A Rare Case of Tuberculous Pyometra in a Young Infertile Female Confirmed by mRNA-based RT-PCR

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Abstract

A 25-year-old female presented to the infertility OPD with complaints of secondary infertility and pain lower abdomen with watery discharge for the past five days. She had history of undergoing hysterosalpingography in a private hospital ten days back. The interventions included drainage of pyometra, endometrial biopsy for routine and AFB smear/ culture, confirmation of diagnosis by mRNAbased RT-PCR for detection of *M. tuberculosis*-specific 85B antigen gene, anti-tubercular therapy. Pyometra and tubo-ovarian masses disappeared and patient resumed her normal period post-treatment. Genital tuberculosis was confirmed by mRNA-based RT-PCR and the disease resolved after antitubercular therapy. We conclude that a combination of high degree of clinical suspicion and 'highprecision' gene detection methods (e.g. mRNA) in culture-negative cases may be useful in diagnosis of tuberculosis. particularly infertile patients presenting genital in with pyometra posthysterosalpingography.

Keywords: Pyometra, tuberculosis, mRNA-based RT-PCR, endometrial biopsy

Introduction

Pyometra is the accumulation of pus in the uterine cavity. It is usually an old age disease. The condition is usually caused by occlusion of the cervical canal secondary to chronic atrophic cervicitis, or benign/ malignant cervical lesions (1). It may also be caused due to foreign bodies, puerperal infections or congenital anomalies (1, 2). However, it is thought to

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Dr. Sudha Prasad, M.D. IVF & Reproductive Biology Centre, Department of Obstetrics and Gynaecology, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi-110002, India Tel: + 91 9968604341 E- mail: drsprasad08@gmail.com be relatively rare in the pre-menopausal age group (3). The usual symptoms of pyometra consist of purulent vaginal discharge and lower abdominal pain (4).

We present a case of 25-year old female who presented to our clinic with in lower abdomen and discharge per vaginum for 5 days. Extensive-up of the patient revealed pyometra and biopsy of the endometrium revealed active genital tuberculosis.

Case Report

A young 25-year old woman reported to the Infertility Clinic of the Department of Obstetrics and Gynaecology of our tertiary care centre with prime complaint of secondary infertility for one year along with the pain in lower abdomen and discharge per vaginum for 5 days. She also had a history of

undergoing hysterosalpingography (HSG) five days ago. There was no history of fever, vomiting, urinary or bowel complaints. She reported no weight loss, fatigue, lack of appetite and evening rise of temperature or other previous systemic symptoms. The patient had undergone laparoscopy seven years ago for infertility in which bilateral salpingostomy was done. This was followed by three cycles of ovulation induction with Intra-Uterine Insemination (IUI). She also had a history of ectopic pregnancy one year back which was managed conservatively. Exposure to tuberculosis or history of anti-tubercular therapy was not reported in her medical history. She was married for ten years. Her general condition was stable and she was afebrile. The abdomen was soft with no tenderness or guarding. Per speculum examination revealed mucoid discharge which was nonpurulent. Significant signs of cervicitis could be seen. On per vaginum examination, uterus was anteverted, bulky, firm, mobile and in both fornices adnexal masses were palpable and tender.

The patient was hospitalized for complete workup. Ultrasound examination revealed pyometra and bilateral tubo-ovarian masses (Fig. 1). The patient was put on intravenous antibiotics (ciprofloxacin-500mg twelve hourly and metronidazole-100 mg eight hourly) for 72 hours. Thereafter, the patient was subjected to cervical dilatation and pyometra drainage and the pus sample obtained was sent for routine culture and sensitivity. Foley's catheter was A week later, the patient underwent inserted. endometrial biopsy and the sample was sent for acid fast bacilli (AFB) smear, culture and sensitivity on BACTEC 460 TB systems, Polymerase Chain and mRNA-based Reaction (PCR) Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Initial pus samples sent for routine bacterial

culture did not show growth of any significant pathogen. Also, AFB smear and culture turned negative. Significantly however, endometrial sample tested positive in DNA-based PCR for 240 bp region of MPB64 gene and mRNA-based RT-PCR for 216 bp region of 85B antigen gene of *M. tuberculosis*, when tested as per the protocol reported by us recently (5, 6).

The patient was then put on anti-tubercular therapy. The treatment comprised of rifampicin (R, RMP) 450 mg, isoniazid (H, INH) 300 mg, ethambutol (E, EMB) 800 mg and pyrazinamide (Z, PZA) 1500 mg for 2 months, followed by the same doses of INH and RMP for 4 months. The follow-up of the patient was uneventful.

Discussion

The incidence of pyometra in gynecological patients is reported to be 0.01–0.5% (7). Cases of tuberculous pyometra are rare, but sporadic cases of postmenopausal tuberculous pyometra have been reported (2). We have not come across any case of 'tuberculous' pyometra in 'young' infertile women at least from India.

In the present case, the patient presented with pain in the lower abdomen and discharge per vaginum after she underwent hysterosalpingography. Ultrasound revealed pyometra for which cervical dilatation was done. Subsequently, both PCR and mRNA-based RT-PCR reports confirmed the diagnosis of endometrial tuberculosis. Although no history was available, but it likely that the patient may have had an underlying tuberculosis infection in the past that flared-up after hysterosalpingography.

It is believed that genital tuberculosis is usually secondary to a primary focus elsewhere in the body, resulting from haematogenous spread from the distant



Figure 2: Ultrasound pictures depicting (a) pyometra and (b) bilateral T.O. masses

primary focus, most commonly affecting the fallopian tubes (92-100%) followed by endometrium (50%), ovaries (10-30%), cervix (5%) and vagina and vulva (<1%). (8, 9). In 80-90% cases, it affects young women between 18-38 years of age and is an important cause of infertility (2, 10). Our patient was also a case of secondary infertility with history of prior ectopic pregnancy.

Review of published literature showed case reports of pyometra in 'post-menopausal' women; and there are only two case reports of 'nontuberculous' pyometra in the 'reproductive' agegroup after ovum retrieval for IVF (7, 11). Both the patients were infertile and possibly pyometra was due to endometritis. Biopsy in one of the cases revealed endometritis, while the other was negative for it.

To the best of our knowledge, this is the first unique case of 'tuberculous' pyometra in a 'young' infertile patient; and hence suspicion of genital tuberculosis, even in AFB negative cases should also be considered in young infertile females presenting with pyometra post-hysterosalpingography. Since the incidence of genital tuberculosis ranges between 1-19% in India, it is mandatory to do pre-menstrual endometrial biopsy before proceeding for HSG (5, 12). We have recently reported that early and reliable diagnosis of genital tuberculosis involving state of the art technology, such as DNA PCR and/or *m*RNA-based RT-PCR; and treatment before development of the fulminant genital tuberculosis has resulted in higher pregnancy rates (5, 13). Genital tuberculosis should thus be considered for differential diagnosis of pyometra in young infertile patients as it may aggravate the disease; and resultant peritonitis which may be life-threatening.

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Disclosure

The authors have no conflict of interest and have nothing to disclose.

References

- 1. Nuamah NM, Hamaloglu E, Konan A. Spontaneous uterine perforation due to pyometra presenting as an acute abdomen. Int J Gynecol Obstet 2006;92:145–6.
- 2. Dutton WA. Postmenopausal tuberculous pyometra. Can Med Assoc J 1966;94:1012-3.
- 3. Chan LY, Lau TK, Wong SF, Yuen PM. Pyometra. What is its clinical significance? The Journal of Reproductive Medicine 2001; 46: 952–6.
- 4. Imachi M, Tanaka S, Ishikawa S, Matsuo K. Spontaneous perforation of pyometra presenting as generalized peritonitis in a patient with cervical cancer. Gynecologic Oncology 1993; 50: 384–8.
- 5. Prasad S, Singhal M, Negi SS, Gupta S, Singh S, Rawat DS, Et al. Targeted detection of 65 kDa heat shock protein gene in endometrial biopsies for reliable diagnosis of genital tuberculosis. Eur J Obstet Gynecol Reprod Biol 2012;160:215-8.
- Jou NT, Yoshimori RB, Mason GR, Louie JS, Liebling MR. Single-tube, nested, reverse transcriptase PCR for detection of viable Mycobacterium tuberculosis. J Clin Microbiol 1997;35:1161-5.
- 7. Nikkhah-Abyaneh Z, Khulpateea N, Aslam MF. Pyometra after ovum retrieval for in vitro fertilization resulting in hysterectomy. Fertil Steril 2010;93:268.
- 8. Varma TR. Genital tuberculosis and subsequent fertility. Int J Gyn Obstet 1991;35:1-11.
- 9. Arora VK, Johri A, Arora R, Rajaram P. Tuberculosis of the vagina in an HIV seropositive case. Tuber Lung Dis 1994; 75: 239-40.
- 10. Crofton J, Horne N, Miller F. Clinical tuberculosis. 1st ed. London: Macmillan Education Ltd. 1992; 502-10.
- 11. Hofmann GE, Warikoo P, Jacobs W. Ultrasound detection of pyometra at the time of embryo transfer after ovum retrieval for in vitro fertilization. Fertil Steril 2003;80:637–8.
- 12. Kumar P, Shah NP, Singhal A, Chauhan DS, Katoch VM, Mittal S, Et al. Association of tuberculous endometritis with infertility and other gynecological complaints of women in India. J Clin Microbiol 2008;46:4068-70.
- 13. John M, Kukkady ZA. Genital tuberculosis and infertility. Int J Gynaecol Obstet 1999; 64: 193-4.