Case Report

Mycoplasma genitalium as a Cause of Pelvic Inflammatory Disease

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A B S T R A C T

Background: Mycoplasma genitalium is an increasingly recognized cause of pelvic inflammatory disease (PID).
Case: A 17-year-old female adolescent presented with chronic pelvic pain and dysmenorrhea. Test results for *Chlamydia trachomatis* and *Neisseria gonorrhea* were negative, and multiple radiologic test results were normal. The patient failed several empiric courses of therapy over 1 year. Laparoscopy revealed findings consistent with PID. Nucleic acid amplification test results were positive for *M genitalium*.
Summary and Conclusion: M genitalium causing PID can be challenging to diagnose because of its often atypical presentation. Further epidemiological studies are needed to understand the burden of disease and to establish testing and treatment guidelines.
Key Words: Mycoplasma genitalium, Pelvic inflammatory disease, Chronic pelvic pain, Dysmenorrhea

Introduction

Since its discovery in 1981 as a cause of male nongonococcal urethritis, *Mycoplasma genitalium (M genitalium)* has emerged as a pathogen associated with both male and female urogenital tract infections.[1,2] In addition, there is increasing evidence of an association between pelvic inflammatory disease (PID) and *M genitalium.* Numerous studies have detected *M genitalium* in up to 22% of women with PID according to the CDC.[3] We describe an adolescent female with a prolonged and indolent course of pelvic pain diagnosed with PID secondary to *M genitalium* infection.

Case

A 17-year-old heterosexual female adolescent initially presented to our pediatric gynecology office complaining of worsening dysmenorrhea and chronic pelvic pain. She had menarche at age 12 and reported having regular menstrual cycles since then. She experienced coitarche at age 15 and had a total of 5 male partners. She reported inconsistent condom use previously, but uses condoms 100% of the time with her current partner. She experienced dysuria only during menstruation. Her abdominal examination findings were benign, and no cervical motion tenderness was noted on bimanual examination. She had no vaginal discharge but did have general tenderness on vulvar and vaginal examination. Nucleic acid amplification test (NAAT) results for *Chlamydia trachomatis* and *Neisseria gonorrhea* were negative, and initial pelvic ultrasound findings were normal. Vaginal cultures were not performed because of the lack of vaginal discharge. She started empiric therapy with a combined oral contraceptive pill (OCP) for presumed primary dysmenorrhea versus endometriosis. She was seen by a urogynecologist 2 weeks afterward, and interstitial cystitis was ruled out.

The patient presented 6 months later with worsening pelvic pain that had prompted 3 emergency department (ED) visits. The OCP therapy moderately improved her dysmenorrhea; however, she complained of breakthrough bleeding with daily pelvic pain. Evaluation during the ED encounters included pelvic ultrasound and computed tomography scan, repeat endocervical *C trachomatis* and *N gonorrhea* NAAT, and routine laboratory work. All results were normal. She was referred to gastroenterology for a clinical diagnosis of constipation, and use of stool softeners was initiated. Over the year, she had multiple follow-up visits for persistent pelvic pain accompanied with dysuria, dyspareunia, and dyschezia. Stool softeners mildly improved her symptoms. Her pelvic examination revealed normal cervical and vaginal mucosa associated with clear-yellow discharge. Evaluation for endometriosis by laparoscopic surgery was recommended, but she initially declined. Results of repeat tests for *C trachomatis* and *N gonorrhea* were again negative. No empiric antimicrobial therapy was given. Preceding laparoscopy, she underwent endoscopy, colonoscopy, cystoscopy, and pelvic magnetic resonance imaging; all examination findings were normal. Her constipation resolved after colonoscopy. She then agreed to a diagnostic laparoscopy.

During laparoscopy, moderate-to-severe adhesions were noted along the fallopian tubes and ovaries extending down to the cul-de-sac presumed to be secondary to PID infection (Figs. 1 and 2). No clear vesicular lesions, classic powder burns, or red lesions concerning for endometriosis were

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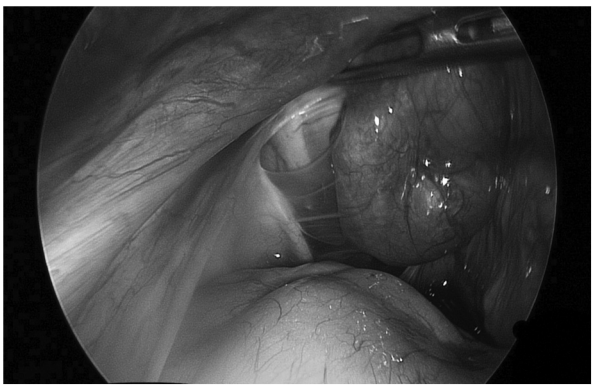

Fig. 1. Clubbed left fallopian tube with adhesions.

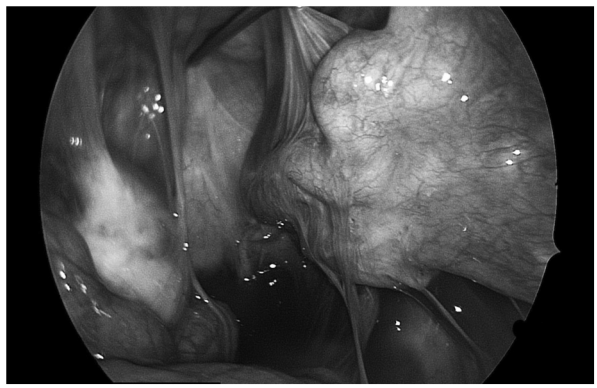

Fig. 2. Agglutinated right fallopian tube with adhesions.

seen. No inflammation or adhesions were seen by the liver. Postoperative gonorrhea and chlamydia testing were negative. Given a recent article identifying *M genitalium* as an underreported cause of PID, the patient underwent *M genitalium* NAAT testing. Results of NAAT performed at the external cervical os were positive, and results of reflex testing for *Ureaplasma* species were also positive. She was prescribed azithromycin 1.5 g for 5 days. She and her partner were referred to an adult infectious disease specialist for treatment and follow-up. Results of repeat *M genitalium* NAAT 1 month after treatment were negative. At that time, the patient was treated with 7 days of doxycycline for *Ureaplasma* spp. to prevent the side effects of taking 2 antibiotics. Her symptoms improved but did not resolve. Infectious disease consultation recommended repeating *M genitalium* NAAT, which was collected 2 months after treatment. The test results returned positive. Results of repeat *Ureaplasma urealyticum and U parvum* were negative. The patient had resumed sexual activity with the same partner. She was retreated with moxifloxacin with improvement of her symptoms, and results of repeat testing 2 months later were now negative for *M genitalium* and *Ureaplasma*. No further gonorrhea and chlamydia testing were performed. In addition to antibiotic treatment for the mycoplasma infection, she was referred to mental health and physical therapy services for chronic pelvic pain management.

Summary and Conclusion

PID is a serious sequela of sexually transmitted infections (STIs) in sexually active adolescent females. The Centers for Disease Control and Prevention (CDC) estimates the prevalence among women 18-44 years to be 4.4% in the United States.[4] *N gonorrhoeae* and *C trachomatis* are the most common causes of acute PID; however, as many as 70% of PID cases have no identified pathogen or are suspected to be polymicrobial.[5] There is increasing evidence that *M genitalium* may contribute to a substantial number of PID cases. In 2003, a case-control study performed in the United Kingdom reported that of a total of 82 women, 13% of the PID cases were positive for *M genitalium,* whereas none of the control subjects tested positive for the organism.[6] A cross-sectional case-control study by Bjartling et al demonstrated that the prevalence of *M genitalium* (2.1%) was comparable to that of C *trachomatis* (2.8%) in women with PID and cervicitis.[2] In a 2015 meta-analysis, *M genitalium* infection was found to be associated with a significantly increased risk of PID, with a pooled odds ratio of 2.14.[7] In addition, a 2019 meta-analysis showed a risk ratio of 1.73 between M *genitalium* and PID.[8]

The clinical manifestations of *M genitalium* infection may be indistinguishable from those of *C trachomatis*.[2] Some patients may also be asymptomatic.[9] Most reports describe symptoms consistent with PID, which include pelvic pain and uterine tenderness, or signs of endometritis and cervicitis.[9] Patients may also have postcoital bleeding, dysuria, and abnormal vaginal discharge.[2]

Most studies have used polymerase chain reaction (PCR) assays to detect *M genitalium*.[7] Recently, the Food and Drug Administration (FDA) approved an Aptima *Mycoplasma genitalium* assay, a NAAT, which can detect the bacteria in urine, urethral, penile meatal, endocervical, or vaginal swabs. The ability to accurately detect *M genitalium* may lead to a better understanding of the true disease burden.

M genitalium infection can be difficult to treat, because the species lacks a cell wall and can rapidly develop antibiotic resistance. In addition, the lack of a cell wall makes the organism intrinsically resistant to antibiotics such as penicillins and cephalosporins that target cell wall biosynthesis.[10] Tetracyclines, macrolides, and fluoroquinolones are standard choices for Mycoplasma species. Doxycycline has been shown to have poor activity against *M genitalium.* Azithromycin, either as a single dose or as a 5-day extended-dose regimen, is considered first-line therapy, but numerous reports of resistant strains have been published and definitive treatment guidelines do not exist.[10] Fluoroquinolone resistance has also been reported; but currently, moxifloxacin has been shown to be the most effective antimicrobial agent.[10] Similar to other STIs, patients are advised to maintain abstinence, to notify their partners, and to undergo treatment until their symptoms have resolved.[10] The recommendation for testing and treating the partner is supported by a systematic review in which up to 50% of infected individuals had a heterosexual partner with *M genitalium*.[8] A test of cure should also be performed 3-6 weeks after treatment because of high rates of resistance.[11]

Our case demonstrates how challenging the diagnosis of *M genitalium* causing PID can be in adolescent females with atypical presentations and significant sequelae. Undetected *M genitalium* can lead to extensive pelvic adhesions with

future fertility issues and chronic pain.[10] Similar to *M genitalium* in that it lacks a cell wall, *U urealyticum* is also part of the normal urogenital flora that could potentially become a co-infection.[1,5] Although *Ureaplasma* has been indicated as a possible cause of PID, its impact is not well understood, and further studies are required.[1,5] Currently, there are no recommendations as to whether *M genitalium* testing should be part of routine annual STI screening. In a patient with signs and symptoms of PID or chronic pelvic pain, *M genitalium* should be included in the differential. Further studies are needed to determine the incidence and prevalence of *M genitalium* in the asymptomatic young, sexually active female population as well as individuals presenting with clinical PID symptoms. These data could then be used to establish standardized testing and treatment guidelines for *M genitalium*.

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