread by any route – Hematogenous spread, lymphatic spread, or direct extension from the primary focus in the body. Rarely, primary route can be the cause of infection introduced by the male partner suffering from TB of genitourinary tract.

3. Which stain is used for the confirmation of TB infection?
 - a) Periodic Acid Schiff stain
 - b) Ziehl Neelson stain – 20%
 - c) Ziehl Neelson stain – 05%
 - d) Ziehl Neelson stain – 01%.

Answer to Question 3: (b)

The concentration of sulfuric acid varies in the ZN stain. About 20% of acid is used for *M. tuberculosis*, 5% of acid is used for *Mycobacterium leprae*, and 1% of acid is used for actinomyces and nocardia.

REVIEW OF THE TOPIC

TB is a significant cause of high morbidity and mortality and is more common in developing countries. TB of the female genital tract is a rare disease and more commonly involves the upper genital tract (fallopian tubes and endometrium) as compared to lower genital tract.^[1,2] TB of cervix is very rare as the stratified squamous epithelium is resistant to the tubercular bacilli.^[3] Cervical TB accounts for 0.1–0.65% of all the TB cases and 5–24% of the genital tract TB cases.^[1,2] The incidence of TB is on rise.^[1] It can occur at any age but commonly affects women of reproductive age group.^[4,5] The two common organisms responsible for genital TB are *M. tuberculosis* or *Mycobacterium bovis*.^[1] Genital tract TB usually occurs from the hematogenous spread of infection from the primary focus. Cervical TB almost always occur secondary to TB of fallopian tube or endometrium and is typically associated with pulmonary TB.^[1,2] It can occur by either hematogenous spread, lymphatic spread, or by direct extension from the primary focus.^[1,6,7] Rarely, primary route can be the cause of infection introduced by the partner suffering from TB of genitourinary tract.^[2,4] Chowdhury

suggested that sputum may also be source of infection when it is used as a sexual lubricant.^[4] The symptoms of genital TB can range from constitutional symptoms to infertility.^[1,2] The common presentations include abdominal pain, menstrual irregularities, discharge per vaginum, postmenopausal bleeding, etc.^[2] Grossly TB can present as papillary or vegetative growth, multiple tiny nodules or ulcer, and on imaging studies (hysterosalpingography or ultrasonography) of cervix, there can be seen diverticular outpouching of cervix with feathery appearance or cervical distortion etc.^[1,3] These features can be easily misinterpreted as cervical carcinoma.^[1] Microscopic examination of a cervical biopsy is characterized by well-formed epithelioid cell granulomas which may be associated with multinucleated Langhans type giant cell reaction and caseation necrosis. Lymphoplasmacytic infiltrates are seen at the rim of granulomas.^[2] TB of cervix needs to be differentiated from other granulomatous diseases, for example, lymphogranuloma venereum, sarcoidosis, schistosomiasis, amoebiasis, brucellosis, foreign body granuloma due to suture, crystal or cotton, and carcinoma cervix.^[2,8-11] The confirmation can be done by demonstration of acid fast bacilli of TB on ZN staining or isolation of mycobacterium.^[2] However, ZN stain and culture may be negative in one-third of the cases. In these cases, identification of typical granulomas is sufficient for the diagnosis of TB, if other causes of granulomatous cervicitis are excluded from the study.^[1,2] Newer diagnostic techniques such as enzyme linked immunosorbent assay or polymerase chain reaction may aid in the diagnosis of TB.^[8,9] The treatment includes anti tubercular therapy. The granulomas disappear after the treatment; however, fertility is low in patients even after the treatment due to subsequent healing by fibrosis and adhesions.^[4,5] The best method of preventing TB is Bacillus of Calmette Guerin vaccination and healthy lifestyle.^[5]

SUMMARY

Genital TB is a chronic disease in females with low-grade symptoms. It commonly involves fallopian tubes and endometrium. Cervix is an uncommon location for genitourinary TB. The gross appearance and imaging studies of cervical TB may mislead as cervical carcinoma. Therefore, microscopic examination and positive ZN stain and culture are diagnostic. TB may lead to fibrosis and adhesion and is a major cause of infertility among females. Therefore, screening for genital TB must be a part while evaluating for the menstrual irregularities or infertility. Early diagnosis and further treatment are the key to avoid the complications associated with TB.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

COMPETING INTEREST STATEMENT BY ALL AUTHORS

There is no conflict of interest in this paper.

AUTHORSHIP STATEMENT BY ALL AUTHORS

Each author has participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article. All authors read and approved the final manuscript. Each author acknowledges that this final version was read and approved.

ETHICS STATEMENT BY ALL AUTHORS

As this is case without identifiers, our institution does not require approval from the Institutional Review Board (IRB).

LIST OF ABBREVIATIONS (In alphabetic order)

AFB – Acid Fast Bacilli
 ATT – Anti tubercular therapy
 BCG – Bacillus of Calmette Guerin
 ELISA – Enzyme linked immunosorbent assay
 PAP – Papanicolaou
 PCR – Polymerase chain reaction
 TB – Tuberculosis
 ZN – Ziehl Neelson.

EDITORIAL/PEERREVIEW STATEMENT

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a **double-blind model** (the authors are blinded for reviewers and vice versa) through automatic online system.

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