

# Amniotic Membrane–Covered Intrauterine Device for Tuberculosis-Associated Secondary Amenorrhea: Serial Endometrial Thickness and Menstrual Recovery in Two Cases

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## HOW TO CITE: ABSTRACT:

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**Background:** Amniotic membrane has been investigated as an adjunct to treatment of intrauterine adhesions, but its role in women with tuberculosis and secondary amenorrhea is uncertain. We describe serial endometrial thickness and menstrual outcomes after antituberculosis therapy and intrauterine placement of an amniotic membrane wrapped plastic intrauterine device (IUD) frame.

**Case presentation:** Two women, aged 32 and 36 years, presented in December 2025 with amenorrhea lasting three and nine months, respectively. Both had positive sputum molecular tests for tuberculosis and had received two months of rifampicin, isoniazid, pyrazinamide, and ethambutol at presentation. The first had undergone diagnostic laparoscopy and hysteroscopic polypectomy approximately one year before amenorrhea; polypectomy histopathology showed an endometrial polyp and chronic granulomatous inflammation suggestive of tuberculosis. The second had recurrent pregnancy loss, curettage, and hysteroscopic resection of a reported 1-cm uterine septum in December 2025; no histopathology result was available for that procedure. Both declined blood investigations. A membrane wrapped plastic IUD frame was placed after removal of the copper wire from its stem. Endometrial thickness increased from 3.0 to 6.5 mm over four months in the first patient and from 2.0 to 7.0 mm over three months in the second. Menstruation resumed at months 4 and 3, respectively, with duration and volume reported as comparable to previous cycles. The frames

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were removed at visits during menstruation. Both reported continued regular cycles for two further months. No adverse events were recorded.

**Conclusion:** Serial endometrial thickening and menstrual resumption were observed after combined care. Concurrent antituberculosis therapy, prior uterine procedures, incomplete diagnostic assessment, and the uncontrolled two-case design prevent attribution of benefit to the membrane or frame. These observations warrant further investigation without establishing efficacy, safety, or fertility restoration.

**Keywords:** secondary amenorrhea; tuberculosis; amniotic membrane; intrauterine device frame; endometrial thickness; case report.

## Introduction

Secondary amenorrhea in a woman with tuberculosis raises concern for genital involvement, particularly when accompanied by intrauterine fibrosis. However, tuberculosis confirmed in a respiratory specimen does not establish endometrial infection. A published report of pelvic tuberculosis with Asherman's syndrome illustrates the association between genital disease, amenorrhea, and infertility, while emphasizing the importance of site-specific diagnostic evidence (Fowler & Mahalingaiah, 2019). Previous uterine instrumentation and other causes of menstrual disturbance must also be considered.

Amniotic membrane has been evaluated as a biological interface after hysteroscopic adhesiolysis. Clinical studies have used amnion with an intrauterine balloon or as part of sequential barrier therapy involving a balloon and IUD (Gan et al., 2017; Wu et al., 2021). These approaches differ from placing amnion around a modified plastic IUD frame in patients receiving antituberculosis treatment. Whether such placement adds benefit beyond infection treatment and other uterine procedures remains uncertain.

This report describes two women with tuberculosis and secondary amenorrhea treated with antituberculosis medication and an amniotic membrane wrapped IUD frame. Serial transvaginal ultrasound measurements and menstrual outcomes are presented alongside the

diagnostic and treatment factors that limit causal interpretation.

## Case presentation

### Case 1

A 32-year-old woman presented to the gynecology outpatient clinic in December 2025 with three months of secondary amenorrhea. She had been married for six years and had never been pregnant. Her menstrual cycles had previously been regular, and she reported no hormonal or nonhormonal contraceptive use. Approximately one year before the onset of amenorrhea, she underwent diagnostic laparoscopy and hysteroscopic polypectomy for an endometrial polyp. Histopathological examination of the tissue obtained during hysteroscopy revealed an endometrial polyp with chronic granulomatous inflammation suggestive of tuberculosis. The patient declined further investigations for tuberculosis at that time. Representative images from the hysteroscopic procedure are shown in Figure 2.

Pulmonary tuberculosis had been confirmed by a positive molecular test on sputum. At presentation, the patient had completed two months of treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol. Her treating pulmonologist planned a total antituberculosis treatment duration of one year. She declined blood laboratory investigations, limiting evaluation of endocrine and other causes of amenorrhea.

Baseline endometrial thickness was 3.0 mm. An amniotic membrane-wrapped plastic IUD frame was placed during outpatient care. Monthly transvaginal ultrasonography recorded endometrial thicknesses of 4.0, 6.0, 6.4, and 6.5 mm at months 1–4, respectively. Spontaneous menstruation resumed five days after the month-4 ultrasound examination, still within the fourth month after frame placement. The frame was removed at a follow-up visit while the patient was menstruating. She reported that the duration and volume of menstruation were comparable to those of her cycles before amenorrhea. Regular menstruation continued for a further two months, according to the patient's report. No adverse events were recorded during follow-up.

## Case 2

A 36-year-old woman presented to the gynecology outpatient clinic in December 2025 with nine months of secondary amenorrhea. She had been married for five years and had experienced three pregnancy losses, the most recent in 2024. She underwent curettage for an incomplete miscarriage in 2024. Before amenorrhea, her menstrual cycles had been regular, and she reported no hormonal or nonhormonal contraceptive use.

She had a diagnosis of septate uterus and underwent hysteroscopic resection of a 1-cm uterine septum in December 2025. Hysteroscopy identified fibrotic tissue. No histopathology result was available, and no genital tract microbiological confirmation of tuberculosis was documented. A sputum molecular test for tuberculosis was positive.

At presentation, the patient had completed two months of treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol. Her treating pulmonologist planned a total antituberculosis treatment duration of one year. She declined

blood laboratory investigations. Baseline transvaginal endometrial thickness was 2.0 mm, and an amniotic membrane wrapped plastic IUD frame was placed during care for amenorrhea. Insertion was performed on a different day from hysteroscopy. The amniotic membrane-wrapped IUD frame was inserted one month after hysteroscopy. Baseline endometrial thickness was measured before frame insertion, and the date of insertion was designated as month 0. All subsequent follow-up intervals were calculated from this date rather than from the date of hysteroscopy.

Monthly transvaginal ultrasonography recorded endometrial thicknesses of 4.0, 6.0, and 7.0 mm at months 1–3, respectively. Spontaneous menstruation resumed one week after the month-3 ultrasound examination, still within the third month after IUD frame placement. The patient reported that the duration and volume of menstruation were comparable to those of her cycles before amenorrhea. The frame was removed at a follow-up visit while she was menstruating. Regular menstruation continued for a further two months, according to the patient's report. No adverse events were recorded during follow-up.

## Comparison of the clinical courses

Table 1 summarizes the two cases. Both women had received an initial two-month course of antituberculosis medication when they presented to gynecology. Their histories of uterine instrumentation differed. The first underwent polypectomy approximately one year before amenorrhea, whereas the second underwent hysteroscopic surgery during the month of presentation. These features are relevant to both the differential diagnosis of amenorrhea and interpretation of subsequent improvement.

**Table 1. Comparison of the clinical courses**

| Characteristic       | Case 1                  | Case 2                  |
|----------------------|-------------------------|-------------------------|
| Age and presentation | 32 years; December 2025 | 36 years; December 2025 |

| Characteristic            | Case 1                                                                              | Case 2                                                                                        |
|---------------------------|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| Amenorrhea duration       | 3 months                                                                            | 9 months                                                                                      |
| Reproductive history      | Never pregnant; married 6 years                                                     | Three pregnancy losses; married 5 years                                                       |
| Prior menstrual pattern   | Regular                                                                             | Regular                                                                                       |
| Contraceptive use         | None reported                                                                       | None reported                                                                                 |
| Uterine procedures        | Diagnostic laparoscopy and hysteroscopic polypectomy about 1 year before amenorrhea | Curettage in 2024; hysteroscopic resection of a reported 1-cm uterine septum in December 2025 |
| TB evidence               | Positive sputum molecular test; histology suggestive of TB                          | Positive sputum molecular test; no histopathology result available                            |
| Blood investigations      | Declined                                                                            | Declined                                                                                      |
| Treatment at presentation | 2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol                     | 2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol                               |
| Menstrual resumption      | Month 4                                                                             | Month 3                                                                                       |
| Frame removal             | At a follow-up visit during menstruation                                            | At a follow-up visit during menstruation                                                      |
| Subsequent menstruation   | Regular cycles reported for 2 more months                                           | Regular cycles reported for 2 more months                                                     |
| Recorded adverse events   | None                                                                                | None                                                                                          |

## Intervention and outcome assessment

### Membrane source and preparation

The amniotic membrane was supplied by the Cell and Tissue Bank–Regenerative Medicine service of Dr. Soetomo General Academic Hospital. The product label specified gamma irradiation at 25 kGy, room-temperature storage, and single use. Published production methods from the bank describe donor screening and consent, separation of amnion from chorion, cleaning, decontamination, freeze-drying, packaging, and gamma irradiation (Suroto et al., 2021). These

methods provide manufacturing background; batch-specific donor and processing records were not available for this report.

A 10 × 10 cm amniotic membrane sheet was soaked for 2–3 minutes in sterile 0.9% sodium chloride infusion solution in a sterile bowl. After hydration, the membrane detached from its supporting gauze, leaving a thin sheet for wrapping. The copper wire around the stem of an Andalan Copper T IUD was removed, leaving the plastic frame as the carrier. The membrane was wrapped around the frame, and the assembly

was loaded into the inserter. Removal of the stem wire was intended to facilitate wrapping and loading. Contraceptive performance of the modified assembly was not evaluated.

The membrane wrapped frame was placed in the uterine cavity using the inserter and the standard insertion technique described by the treating team. Both frames were removed at follow-up visits during menstruation. The exact insertion and removal dates, confirmation of post-insertion position, and handling of any other copper components were not available.

### Serial ultrasonography and menstrual assessment

Both patients underwent monthly transvaginal ultrasonography. The reported series begins with the baseline assessment and continues to the visit associated with menstrual resumption (Table 2 and Figure 1). The absolute increase from baseline was 3.5 mm in the first patient and 5.0 mm in the second. No month-4 value was supplied for the second patient, and none was imputed.

**Table 2. Serial ultrasonography and menstrual assessment**

| Follow-up time                                                   | Case 1<br>thickness in<br>mm | Case 2<br>thickness in<br>mm | Remarks                                                                                                                                                |
|------------------------------------------------------------------|------------------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Baseline                                                         | 3.0                          | 2.0                          |                                                                                                                                                        |
| Month 1                                                          | 4.0                          | 4.0                          |                                                                                                                                                        |
| Month 2                                                          | 6.0                          | 6.0                          |                                                                                                                                                        |
| Month 3                                                          | 6.4                          | 7.0                          | Case 2 : Menstruation resumed one week after the endometrial thickness measurement. The amniotic membrane-wrapped IUD frame was subsequently removed.  |
| Month 4                                                          | 6.5                          | -                            | Case 1 : Menstruation resumed 5 days after the endometrial thickness measurement, and the amniotic membrane-wrapped IUD frame was subsequently removed |
| Change from<br>baseline to the final<br>ultrasound<br>assessment | +3.5                         | +5.0                         |                                                                                                                                                        |

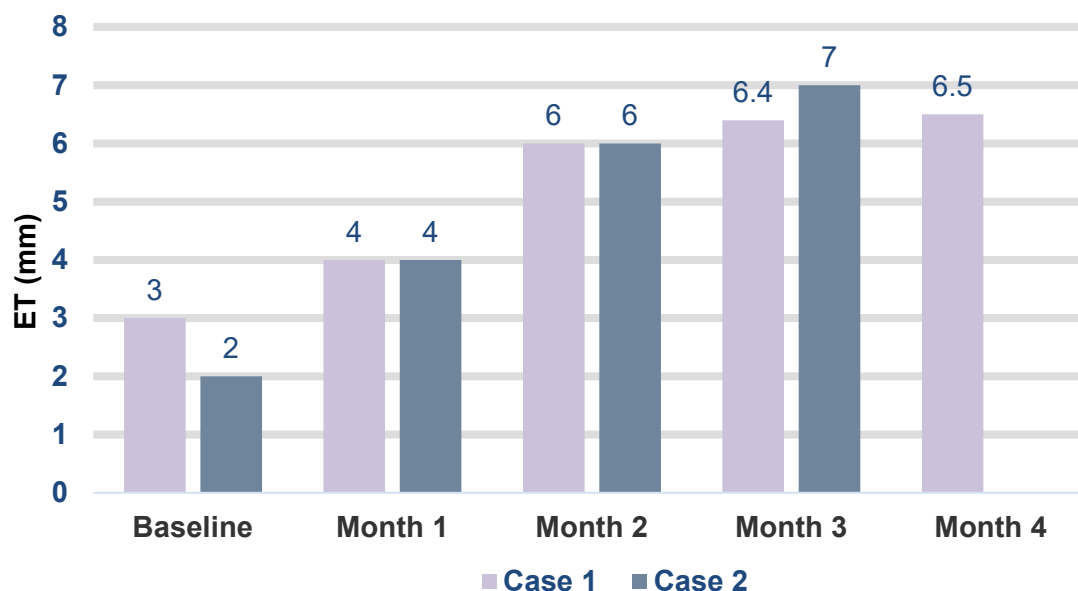


**Figure 1. Serial transvaginal ultrasound measurements. Bars represent reported observations. The second patient's series ends at month 3; the absence of a month-4 value is not a zero measurement.**

Menstrual resumption was based on the reported return of spontaneous bleeding. Both patients described the duration and amount as comparable to their previous menstrual cycles and reported regular cycles for the following two months. Bleeding volume was not quantified

with a validated instrument. The ultrasound plane, operator consistency, and cycle timing at each measurement were not specified. The results are presented descriptively without inferential statistical testing.

### Hysteroscopic images

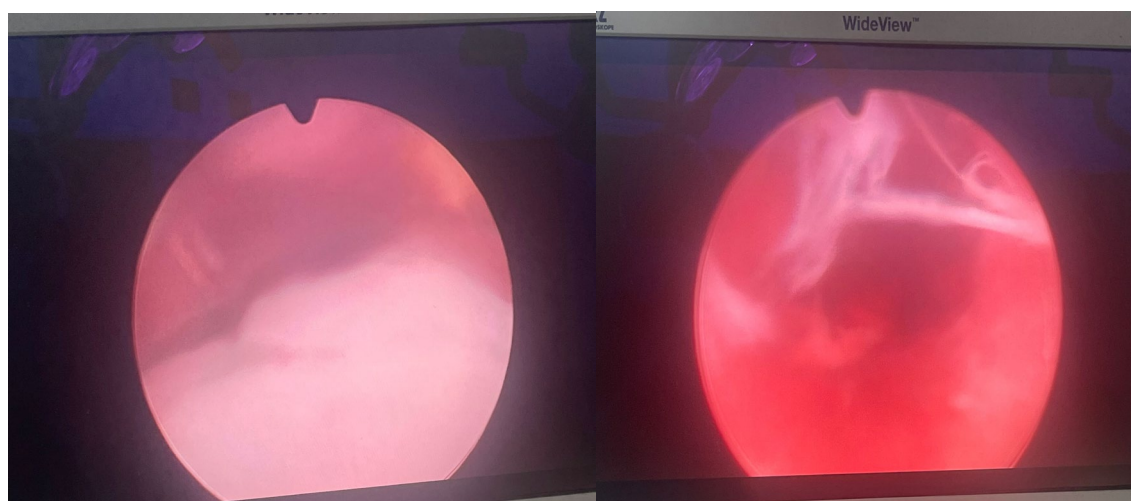


**Figure 2. Representative hysteroscopic images obtained during polypectomy in Case 1, approximately one year before the onset of amenorrhea. Histopathological examination of the resected tissue revealed an endometrial polyp with chronic granulomatous inflammation suggestive of tuberculosis.**

## Discussion

### Clinical findings and diagnostic context

Both patients showed increasing endometrial thickness during monthly follow-up, with menstrual resumption at three and four months. The additional report of regular cycles for two further months extends the observation beyond the first bleeding episode. However, neither menstrual resumption nor thickness alone demonstrates restoration of endometrial histology, ovulation, receptivity, or fertility.

The first patient had pulmonary tuberculosis and histopathological findings of an endometrial polyp with chronic granulomatous inflammation suggestive of tuberculosis. These findings support suspected genital involvement, but the specimen predates amenorrhea by approximately one year and does not establish microbiological confirmation or a causal relationship with the later menstrual disturbance. In the second patient, no histopathology result was available. Fibrotic tissue on hysteroscopy is nonspecific, particularly after uterine instrumentation. Neither case had documented genital tract microbiological confirmation; positive sputum testing does not establish endometrial infection.

Previous intrauterine procedures are important competing explanations. The first patient underwent diagnostic laparoscopy and hysteroscopic polypectomy approximately one year before amenorrhea. The second had curettage following miscarriage and hysteroscopic resection of a reported uterine septum in December 2025. Membrane placement occurred on a different day from hysteroscopy. These histories complicate attribution of menstrual disturbance to tuberculosis and of recovery to the membrane. The effects of hysteroscopic treatment cannot be separated from those of medication or frame placement. Declined blood testing further limited investigation of endocrine causes. Previous regular cycles and absence of contraceptive use add clinical context but do not exclude other causes of amenorrhea.

### Rationale and relationship to existing evidence

The plastic IUD frame acted as a carrier for intrauterine delivery of amnion. A possible biological interface and a temporary mechanical role provide a rationale for investigation, but tissue contact, adhesion prevention, and biological activity were not measured. A T-shaped frame should not be assumed to separate the entire endometrial surface.

Laboratory studies from the tissue bank provide material characterization rather than evidence of intrauterine efficacy. Suroto et al. (2024) evaluated morphology, cytotoxicity, and residual water content of human and bovine freeze-dried amnion; human preparations showed favorable cytocompatibility under the tested conditions and mean water content of approximately 6.8%. These findings cannot be assigned to the individual clinical grafts without their batch records. A separate study found reduced TGF- $\beta$  and bFGF levels after gamma irradiation, indicating that biological properties may change during processing (Suroto et al., 2021).

In a randomized trial of 88 women after adhesiolysis, Gan et al. (2017) compared an intrauterine balloon with or without freeze-dried amnion. Adhesion and menstrual scores favored amnion, but recurrence and pregnancy rates did not differ significantly. Wu et al. (2021) retrospectively studied 45 patients using sequential barrier therapy after adhesiolysis. A meta-analysis of four trials found improved menstrual blood volume without significant differences in adhesion recurrence or pregnancy rates (Zheng et al., 2018). These studies differ in indication, accompanying surgery, and carrier device. They do not establish the additional benefit of the present approach during antituberculosis treatment.

### Treatment timing and safety considerations

Both patients had received two months of a four-drug antituberculosis regimen at gynecology presentation, and further therapy was planned by their pulmonologist. Subsequent endometrial and menstrual changes could therefore reflect the response to infection treatment, uterine

procedures, the membrane/frame intervention, or several factors together. Exact treatment dates, continuation drugs, and documented infection status at insertion are needed to assess the clinical sequence more precisely.

The U.S. Medical Eligibility Criteria classify initiation of copper or levonorgestrel contraceptive IUDs in pelvic tuberculosis as category 4 because placement may worsen the condition (Centers for Disease Control and Prevention [CDC], 2024). Those classifications do not validate or establish eligibility for the modified plastic carrier reported here. The distinction between confirmed pulmonary disease and suspected genital involvement, together with clinical assessment before insertion, remains important. Absence of recorded adverse events in two patients does not establish safety; the available information does not specify a standardized surveillance protocol.

### **Limitations and future investigation**

The uncontrolled two-case design prevents causal inference. Diagnostic evaluation was incomplete, uterine surgical histories were heterogeneous, and the contribution of hysteroscopic treatment during the month of presentation in the second patient was unresolved. Although monthly measurements were available, cycle timing and ultrasound standardization were not documented. Menstrual volume and regularity were patient-reported, and the two-month continuation of cycles does not establish long-term recovery. Exact removal dates were not available, so this observation should not be presented as a precisely timed post-removal outcome.

Fertility outcomes were not available despite the first patient's absence of previous pregnancy and the second patient's recurrent pregnancy loss. The report does not establish that either reproductive history was caused by tuberculosis or that this intervention improves conception or live birth. Future studies would require documented diagnostic categories, a standardized protocol, an appropriate comparison group, and longer follow-up of cavity findings,

menstruation, adverse events, and reproductive outcomes under appropriate ethical oversight.

### **Conclusion**

Two women with tuberculosis and secondary amenorrhea showed serial endometrial thickening and menstrual resumption after antituberculosis treatment and intrauterine placement of an amniotic membrane wrapped plastic IUD frame. Both reported menstrual duration and volume comparable to their previous cycles and regular menstruation for two further months. Concurrent treatment, prior uterine procedures, incomplete diagnostic assessment, and the small sample prevent attribution of benefit to the membrane or frame. These findings remain exploratory and do not establish efficacy, procedural safety, or fertility restoration.

### **Declarations**

#### **Ethics and consent**

Both patients agreed to publication of their cases. Written informed consent was obtained from both patients for publication of their clinical information and accompanying images.

#### **Competing interests**

The authors declare no competing interests.

#### **Clinical care coverage and funding**

The costs of antituberculosis medication, the amniotic membrane wrapped IUD intervention, and serial transvaginal ultrasonography were covered by Indonesia's National Health Insurance program (BPJS Kesehatan), with no out-of-pocket costs to either patient. This study received no specific research funding.

#### **Author contributions**

Sintia Damayanti: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. Sri Ratna Dwiningsih: Supervision. Arif Tunjungseto: Supervision.

#### **Data availability**

The clinical data relevant to this case report are included in the article. Individual patient medical

records are not publicly available to protect patient confidentiality.

### Patient perspective

Both patients expressed satisfaction with the return of menstruation and with receiving

treatment without out-of-pocket costs. This statement summarizes their reported views and is not a verbatim quotation.

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