

Case Report

Tuberculosis Causing Infertility

Lim PS (✉), Muhammad Azrai A, Chew KT

Department of Obstetrics & Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia

Abstract

Genitourinary tuberculosis was the second most common form (30%) of extrapulmonary tuberculosis after peripheral lymphadenopathy. We reported a case of tuberculosis of the cervix and endometrium presented with secondary amenorrhoea and infertility. The diagnosis was based on histological examination. Despite tuberculosis treatment, she did not gain back her menses.

Keywords: Extrapulmonary tuberculosis; genitourinary tuberculosis; infertility; reproductive organ; secondary amenorrhoea

Correspondence:

Lim Pei Shan. Department of Obstetrics & Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia. Tel: +603-91455950 E-mail: pslim@ppukm.ukm.edu.my

Introduction

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*. Pulmonary infection was generally the primary focus and most were self-limited. Genitourinary tuberculosis was the second most common form (30%) of extrapulmonary tuberculosis after peripheral lymphadenopathy (1). The actual incidence could not be assessed accurately since about 11% of patients were asymptomatic, (2) and it varied in different countries. It was less than 1% in the United States and Australia but nearly 13% in India (3, 4).

Case Report

A 37-year-old teacher para 3 presented with secondary infertility for four years and secondary amenorrhoea of 11 months. She had three uncomplicated pregnancies and normal deliveries prior. The couple had regular unprotected coitus. Three years after her last childbirth she became amenorrhoeic. The urine pregnancy test was checked on a few occasions but remained negative. She had no galactorrhoea, excessive weight gain, hirsutism, acne, vaginal discharge, or menopausal symptoms. There was no other significant history. She remained amenorrhoeic after a

progesterone challenge with no abdominal pain. Hormonal profiles were in the normal range. She was counselled for diagnostic laparoscopy and hysteroscopy with D&C to exclude a uterine cause of secondary amenorrhoea.

She was 158 cm tall and weighed 66.3 kg with a BMI of 26.5 kg/m², which was overweight. Her general condition was satisfactory. She was not pale or jaundiced with normal blood pressure and pulse rate. The abdomen was soft and non-tender. There was no abnormal mass, organomegaly, or ascites. The vulva and vaginal were normal. The cervix was normal and the os was closed. The uterus was anteverted, normal-sized, and mobile. There was no adnexal mass and the pouch of Douglas was normal. The uterosacral ligaments were not thickened. Other examinations were unremarkable.

Her haemoglobin was 11.9 g/d. The white cell count and platelet count were normal. Her Pap smear revealed benign cellular changes associated with *Candida* spp. infection. Transabdominal ultrasound scan revealed a normal sized uterus 8.8 x 4.0 cm, which was anteverted. The endometrial thickness was 5.5 mm. The right ovary was 3.2 x 2.6 cm and the left

ovary was 3.5 x 2.1 cm. Her chest radiograph was normal.

She underwent diagnostic laparoscopy, hysteroscopy, and diagnostic dilatation and curettage. Intra-operatively, her vulva and vagina appeared normal. The cervix was tubular and healthy looking with closed os. The uterus was normal-sized anteverted. Ovaries were felt normal with no mass at the pouch of Douglas and the uterosacral ligaments were not thickened. There were multiple small endocervical polyps seen during hysteroscopic examination, which were removed and sent for histopathological examination. Both uterine ostia were visualised. Upon diagnostic laparoscopy, there was no adhesion noted in the peritoneal cavity. The uterus appeared normal and anteverted. Both ovaries appeared normal. Right hydrosalpinx was noted at the ampullary region with the left tube having normal looking. Both tubes were blocked upon dye test.

The histopathological results revealed: cervical tissue with multiple foci of granuloma formation accompanied by lymphoplasmacytic infiltration and occasional giant cells. There were few fragments of tissue composed of caseating necrosis and rimmed by epithelioid cells, lymphocytes, plasma cells, and multinucleated giant cells. Few endocervical glands were also seen. Special stains for acid-fast bacilli and fungal bodies were negative. Consistent with tuberculosis of the cervix and endometrium.

In view of the histology, a Mantoux test and ESR were done. Her Mantoux was positive measuring 5x6 cm and ESR was 30 mm/Hr. She was referred to the Respiratory Unit and was started on EHRZ regime (Isoniazid 300 mg daily, Rifampicin 600 mg daily, Ethambutol 900 mg daily, Pyrazinamide 1.2 g daily, and Pyridoxine 10 mg daily). An ophthalmology assessment was also performed. She was given anti-tuberculous agents for nine months and a repeat endometrial sampling at the end of therapy was negative for granuloma with acid-fast bacilli stain still negative. She remained amenorrhoeic despite hormonal treatment.

Discussion

TB can infect any of the reproductive organs. Fallopian tube involvement was in at least 90% of the cases following bloodstream spread (5). The tubes might appear normal on external appearance or might show a hydrosalpinx, pyosalpinx, or even calcification. (3). Ovarian involvement was seen in about 20-25% of cases whereas infection of endometrium was encountered in 50-70% of cases, cervical involvement was only 5% (1, 2). In this patient, the infection

involved both fallopian tubes, as evidenced by hydrosalpinx and tubal blockage, thin endometrium, and cervix. Both her ovaries were normal.

The commonest presenting complaint was infertility. This was seen in 70-85% of cases even without tubal blockage (1, 2). The other symptoms were lower abdominal pain (25-50%) and menstrual disturbances (50%) (1). In this patient, she presented with secondary subfertility and amenorrhoea. Amenorrhoea accounted for about 14.3% of all menstrual disturbances (5).

The diagnosis of genital tuberculosis was often made during the course of acute pelvic peritoneal infection, investigation of adnexal mass, menstrual irregularity, or infertility workup. The fallopian tubes had typical changes on hysterosalpingography (HSG) such as calcification, lead pipe appearance with ampullary distension, golf club appearance, and Maltese-cross appearance (1). Intra-uterine adhesions might result in a glove finger appearance or mimic different Mullerian anomalies on HSG. Endometrial biopsy for histological examination was one of the simplest diagnostic methods and was best done at the early menstrual phase with special attention to the cornual areas. A 50% detection rate had been reported by histopathological changes (3). This patient's Mantoux test was positive and she had hydrosalpinx on the right ampullary tubal region with bilateral blocked tubes. Her endometrial tissue showed caseating necrosis and cervical polyps showed granulomas with lymphoplasmacytic infiltration. However, the special stain for acid fast-bacilli and culture were unable to grow the organism. Although a definitive diagnosis requires isolation of tubercle bacilli via culture, most authorities accept the diagnosis based on histologically characteristic granulomas or a positive tuberculin test (6).

Management comprised of treatment for the infection and its sequelae. Combination of anti-tuberculous agents for 9-12 months, which was the mainstay of treatment, would expect a more than 95% cure rate (1). Surgical treatment, usually consisting of total abdominal hysterectomy and bilateral salpingo-oophorectomy, was indicated if persistent or recurrent disease/pelvic masses persist after medical therapy, unhealed fistula, or multi-drug-resistant disease. This patient was treated with anti-tuberculous therapy for nine months and a repeat endometrial sampling showed no granuloma.

In vitro fertilisation (IVF) was the only chance of conception in infertile women with genital tuberculosis (1). However, in this patient, her

endometrium was atrophic. Marcus et al. (1994) demonstrated a 0% pregnancy rate if the endometrium was atrophic. Tubal reconstruction surgery was not advisable as reactivation of silent pelvic tuberculosis had been reported with a risk of ectopic pregnancy (1). Partial or total intra-uterine synechiae might present in endometrial infection (8). Hysteroscopy evaluation and lysis of adhesions were needed prior to infertility treatment (1, 3) but recurrence was as high as 48.9% (9). Nonetheless, a pregnancy rate per transfer of 16.6% had been reported following IVF. There was no intra-uterine adhesion noted in this patient except for endocervical polyps which were infected. There was a case of an endometrial polyp infected with TB in a 70-year-old lady being reported (6).

Conclusion

Despite the wide coverage of BCG vaccination in Malaysia, we do still see extrapulmonary tuberculosis. This particular case demonstrated an extra-pulmonary tuberculosis with secondary infertility and secondary amenorrhoea although she was not immunocompromised and had no history of exposure to TB patients. Infertility was the most common feature of genital tuberculosis. In infertility patients with secondary amenorrhoea, the possibility of genital TB needs to be considered after exclusion of other common causes of these two conditions. Positive culture though is diagnostic, histopathological finding is sufficient for initiation of therapy. IVF offered the only realistic chance of conception despite the high success in eradicating the infection by medical therapy. Unfortunately, she remained amenorrhoea following TB treatment and IVF was too costly for her.

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