Asian Journal of Health Research
Journal Homepage: https://a-jhr.com
Published by Ikatan Dokter Indonesia Wilayah Jawa Timur

Case Report

Asherman's Syndrome due to Endometrial Tuberculosis: A Case Report and Literature Review

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ARTICLE HISTORY
Received: 29 May 2025
Revised: 28 June 2025
Accepted: 28 July 2025

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KEYWORDS
Amenorrhea; Infertility; Hysteroscopic Surgery; Female Genital Tuberculosis; Endometrial Adhesion

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ABSTRACT

Introduction: Female genital tuberculosis, a rare form of extrapulmonary TB, often goes underdiagnosed despite its potential to cause significant reproductive complications such as amenorrhea and infertility. The theory behind this case emphasizes the need for heightened awareness and improved diagnostic approaches to effectively manage endometrial TB and its associated intrauterine adhesions.

Case Presentation: A 31-year-old woman presented with a four-year history of oligomenorrhea and 3.5 years of primary infertility, undergoing various treatments including hormone therapy and ultrasound evaluations that revealed intrauterine masses and cervical issues. Following a hysteroscopic surgery that identified cervical stenosis and a tuberculous mass, she was treated for endometrial tuberculosis with anti-tuberculosis medication. Despite treatment, she continued to experience abnormal menstrual cycles, leading to further hysteroscopic evaluations that indicated significant uterine fibrosis and chronic cervicitis. The patient declined the insertion of a levonorgestrel-releasing intrauterine system (LNG-IUS) but received a Depo Medroxy Progesterone Acetate (DMPA) injection and was fitted with an IUD, alongside hormonal therapy with cycloproginova, with ongoing assessments showing improvements in uterine vascularity and visibility of the fallopian tubes.

Conclusion: This case highlights the complexities of managing secondary amenorrhoea due to genital tuberculosis, which disrupts endometrial function and results in significant intrauterine adhesions. A multidisciplinary approach, involving hysteroscopic adhesiolysis, anti-tubercular therapy, and postoperative hormonal interventions, is crucial for effective treatment. Despite the restoration of menstrual cycles, ongoing fertility risks and pregnancy complications necessitate thorough preconception counselling and long-term monitoring.

Cite this as: Pratama AJ, Prabowo A, Tantular R, Fadli ML (2025) Asherman's Syndrome due to Endometrial Tuberculosis: A Case Report and Literature Review. *Asian J Heal Res*. 4 (2): 44–49. doi: 10.55561/ajhr.v4i2.251

INTRODUCTION

Tuberculosis (TB) is a chronic granulomatous disease primarily affecting the lungs, with genitourinary involvement being an uncommon but potential secondary complication in women. Among these, female genital tuberculosis remains an underrecognized form of extrapulmonary TB that typically arises secondary to pulmonary or abdominal infection. Endometrial TB is found in 50-80% of female genital TB cases and can cause progressive damage to uterine structure and function. Patients are usually asymptomatic but could present with menstrual irregularity and infertility [1,2].

In advanced stages, adhesions may cause distortion to total obliteration of the uterine cavity, often leading to amenorrhea secondary to organ failure. While advances in diagnostic techniques, especially with hysteroscopy, have improved the detection of intrauterine adhesions, the prevalence of endometrial TB is still often underdiagnosed, especially in areas with high rates of genital TB. Diagnosis is often delayed due to non-specific symptoms or lack of awareness about the association between genital TB and the development of secondary amenorrhea [1,3].

This case report aims to highlight a rare case of endometrial TB accompanied by intrauterine adhesion, highlighting the clinical, diagnostic, and management challenges in such cases. By understanding the relationship between these two conditions, we can further improve patient management and prevent long-term complications.

CASE PRESENTATION

A 31-year-old lady approaches with a primary complaint of oligomenorrhea for the past four years and primary infertility for 3.5 years, seeking treatment at a private hospital for the past year. The patient had hormone therapy, resulting in a normal menstrual cycle; however, it became abnormal again in the final six months, even with hormonal therapy. She sought treatment at another private hospital, where the ultrasound results indicated a mass in the intrauterine cavity; thereafter, she was directed to Saiful Anwar General Hospital. The patient was examined in the outpatient clinic, showing vital signs within normal limits, a BMI of 24 kg/m², and resistance was observed during uterine sondage in the gynaecological examination. The uterus appeared somewhat enlarged, indicative of 12 weeks of gestation. Ultrasound findings revealed cervical thickening and hypervascularity, indicative of cervicitis, accompanied by left hematosalpinx and hematometra, with differential diagnoses including left pyosalpinx and pyometra. The laboratory findings for the patient revealed progesterone at 0.11 ng/ml, prolactin at 374.6 uIU/ml, oestradiol at 50.38 pg/ml, and FSH at 7.14 mIU/ml. The patient was scheduled for an elective hysteroscopy to evaluate the diagnosis.

Hysteroscopic surgery identified cervical stenosis, and dilation was subsequently conducted. A mass of irregular shape was present in the cavum uteri, exhibiting minor vascularization, and the tubal ostia were not distinctly observable; the impression suggested the presence of purulence. Resection and ablation of the hemorrhagic source, along with the evacuation of pus and debris, were executed. Fibrosis is present in the cervix, corpus, and fundus of the uterus. The hysteroscopic PA mass biopsy revealed a tuberculous process. The thoracic radiograph indicated left lung fibrosis resulting from prior inflammation, with no infiltrates present.

The patient was then referred to a pulmonary specialist for joint management, exhibiting no symptoms of fever, weight loss, or night sweats. Assessment of *Ziehl-Neelsen* (ZN) stain sputum negative, rapid HIV negative, and diagnosed with endometrial tuberculosis, treated with anti-tuberculosis medication 4 FDC (Fixed Drug Combination) 1x3 tablets (1 month), followed by a continuation phase lasting up to 12 months. After 12 months, the patient continued to experience abnormal menstrual periods. A hysteroscopy was conducted, revealing significant fibrosis within the uterine cavity, a thin endometrium, and unclear visibility of the left and right tubal ostia. The endometrial biopsy indicated chronic cervicitis with squamous metaplasia, and the insertion of an LNG-IUS (levonorgestrel-releasing intrauterine system) was proposed, but the patient declined.

The patient subsequently received a DMPA (Depo Medroxy Progesterone Acetate) injection for three months, was fitted with an IUD, administered cycloproginova (Estradiol valerate–norgestrel) for up to three cycles, and underwent hysteroscopy. The assessment results indicated minimal connective tissue, visibility of both tubes, and a profusion of blood vessels in the endometrium. The patient was scheduled to get an additional three cycles of cycloproginova.

DISCUSSION

The patient has been evaluated from the prior hospital, exhibiting negative findings for the progesterone challenge test and the estrogen-progesterone challenge test, indicating a probable uterine outflow obstruction in this instance. However, the follow-up for this patient is prolonged and delayed, taking up to one year, which exacerbates the severity of intrauterine adhesions. Non-specific and frequently asymptomatic manifestations in the initial stages of endometrial TB lead to postponed treatment and referral [4].

The early symptoms of amenorrhoea may have eased with progesterone treatment, leading to the patient's referral only after the discovery of an intrauterine mass and the subsequent exacerbation of amenorrhoea. The patient ought to have undergone a curettage biopsy or histological assessment upon the prior discovery of endometrial thickening or an intrauterine mass. The discovery of resistance during the uterine sondage confirmed this notion, but the laboratory results remained within normal parameters.

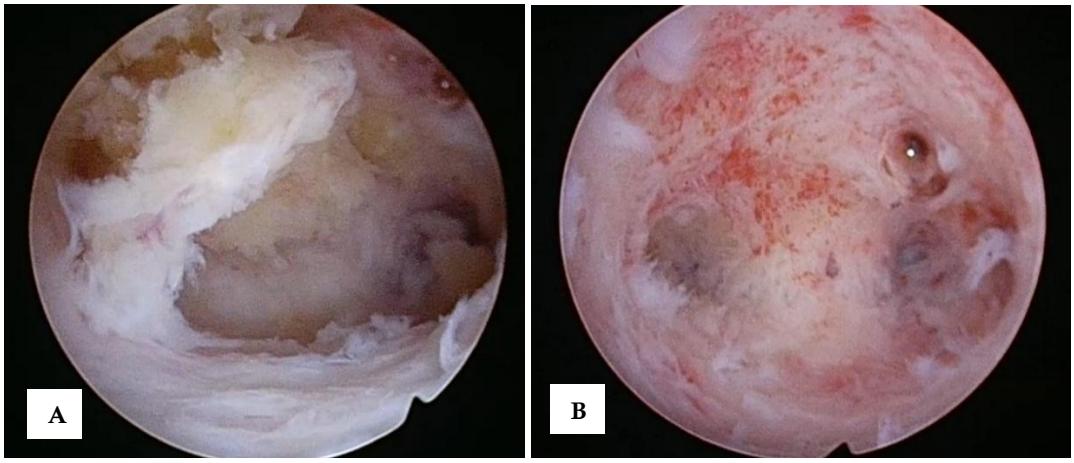


Fig. 1. **(A)** A mass of irregular shape with fibrotic and purulence in cavum uteri found on the first hysteroscopy; and **(B).** Uterine cavity after resection, ablation and evacuation of pus and debris.

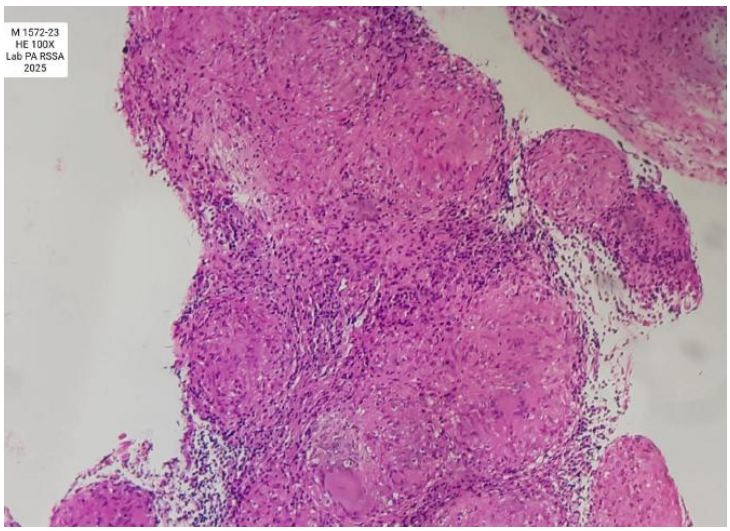


Fig. 2. Histopathological exam of the mass shown tuberculosis process, showing granulo-matous inflamed cells, epitheloid cells, Langhans giant cells and pale Caseous Necrotic tissue.

Hysteroscopy was used to verify the diagnosis, revealing an irregular mass in the uterine cavity accompanied by significant fibrotic tissue, cervical stenosis, and purulence in both fallopian tubes. Histopathological findings indicated a tuberculous process. Due to the paucibacillary nature and cyclical shedding of the endometrium, TB endometritis often shows early-stage granulomas and low AFB detection by ZN staining [5]. The identification of outflow obstruction or uterine wall adhesions may result from multiple factors, including prior trauma to the uterine cavity, congenital abnormalities, genetic susceptibility, and infection [6,7].

This instance illustrates a particular case of endometrial tuberculosis based on the histological findings. The process commences with *Mycobacterium tuberculosis* infection infiltrating the endometrial tissue, resulting in persistent inflammation. This chronic inflammation leads to fibroblast proliferation and the production of connective tissue (fibrosis) that supplants the endometrial stroma. Furthermore, this fibrotic tissue compromises the endometrium's ability to facilitate the menstrual cycle. The functional layer of the endometrium, which is intended to regenerate with each menstrual cycle, transforms into a dormant cuboidal or columnar epithelial layer and loses its responsiveness to hormonal stimuli, including oestrogen and progesterone. Furthermore, alterations in the endometrial basal layer, which serves as a source for the regeneration of endometrial cells, result in a diminished capacity for the endometrium to recover and function effectively. Chronic inflammatory tuberculosis induces

the production of epithelioid granulomas to manage infection, which subsequently disturbs the normal architecture of the endometrium and may result in significant adhesions inside the uterine cavity and secondary amenorrhoea [6,8].

Genital tuberculosis is predominantly a subsequent manifestation of pulmonary or extrapulmonary tuberculosis, especially affecting the kidneys, bones, meninges, or gastrointestinal tract. The infection disseminates through haematogenous, lymphatic, and direct extension pathways. The most frequently impacted locations are the fallopian tubes (95–100%), endometrium (50–60%), ovaries (20–30%), cervix (5–15%), and infrequently, the vagina or vulva (1–3%) [9]. The thoracic assessment of this patient indicated left lung fibrosis, implying latent pulmonary tuberculosis with potential haematogenous dissemination to the genital system, specifically affecting the fallopian tubes, endometrium, and cervix [10].

The objective of intrauterine adhesion therapy is to restore the normal anatomy and functionality of the uterine cavity, avert the recurrence of adhesions, and enhance endometrial regeneration. Diverse techniques have been employed, including the expectant approach, outmoded 'blind' dilatation and curettage, and hysterotomy, which is reserved for severe instances. Currently, hysteroscopic adhesiolysis is the gold standard due to its minimally invasive nature and the capability for direct vision during adhesion removal [11]. The surgery may be facilitated by laparoscopic guiding, transabdominal ultrasonography, or fluoroscopy to prevent problems such uterine perforation, particularly in cases of dense adhesions. Additional developments, including the application of laminaria, the PLUG (Pressure Lavage Under Guidance) approach, and the transformation of 'blind' hysteroscopic procedures, have been documented for intricate cases. The hysteroscopic adhesiolysis technique was employed as the major method for this patient [12].

The principal treatment for endometrial tuberculosis infection should be conducted in collaboration with a pulmonary specialist. Patients get the conventional anti-tuberculosis regimen of rifampicin, isoniazid, pyrazinamide, and ethambutol for a minimum of six months to achieve eradication and avert recurrence of the infection [13]. Nevertheless, menstruation had not returned to a regular pattern even after one year. The treatment of endometrial adhesions resulting from tuberculosis involves hysteroscopic adhesiolysis to reconstruct the anatomy of the uterine cavity using minimally invasive methods, such as cold knife or electrocautery. Additionally, prevention of re-adhesion is achieved through hormonal therapy (oestradiol and progestin), the insertion of an IUD or LNG-IUS, or the application of anti-adhesion agents like hyaluronic acid and Platelet-Rich Plasma (PRP). Oestrogen treatment contributes to postoperative endometrial regeneration, whereas PRP may enhance endometrial proliferation and implantation efficacy. A follow-up evaluation, comprising a repeat hysteroscopy and endometrial biopsy, is essential to monitor therapy efficacy and reproductive status. Due to the potential permanence of endometrial damage caused by tuberculosis, reproductive interventions like IVF may be necessary. Women with genital TB have a poor prognosis for fertility, even after treatment. Estimates of posttreatment conception rate vary from 12% to 23% (12). A comprehensive approach is advised to promote the patient's emotional well-being and provide extensive knowledge regarding the long-term effects of tuberculosis on reproduction [10,14,15].

The patient underwent sufficient anti-tuberculosis treatment and hysteroscopic adhesiolysis was conducted. The initial postoperative treatment excluded IUD placement because of extensive infection characterised by intrauterine to tubal pus. Upon completion of TB treatment, the patient underwent a subsequent hysteroscopy and was scheduled for LNG-IUS insertion to preserve cavum uteri patency; however, the patient declined and opted for a DMPA injection followed by a re-evaluation hysteroscopy. Following examination, an intrauterine device (IUD) was placed, and Cycloprogynova was prescribed for 3-6 cycles, resulting in regular menstrual cycles occurring every 28 days for a duration of 7 days. Typically, assessment of the uterine cavity post-treatment is advised one to two months following the initial surgery. Ultrasonography, hysterosalpingography (HSG), and hysteroscopy are the predominant follow-up techniques employed. Hysteroscopy is the sole technique that facilitates precise assessment of adhesion recurrence and is the most frequently employed procedure in clinical practice, including this instance. The patient underwent multidisciplinary treatment and obtained effective management. The subsequent stage is to guarantee optimal fertility. This is achieved by verifying tubal function using HSG and assessing the partner's sperm, and if required, proceeding to interventions such as IVF [6,8].

Intrauterine adhesions resulting from tuberculosis endometritis, despite enhancements in menstrual cycles through hysteroscopy and tissue ablation or resection, continue to pose a significant risk for fertility and obstetric difficulties during pregnancy. The risk of spontaneous miscarriage, ectopic pregnancy, and uterine rupture may escalate following hysteroscopic adhesiolysis; thus, vigilant monitoring of these individuals is crucial from the pre-pregnancy phase through to delivery [16,17].

CONCLUSION

This case illustrates the intricate pathophysiology and management challenges associated with secondary amenorrhoea resulting from genital tuberculosis, which impairs endometrial function and leads to considerable intrauterine adhesions. The delayed diagnosis due to non-specific early symptoms facilitated the progression of fibrosis and outflow obstruction. Consequently, a multidisciplinary approach that encompasses hysteroscopic adhesiolysis, anti-tubercular therapy, and postoperative hormonal and structural interventions is required. Early diagnosis during the latent phase can be achieved through the identification of subtle hysteroscopic changes, in conjunction with TB-PCR testing. Menstrual cycles have been reinstated; however, the potential for infertility and complications during pregnancy remains a concern. To optimise reproductive outcomes, preconception counselling, fertility assessment, and long-term monitoring are essential.

ACKNOWLEDGMENT

We thank all the authors of the articles reviewed in this article.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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