

Assisted conception, endometrial tuberculosis with secondary infertility, treatment and subsequent live birth: A case report

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Abstract

Female genital tuberculosis is a latent cause of infertility in our milieu and is barely looked for as part of usual evaluation of infertility. With a radical incidence of Tuberculosis in the face of the developing countries, it is important to always have genital tuberculosis in mind particularly when no erstwhile reason is found for the infertility. Woman genital tuberculosis is a significant cause of secondary infertility in developing countries or where tuberculosis is endemic. In the current study we present a case in which endometrial tuberculosis was a cause of secondary infertility of almost 10 long years. From February 2013 to October 2013, we performed, laparoscopy, trans- vaginal Study, pelvic scan for infertile patient. The patient had secondary infertility; therefore, she underwent the process of the endometrial biopsy and hysteroscopy. The laparoscopic discovery confirmed normal ovaries and uterus in the patient; evenough the fallopian tube of the patient was normal. Hysteroscopy results concluded that the endometrial layer was atrophied in the patient, and biopsy results revealed the presence of acid-fast bacilli using Zeihl-Neelsen stain further confirmation by the ABITM Rt-PCR. We concluded that patients with endometrial tuberculosis possibly have no clear filed record of tuberculosis or may have proof evidence of tuberculosis grazes somewhere else in the body. Histopathological confirmation from the biopsies of pre-menstrual endometrial tissue or expression of tubercle bacilli in cultures of endometrial curetting or menstrual blood is required to reach a decisive diagnosis of the disease or indications. When our patients were treated with antituberculosis treatment (ethambutol 800 mg + isoniazid 300 mg + pyrazinamide 750 mg + rifampicin 450 mg.) for 6 months they regained with the endometrial tuberculosis, and achieve pregnancy via assisted conception. Gynaecologists in developing countries must consider genital tuberculosis as an important cause of secondary infertility.

Keywords: *Mycobacterium Tuberculosis*, Anti-TB therapy, Assisted reproduction

1. Introduction

Tuberculosis or TB is a bacterium (*Mycobacterium Tuberculosis*) that can impinge on any part of your body, but most frequently affects the respiratory system, lungs. On the other hand in some case the TB infection travels through the blood to various other parts of the body. It can thus be a reason for secondary infections in the genital tract (fallopian

tubes, uterus, and ovaries), pelvic area, brain, spine and kidneys. When the bacillus reaches the genital tract it causes pelvic TB or genital tuberculosis. It affects the genital tract (in both men and women). In some of the rare cases it also affects the cervix, vulva and vagina. Genital tuberculosis is one of the foremost latent causes of female infertility and tubal disease in developing countries. Still Tuberculosis continues a foremost civic health problem worldwide and is of most concern in developing countries with a comprehensive mortality of 1.2 to 1.5 million in 2010. India holds one-fifth of the global load of TB

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with more than 350,000-400,000 deaths each year. Though pulmonary TB (PTB) cases, report for the immense majority of the total TB burden, almost 10-15 per cent. Of total cases are extra-pulmonary (1, 2). The prevalence of female infertility is elevated globally, with discrepancy in predominance of aetiology between the developed realm sphere where an ovulation is widespread; and the not so developed nations where tuboperitoneal smash up from infectious disease holds influence (3). Genital tuberculosis (endometrial) is an identified cause of infertility in women (4, 5).

Genital TB is a form of extra pulmonary tuberculosis and is always secondary to TB infection elsewhere (usually pulmonary) in the body part of pelvic TB with a express extension to the endometrium in almost about half of the cases found (5-7) Statistics regarding the concrete prevalence rates of genital TB in the common population is insufficient due mainly to its understated presentation (8). In the infertility treatment centre globally, a vague 5%-9% of the women currently is having genital TB with incidence value ranging from less than 1% in the developed nations to a reportedly increasing leaning in the developing nations (8, 9). Genital TB is usually a latent infection with no clear evident symptoms as the bacteria may remain latent in your body for as long as 10 to 15 years.

Though, some of the indication to look out for include: irregular menstrual cycle, pelvic pain, vaginal discharge, infertility sometimes, the lack of symptoms makes it complex to diagnose genital tuberculosis. Depending upon your symptoms, your doctor may advise you to get tests to authenticate the diagnosis. Other expression include menstrual irregularities lower abdominal pain or chronic pelvic or. It is more or less always acquired by haematogenous extension from an extra genital source such as pulmonary. However the first and the foremost the fallopian tubes are most commonly affected genital organs, followed by endometrium, ovary, and cervix (7, 10).

Spread of the genital TB most likely to acquire if people have low immunity and spend a long time in close contact with an infected person or genital tuberculosis may also spread due to sexual contact with an infected person.

Brief contact with an infected person while, say, commuting on buses or trains,, sharing food, talking or shaking hands, will not give you TB. Only people who have an active infection of TB in the lungs are infectious. When they sneeze or cough, TB is spread, quite like the common cold.

When a person breathes in the TB bacterium, it settles in the lungs and begins to grow.

2. Case Presentation

2.1. Female Profile

A 36 year old woman, resident in the suburbs of South-Bangalore India, initially reported her case at the gynaecological clinic with complaints of failure to conceive after 10 years of marriage regardless of passable unprotected sexual intercourse. She got menarche at 13 years of age, and menstruated for 5 days in a regular 26-28day cycle. The menstrual flow was usual. She had no vaginal itching, dysmenorrhoea, dyspareunia or abnormal vaginal discharge or any such symptoms. There was no history of, early morning vomiting, nausea, epigastric pain, neck swelling, breast discharge, abdominal swelling, chronic cough, blurred vision, and headaches.

She did not have any preceding consultations for infertility in the formal health sector. She was not a known Hypertensive, diabetic nor obesity, patient and had no kin history of alike. Test revealed a healthy gaze woman. She was not feverish (Temp 36.6''c), fair. Her BMI was 23.8kg/m². She had normal pulse of 80beats/minute and blood pressure of 100/80mmHg. Trans Vaginal study (TVS) shown a normal vagina and vulva normal sized uterus. The Pouch of Douglas was empty.

2.2. Male Profile

Her husband was 39 years old, and his semen analysis was normal.

A) Semen analysis report

Collection time: 5:30 pm
Incubation Time: 30
Days of Abstinence: 4 Days

B) Physical examination

Volume: 2.3ml
Coagulated immediately: Yes
Liquefaction: Normal
Color: Grey white
pH: 8.0

C) Microscopic observations

Sperm concentration/ml: 120 × 10⁶/ml
Vitality: 75 %
Total count: 300 Millions
Dead: 25 %

Motility (%)		1 hour	2 hour	4 hour	24 hour
Excellent Progression	(%) Grade IV:	12 %	6 %	0%	0%
Rapid Progression	(%) Grade III:	21 %	15 %	10 %	0%
Slow Progression	(%) Grade II:	25 %	16 %	11%	0%
Non-Progressive	(%) Grade I:	13 %	8 %	3 %	0%
Immotile	(%) Grade 0:	29%	55%	76%	100%

D) Morphological abnormalities

Head defects: 21% defects in head
 Mid-piece defects : 17 % defects in mid-piece
 Tail defects: 23 % defects in tail
 Head, mid-piece & neck: 11 %
 Multiple defects: 03 % defects in multiple
 Percentage of overall defects: 75%

E) Agglutination: Absent

F) Cellular debris

Present (+ + +)
 RBC's: NO
 Epithelial cells: 0-1 HPF

G) Sperm function test report

Hypo Osmotic Swelling: 58%
 Acrosome Intactness: 55%
 Nuclear Chromatin Decondensation: 47%
 Mitochondrial Activity Index: 48.5

H) Method of Preparation: Density Gradient

Cont Motility: 60mil
 Post wash: 40mil

2.3. Investigation carried out included

A diagnosis of primary Infertility due to endometrial tuberculosis pathology was made. Because of the histological examination of the biopsied endometrium showed no adhesions or granulomas but endometrium-TB RT PCR (High Copy Number) Positive, culture of the endometrium yielded Mycobacterium tuberculosis (MGIT-9600) positive results.

2.4. Disease index of suspicion

Confirmation by ABI Real Time PCR Targeting IS6110 and TCR4 targets, MGIT-9600 Bactec Culture and Zeil Nilson Stains.

2.5. Treatment

Antituberculosis chemotherapy was started after the confirmation of the disease with Rifampicin, Isoniazid, Pyrazinamide and Ethambutol. Brand Name-AKT4 Duration-6 Months.

2.6. Ovarian stimulation protocol and fertilization

The antagonist protocol used (Long Protocol). Subsequently ICSI was performed. (Table1 and 2). Then on day 5 one blastocyst was transferred (Figure 1).

Table 1. Oocyte and IVF characteristics

Oocyte No	1	2	3	4	5	6	7	8
Maturity	MII	MII	MII	MII	MII	MII	MII	MII
Irregular	No	No	No	Yes	No	No	No	No
Vacuoles	No	No	No	Yes	Yes	No	No	No
Granular	Yes	No	No	Yes	Yes	Yes	No	Yes
Dark Cytoplasm	No	No	No	No	No	No	Post Mature	No
Irregular PB	Single	Fragmented	Single	Single	Single	Single	Fragmented	Single
PB position	12:00	12:00	12:00	12:00	12:00	12:00	12:00	12:00
Re-Injection	No	No	No	No	No	No	Nil	No
Tough ZP	Thick	No	No	Yes	Yes	No	Thick	No
Lyed	No	No	No	No	No	No	No	No
Damaged	Null	Null	Null	Null	Null	Null	Null	Null

Table 2. Fertilization characteristics of oocytes

Day 1	6 Fertilized	Grade Of 2 PN	6 PN
Day 2	5 Fertilized	Grade Of Division	3Grade A, 2Grade B
Day 3	5 Divided	Grade Of Division	3Grade A, 2Grade B(FROZEN at day 3)
Day 4	3 Divided	Grade Of Division	3 Morulla
Day 5: Blastocyst stage	1 Expanded	Grade Of Blastocyst	3: 1: 1



Figure 1. Transferred Blastocyst

4. Discussion

Patients with endometrial tuberculosis may have no defined history of tuberculosis or may have confirmation of tubercular grazes somewhere else in the body. Abdominal and vaginal inspections may be routine checkups. In conclusion, the case presented detailed aetiology of the infertility because of the genital tuberculosis (Endometrial) need to consider even in apparently low risk patients. In spite of the successful fertility upshot in our patient, we do not think that this case was a challenge to preceding perceptions of endometrial tuberculosis.

An increased erythrocyte sedimentation rate and a positive test for Mantoux are non specific, and consequently cannot endow with an exact and accurate finding of genital tuberculosis. Chest X-rays are usual in majority of the cases; however, hysterosalpingography and pelvic ultrasound assessments may assist in the findings and diagnosis. Histopathological proof from biopsies of premenstrual endometrial tissue or the display of mycobacterium tubercle bacilli in cultures of menstrual blood or endometrial curetting is obligatory to give a irrefutable diagnosis of the ailment (11-13).

During our study, pulmonary abrasion was not seen in the accounted cases. The patients refused to have any contact with active tuberculosis. Chest X-ray was not carried out for the patients, as there were no indications to indicate its requirement. Zeihl-Neelsen staining of acid-fast bacilli (AFB) necessitates a huge number of bacteria (a minimum of 105/ml) to be present in the specimen of identification. In our cases, Histopathological, microbiological studies and polymerase chain reaction showed positive ZN staining for AFB and Real time polymerase chain reaction, and this was our main diagnostic method that confirmed our medical diagnosis (10). It has been approximated that (5 to 10%) of infertile cases are a result of female genital tuberculosis and even this rate is higher with patients with tubal factor infertility (39- 41%) fallopian tubes (95-100%), endometrium (50-60%), and ovaries (20-30%) (14-16) respectively.

The chemotherapy is mainstay for this treatment, in this case which is been responding for the patient. Here we describe single case of assisted conception with a normal pregnancy resulting in a patient with Mycobacterium tuberculosis infection of the endometrium. The *In vitro* fertilization and embryo transfer are usually the most suitable options for these patients as been assisted in this case. However the pregnancy remained eventful, and the patient delivered a normal male infant, 3,260 g at term. Examination of the placenta and uterus was performed, but there were no adhesions or any such features of chronic inflammation of any sign.

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