CASE REPORT

Co-infection of *Mycoplasma genitalium* and *Chlamydia trachomatis* in an infertile female patient with genital tuberculosis

Prathyusha Kokkayil, Jyoti Rawre, Neena Malhotra[1], Benu Dhawan

Departments of Microbiology and [1]Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence:
Dr. Benu Dhawan, Department of Microbiology, All India Institute of Medical Sciences, New Delhi -110 029, India.
E-mail: dhawanb@gmail.com

ABSTRACT

Genital tuberculosis is a common cause of female infertility in India. But, it is important to screen for other agents like *Chlamydia trachomatis* and genital Mycoplasmas as well to avoid persistence of infection and its long-term sequelae. Timely diagnosis of these infections using nucleic acid amplification tests and institution of appropriate therapy will improve the conception rates in infertile women. We report a case of co-infection of *Mycoplasma genitalium* and *Chlamydia trachomatis* in an infertile female patient with genital tuberculosis. The infections were diagnosed using polymerase chain reaction, and the patient responded to a combination of antituberculosis therapy and 1 g single-dose Azithromycin.

KEY WORDS: *Chlamydia trachomatis*, co-infection, female infertility, genital tuberculosis, *Mycoplasma genitalium*

Access this article online
Website: www.ijpmonline.org
DOI: 10.4103/0377-4929.125371
Quick Response Code:

INTRODUCTION

Female infertility is caused by anatomical, endocrinal or infectious pathologies. While vaginal infections and endometritis are mild, tubal infections are harsher and tubal infertility is a frequent long-term sequelae of pelvic inflammatory disease (PID). Organisms that cause female infertility include *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, genital Mycoplasmas viz. *Mycoplasma genitalium*, *Mycoplasma hominis* and Ureaplasma sp., etc.[1] Their clinical spectrum ranges from asymptomatic to frank, severe disease. Subclinical, mild and transient infections may persist and lead to tubal blockage, leading to infertility and ectopic pregnancies.[1] Timely detection and institution of appropriate treatment are essential for improved conception rates in such patients.

We report the case of a young infertile woman having co-infection with *Mycobacterium tuberculosis, Chlamydia trachomatis* and *Mycoplasma genitalium*.

CASE REPORT

A 34-year-old lady presented to the Infertility Clinic of a tertiary care hospital in New Delhi with complaints of inability to conceive after 8 years of marriage. The patient gave no history of genital discharge or lower abdominal pain.

The patient was initially screened at the Obstetrics and Gynaecology Department by pelvic ultrasound scans and transvaginal sonography performed in the follicular phase of the ovarian cycle. The hysterosalpingography revealed a left tubal block with thick fibrosed fallopian tube and dense peritubal adhesions. Anomalies like polycystic ovarian syndrome (PCOS), uterine fibroid, endometriosis and other structural anomalies were ruled out. A basal hormone evaluation was also performed between Day 2 and Day 5 of the ovarian cycle to rule out endocrinal pathology. Semen analysis of the male partner was also performed, which excluded male factor infertility.

A pre-menstrual endometrial aspirate was collected and sent for Ziehl–Neelsen stain for acid fast bacilli and *Mycobacterium tuberculosis* DNA polymerase chain reaction (PCR), which targets a 240 bp region of the *mpt64* gene.[2] The Ziehl–Neelsen staining was negative but the *Mycobacterium tuberculosis* DNA PCR was positive. Gram staining and endocervical swab culture for *Neisseria gonorrhoeae* were also negative.

Endocervical swabs were also sent for the detection of genital Mycoplasmas and *Chlamydia trachomatis*. The processed samples were inoculated into PPLO (Pleuro Pneumonia Like Organisms) broths

containing arginine and urea for the isolation of *Mycoplasma hominis* and Ureaplasma sp., respectively. The broths were incubated at 37°C under 5% CO_2 and inspected twice daily. DNA was extracted from the processed samples using an QIAamp Mini Kit (Qiagen, Hilden, Germany) and stored at −20°C until further testing. A multiplex PCR targeting the urease gene of Ureaplasma sp. and the 16Sr DNA of *Mycoplasma hominis* was performed. A PCR was also performed to detect *Mycoplasma genitalium* by targeting the 140 kDa adhesion gene using primers MgPa-1 and MgPa-3.[3]

To detect *Chlamydia trachomatis* infection, a DNA PCR was performed targeting the cryptic plasmid using primers KL-1 and KL-2, and confirmed by a second PCR targeting the *omp1* gene.[3]

The patient's sample was negative for *Mycoplasma hominis* and Ureaplasma sp by both culture and multiplex PCR. *Mycoplasma genitalium* infection was present as the 140 kDa adhesion gene was amplified [Figure 1]. Moreover, both cryptic plasmid PCR and the omp1 gene PCR were positive for *Chlamydia trachomatis* [Figure 2].

DISCUSSION

The patient in our report was suffering from genital tract infection due to multiple etiological agents, namely *Mycobacterium tuberculosis, Chlamydia trachomatis* and *Mycoplasma genitalium*. She was treated with antituberculosis therapy (ATT) and 1 g single-dose Azithromycin. The follow-up samples of the patient after institution of therapy were negative.

The incidence of female genital tuberculosis is high in India, and is around 19%.[4] The most common presentation is tubal blockage and infertility.[5] For infertile women with a positive lab finding of genital tuberculosis like positive AFB smear, culture or DNA PCR, ATT is instituted.[5] But, very often, other infectious agents causing infertility are overlooked.

Chlamydia trachomatis is a major cause of PID, with an increasing proportion of infections being silent, delaying medical care and increasing long-term sequelae like tubal block and infertility. Approximately 20% of women with Chlamydial lower genital tract infection develop PID, 4% chronic pelvic pain, 3% infertility and 2% adverse pregnancy outcome.[6] Real-time PCR shows a relatively high prevalence of *Chlamydia trachomatis* among infertile women, as determined by one of our recent studies that shows a prevalence of 13.5%.[7] Recommended treatment regimens are Azithromycin 1 g orally in a single dose or Doxycycline 100 mg orally twice daily for 7 days.

Mycoplasma genitalium infection, like *Chlamydia trachomatis*, is often asymptomatic and increases the likelihood for silent PID and long-term sequel like tubal blockage and infertility. A study conducted among 132 women with tubal infertility showed the presence of *Mycoplasma genitalium* antibodies in 22% of the women in comparison with 6% women with non-tubal infertility.[8] Grzesko *et al*. detected *Mycoplasma genitalium* more often in cervical swabs from infertile patients (20%) compared with fertile women (4%).[9] Thus, it is evident that *Mycoplasma genitalium* could be an independent cause of tubal factor infertility. For treatment, 1 g single-dose Azithromycin is more effective than 7-day multidose Doxycycline.

Although Azithromycin and Doxycycline can combat both *Chlamydia trachomatis* and *Mycoplasma genitalium*, ATT cannot eradicate these organisms. In fact, genital Mycoplasmas are resistant to Rifampicin due to a single amino acid mutation at position 526 in the beta subunit of RNA polymerase.[10] Therefore, in this patient, instituting ATT alone would not have cured her genital tract infection. Eradication of *Mycobacterium tuberculosis* infection alone would not be effective as two other etiological agents of tubal infertility, *Chlamydia trachomatis* and *Mycoplasma genitalium*, would persist and continue to cause long-term infection and sequelae. Hence, it was essential to treat the patient with a combination of ATT and Azithromycin to result in complete cure.

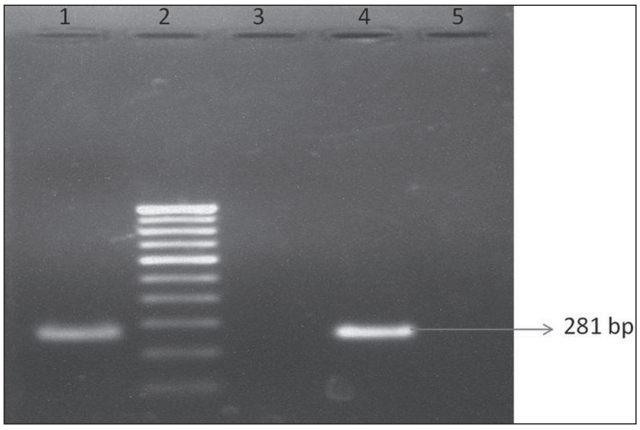

Figure 1: Polymerase chain reaction for *Mycoplasma genitalium*
Lane 1: Positive control Lane 2: 100 bp DNA ladder Lane 3: Clinical sample — negative Lane 4: Clinical sample — positive Lane 5: Negative control

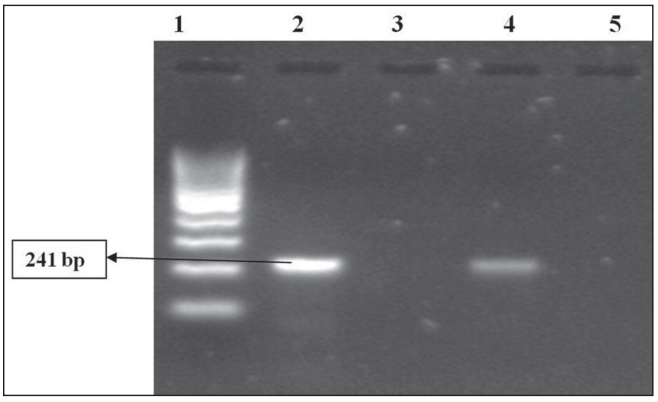

Figure 2: Polymerase chain reaction for *Chlamydia trachomatis*
Lane 1: 100 bp DNA ladder Lane 2: Positive control Serovar D (ATCC VR 885) Lane 3: Negative control Lane 4: Clinical sample — positive Lane 5: Clinical sample — negative

This case report serves as a reminder to treating physicians that in cases of tubal infertility, it is imperative to screen the patient for *Chlamydia trachomatis* and genital Mycoplasma infections using appropriate diagnostic techniques like the nucleic acid amplification test. Timely diagnosis of these agents will result in the institution of appropriate therapy and prevent the sequel of infection.

REFERENCES

1. Baecher-Lind LE, Miller WC, Wilcox AJ. Infectious disease and reproductive health: A review. Obstet Gynecol Surv 2010;65:53-65.
2. Bhanu NV, Singh UB, Chakraborty M, Suresh N, Arora J, Rana T, *et al*. Improved diagnostic value of PCR in the diagnosis of female genital tuberculosis leading to infertility. J Med Microbiol 2005;54:927-31.
3. Ghosh A, Dhawan B, Chaudhry R, Vajpayee M, Sreenivas V. Genital mycoplasma and Chlamydia trachomatis infections in treatment naïve HIV-1 infected adults. Indian J Med Res 2011;134:960-6.
4. Singh N, Sumana G, Mittal S. Genital tuberculosis: A leading cause for infertility in women seeking assisted conception in North India. Arch Gynecol Obstet 2008;278:325-7.
5. Tripathy SN, Tripathy SN. Infertility and pregnancy outcome in female genital tuberculosis. Int J Gynecol Obstet 2002;76:159-63.
6. Weström LV. Sexually transmitted diseases and infertility. Sex Transm Dis 1994;2(Suppl):S32-7.
7. Dhawan B, Rawre J, Ghosh A, Malhotra N, Ahmed MM, Srinivas VB, *et al*. *Chlamydia trachomatis* infection in infertile women in north India: Diagnostic efficacy of a real-time PCR assay. Indian J Med Res 2013 [In Press].
8. Clausen HF, Fedder J, Drasbek M, Nielsen PK, Toft B, Ingerslev HJ, *et al*. Serological investigation of *Mycoplasma genitalium* in infertile women. Hum Reprod 2001;16:1866-74.
9. Grzesko J, Elias M, Maczynska B, Kasprzykowska U, Tiaczala M, Goluda M. Occurrence of *Mycoplasma genitalium* in fertile and infertile women. Fertil Steril 2009;91:2376-80.
10. Fraser CM, Gocayne JD, White O, Adams MD, Clayton RA, Fleischmann RD, *et al*. The minimal gene complement of *Mycoplasma genitalium*. Science 1995;270:397-403.

How to cite this article: Kokkayil P, Rawre J, Malhotra N, Dhawan B. Co-infection of Mycoplasma genitalium and Chlamydia trachomatis in an infertile female patient with genital tuberculosis. Indian J Pathol Microbiol 2013;56:457-9.

Source of Support: Nil **Conflict of Interest:** None declared.