

Asherman's Syndrome and Blocked Tubes, Caused by Female Genital Tuberculosis; Case Report and Literature Review

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Citation: Tesfai B, Estifanos D, Gebremariam H, Sereke D, Gebrejesus T, et al. (2025) Asherman's Syndrome and Blocked Tubes, Caused by Female Genital Tuberculosis; Case Report and Literature Review. Anna Clin Rev Cas Rep: ACRCR-154.

Received Date: 21 May, 2025; **Accepted Date:** 28 May, 2025; **Published Date:** 06 June, 2025

Abstract

Female genital tuberculosis is one cause of infertility and secondary amenorrhea in developing countries, and subfertility might be the only presenting symptom. Here, we present a case of endometrial tuberculosis came with secondary amenorrhea of eight years and primary infertility of five years. She denies any symptom complex history of tuberculosis, but she had a contact history in which her father was treated for pulmonary tuberculosis 10 years back. Hormonal analysis was normal and hysterosalpingography showed signs of Asherman's syndrome with bilateral tubal blockage. Endometrial sampled histopathologic analysis revealed signs of endometrial tuberculosis. She took full course of anti-tuberculosis treatment and laparoscopy, and hysteroscopy was performed to diagnose and prevent the complications. With the double burden of diagnostic challenge and tuberculosis endemicity in low-income countries, high index of suspicion for an early detection and treatment is mandatory to mitigate related complications.

Keywords: Endometrial tuberculosis, Asherman's syndrome, Secondary amenorrhea, Infertility.

Introduction

Female genital tuberculosis (FGTB) is an important etiological cause of female infertility in countries with high prevalence of tuberculous (TB). (1) TB is thought to reach the genital tract via either hematogenous dissemination, lymphatic system, and/or direct spread from adjacent abdominal organs. (2) Within FGTB, the most infected sites are the fallopian tubes (95–100%), endometrium (50–60%), ovaries (20–30%), cervix (5–15%), myometrium (2.5%), and the vulva/vagina (1%). (3, 4) The worldwide incidence of FGTB in infertile women is approximately 5–10% with higher incidence rates found among developing compared to developed countries. (1) Incidence of FGTB at infertility clinics varies due to differences in the overall prevalence of TB, clinical awareness of FGTB, and regional variation in the availability and use of sensitive and accurate diagnostic tests and diagnostic hysteroscopy and endometrial biopsy are often used to arrive diagnosis. (2)

FGTB is typically asymptomatic and is often diagnosed incidentally (1, 2) and symptomatic FGTB may present with a variety of gynecological symptoms of infertility, menstrual disturbance, chronic pelvic pain, dyspareunia (1,3, 5-7, 8) and/or abnormal vaginal discharge. (2, 9) Infertility is considered a long-term complication of FGTB as the symptomless nature of the infection delays individuals to seek treatment, allowing the infection to fester and damage the reproductive organs. (2) In addition to the diagnostic challenge, fertility outcomes after treatment are not impressive. (5) Thus, early diagnosis and on-hand available treatment of anti-TB medication are crucial to prevent the development FGTB and/or permanent damage to reproductive organs. (1, 2)

The prevalence of endometrial TB in this study (Ethiopia) was 4.6% while culture proven endometrial TB was 2.6%. However, histological examination identified only 1.3% endometrial tuberculosis. This study has also shown that the magnitude of endometrial TB is high in gynecologic patients visiting outpatient departments for various complaints. (10) The prevalence of FGTB as a cause of infertility has neither been previously documented nor assessed in Eritrea. We report a case with primary infertility and secondary amenorrhea and histopathological confirmed endometrial tuberculosis.

Case Report

A 29-year-old nulliparous woman presented with infertility of five years. After her menarche, she had regular menses for three years followed by oligomenorrhea of few months and secondary amenorrhea for eight years. Her father was treated for pulmonary tuberculosis 10 years back, and she had no history of vaginal discharge, dyspareunia, weight loss or night sweating. Hormone analysis and chest x-ray revealed normal findings but hysterosalpingography showed signs of Asherman's syndrome with bilaterally blocked tubes (Figure: 1a). Besides, laparoscopic pelvic organ exploration revealed extensive adnexal adhesions and dye test confirmed the tubal blockage. Hysteroscopy based endometrial sampling and histopathologic evaluation revealed endometrial fibrosis, granuloma formation and multiple giant cells caseous necrosis with chronic inflammatory cells, which suggests tuberculosis of the endometrium.

With the diagnosis of FGTB, she was started on anti-tuberculosis treatment with 2-months intensive phase with isoniazid, rifampin, ethambutol, and pyrazinamide, followed by a 4-month continuation phase with isoniazid and rifampin. She

was given these medications with Directly Observed Therapy (DOTs) to prevent treatment failure and drug adherence for effective outcome. She was followed regularly with liver function test, renal function test and chest x-ray, which all were within the normal range.

After completion of anti-tuberculosis treatment, diagnostic and therapeutic hysteroscopy was performed, and cure of endometrial tuberculosis was confirmed by endometrial

sampling taken during hysteroscopy. Her hysterosalpingography was repeated and revealed bilaterally blocked tubes, with formed endometrial cavity. (Figure: 1b, c) Different treatment modalities (progesterone releasing IUD, oral contraceptive pills, norethisterone and estrogen) were tried, which all didn't show any improvement, and she had never menses yet. Currently, she is on follow-up for her infertility condition for possible in vitro fertilization.



Figure 1: Hysterosalpingography (HSG) (a) before treatment: a uterus with marked narrowed cavity of irregular wall and irregular contrast filling, and the uterine tubes were not visualized and no free spillage seen in the peritoneum; which all are suggestive with chronic inflammatory process likely Asherman's syndrome and bilaterally blocked tubes (b) after anti-tuberculosis treatment revealed bilaterally blocked tubes and partially formed cavity and extravasation of contrast (c) after completion of treatment and hysteroscopy based dilatation and curettage, well-formed endometrial cavity with bilaterally blocked tubes.

Discussion

Patients with FGFB are often asymptomatic and commonly present to a health facility once symptoms of infertility and/or menstrual irregularity had arisen. Hence, health seeking behavior, diagnosis and delayed treatment which allow the infection to fester and develop chronic complications, as infertility, Asherman's syndrome, and blocked tubes with poor fertility outcome even after completion of anti-TB treatment, consistent with other literature. (2)

Our patient has primary infertility and secondary amenorrhea but denied any vaginal discharge; findings which are commonly found within various studies. (1, 5, 9, 11) Vaginal discharge is likely identified with post-menopausal compared to reproductive-aged women with endometrial TB. (4, 12) She had prolonged amenorrhea due to severe endometrial adhesions and loss of the functional layer of the endometrium with intact ovaries as her hormonal analysis was normal. One case report stated that patients notice the return of cyclic spotting, indicating possible return of menses, but as to date, our patient menstruation has not yet returned. (7)

Although her father was the only known TB contact, she had neither diagnosed of TB nor had any weight loss, sweating, or cough. Chest x-ray appeared normal which aligns with other reports with most FGFB women may have normal chest radiography and no prior history of TB. (2) But, approximately 20% of FGFB patients have a family history of TB. (11) The patient likely contracted TB from her father which became latent within her genital tract and, after years, the infection had flared and damaged her reproductive organs, causing amenorrhea and infertility. The fact that the patient had regular menses three years past her father's treatment, followed later by irregular menses and amenorrhea strongly suggest latent tuberculosis infection in the genital tract. The challenge of diagnosing genital

TB in the female genital tract during subfertility investigations and after a complicated pregnancy in a woman without a history of or symptoms of TB is highlighted. (13)

Laparoscopy and hysterosalpingography indicated bilaterally blocked fallopian tubes with severe endometrial adhesions, which stand clues for TB involvement of fallopian tubes and uterus. This was consistent with literatures that, the most common female genital organs involved are the fallopian tubes, endometrium, and ovaries. (1, 7, 11, 14) Histopathological analysis of endometrial biopsy revealed endometrial fibrosis, granuloma formation, multiple giant cells with caseous necrosis, like other study. (2) In this case, the family history of TB, clinical presentation (infertility and amenorrhea), diagnostic procedures (hysterosalpingography, hysteroscopy and laparoscopy), and histopathological findings were consistent with FGFB. And further confirmation of the histopathologic diagnosis via polymerase chain reaction and isolation of *M. tuberculosis* complex may further strengthen the evidence for this case report.

Functional loss of the endometrium and bilaterally block tubes are the main cause of infertility for this case as the uterus can no longer sustain pregnancy. However, as the patient's hormonal and ovarian condition are normal, surrogacy or adoptions are available options to experience motherhood. (1, 5, 15) Fertility in some cases may return, as in one case, after completion of therapy, the patient spontaneously conceived and delivered a healthy full-term baby. (1) Besides, subsequent to diagnosis, continuous TB medications had excellent clinical outcome in two patients (pregnant in 18 months after undergone laparoscopy). (8) And, another study reported anti-tubercular treatment may reverse the reproductive capability and prevent permanent damage to the female reproductive organ, as the

pregnancy rate of 64.7 % in secondary infertility and 20.8 % in primary infertility was very much promising. (16)

As poor fertility outcome is likely due to the complications of FGTB, an endometrial biopsy should be advocated in every patient with unexplained female infertility, especially in TB endemic areas. As in our case, since the patient had an eight-year history of amenorrhea, an endometrial biopsy was needed.

This corresponds with other literatures that routine endometrial biopsy should be taken in patient with subfertility. (15)

Conclusion
FGTB is one cause of infertility in TB endemic countries with poor fertility outcome even after completion of treatment. In low-income countries, diagnostic challenges, and high index of suspicion for an early detection and treatment of FGTB is mandatory to mitigate the complication.

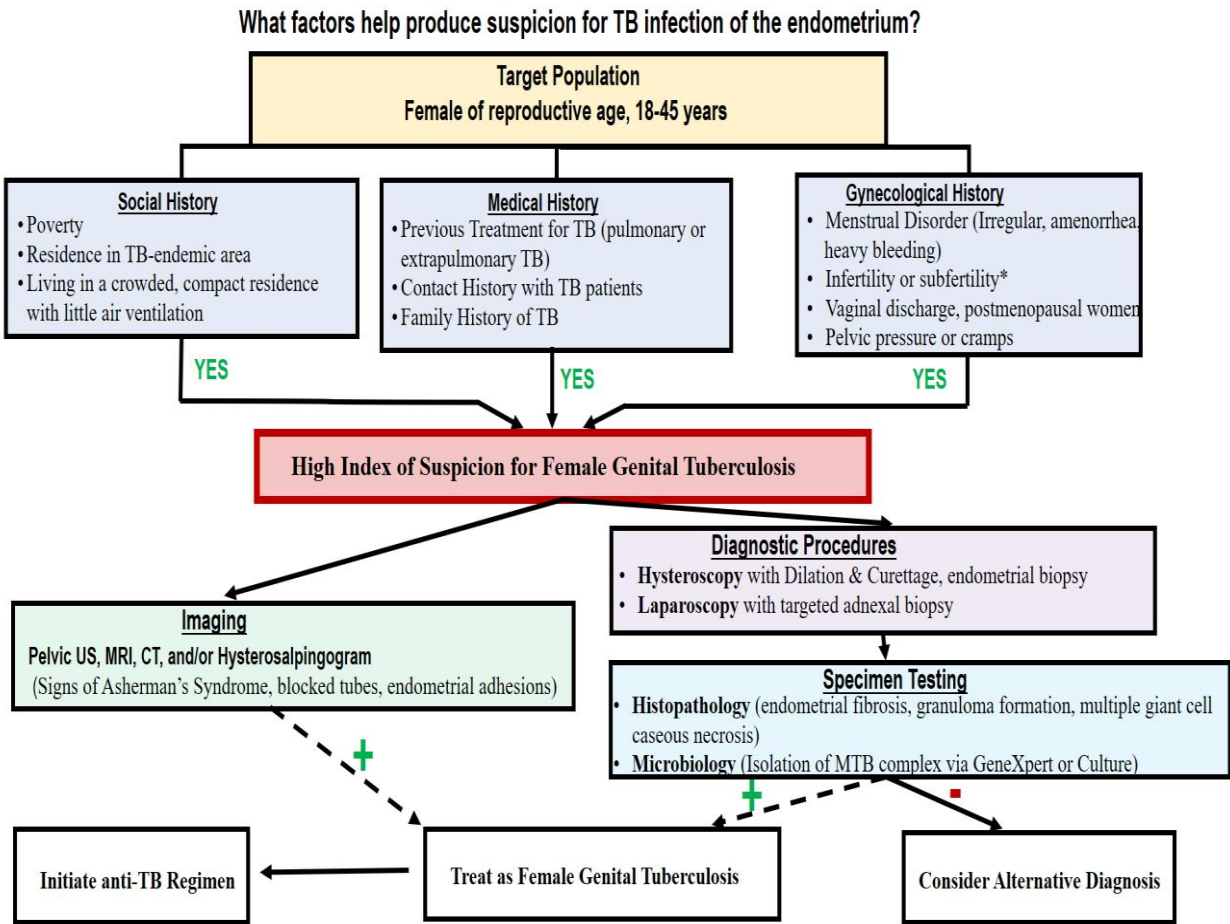


Figure 2: Algorithm regarding risk factors and suggested steps for a high index of suspicion of FGTB. Dash arrows signify both imaging and specimen testing are required to arrive to diagnosis of FGTB. (This was partially adopted from Tzelios et. Al, modified and created by the authors)

Declarations

Acknowledgments: Authors acknowledges Orotta National Referral Maternity Hospital staff and pathology department for their investigative analysis.

Abbreviations: Tuberculosis (TB), Female genital tuberculosis (FGTB), Bacillus Calmette-Guérin (BCG) vaccine.

Informed consent: A written informed consent was obtained from the patient to present and publish the case report for teaching purpose.

Conflict of interest: Authors have no conflict of interest to disclose

Availability of data and material: All available information is included in the manuscript

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