Case Report

A Clinical Conundrum: Chronic Cervicitis

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A B S T R A C T

Background: Cervicitis is most commonly caused by sexually transmitted infections. "Normal vaginal flora" are rarely responsible for inflammation of the cervix.
Case: We describe a 22-year-old female patient with chronic cervicitis who had negative test results for bacterial and viral pathogens most commonly responsible for cervicitis. After 21 months of symptoms and multiple courses of empiric antibiotics addressing the most common causes of cervicitis, a course of antibiotics targeting group B streptococcus found on a genital culture resolved the patient's illness.
Summary and Conclusion: Bacteria considered to be "normal vaginal flora" in a nonpregnant young female adult should be considered as a potential pathogen when test results for more routine pathogens associated with cervicitis are negative.
Key Words: Chronic cervicitis, Group B streptococcus

Introduction

Cervicitis is defined most often as inflammation of the uterine cervix; other definitions might also include the presence of abnormal mucopurulent discharge and/or friability of the cervix.[1,2] In many cases, cervicitis is completely asymptomatic. Cervicitis is generally classified as being either acute or chronic. Acute cervicitis is commonly caused by infection, most often by sexually transmitted infections; chronic cervicitis has longer-lasting symptoms and is often caused by mechanical or chemical irritation, such as douching, or by untreated acute cervicitis.[1] Approximately half of all cervicitis cases are caused by either *Chlamydia trachomatis* or *Neisseria gonorrhoeae* (GC); most of the remaining cases originate from unknown etiology.[2,3] We present a case of chronic cervicitis; the cause of the cervicitis presented a clinical conundrum for more than 1.5 years.

Case

The patient is a 22-year-old woman with a medical history significant for headaches and acne (receiving doxycycline 100 mg twice daily) who presented to the adolescent medicine clinic for her first, routine PAP smear. The patient had no complaints; she had vaginal intercourse for the first time with a male partner within the 3 months before the visit. On examination, her vulva was red and irritated, with thick white discharge present. Her cervix was inflamed and was extremely friable; it bled on contact during examination. The PAP smear was negative for pathology, and routine sexually transmitted infection screening was ordered and was negative. Wet prep was negative for trichomonads, and rare fungal elements were noted. Fluconazole 150 mg (1-time oral dose) was prescribed.

At a 2-week follow-up visit, the patient's cervix and vaginal wall were tender and inflamed. The patient was now complaining of pain and bleeding with intercourse and tampon use. The appearance of the cervix remained inflamed and friable with deep crypts/ulcerations. She was given 1 g of azithromycin empirically, and she completed the previously ordered testing for GC, *C trachomatis*, herpes simplex virus (HSV) (HSV1 and HSV2, polymerase chain reaction [PCR]), and HSV serology. All test results were negative. At a visit 2 months later, the patient was still experiencing pain. The cervix appeared unchanged and an endocervical swab was sent for evaluation; gram stain, genital culture, and anaerobic cultures all revealed normal vaginal flora. Cultures for *Ureaplasma urealyticum* and *Mycoplasma hominis* were negative. Over the next several months, the patient's symptoms did not improve; further testing revealed negative cytomegalovirus immunoglobulin (Ig)M, negative Epstein Barr virus (EBV) IgM, positive EBV IgG, positive EBV early antigen, and positive EBV nuclear antigen—indicating possible reactivated or convalescent EBV infection.

Approximately 6 months after initial presentation, the patient was referred to gynecology; she now had a history of having had 4 male sexual partners with inconsistent condom use. Appearance and degree of inflammation of the cervix remained relatively unchanged. An endocervical swab (Tem-PCR Women's 15:1 Health Panel, Diatherix Eurofins Clinical Diagnostics) was obtained revealing negative results for *Atopobium vaginae*, *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida tropicalis*, *C trachomatis*, HSV1, HSV2, *Mycoplasma genitalium*, *Mycoplasma hominis*, GC, and *Trichomonas vaginalis*. Positive results were found for *Ureaplasma urealyticum*, *Gardnerella vaginalis*, and *Candida parapsilosis*. Cervical biopsy revealed chronic

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inflammation only. The patient was treated with fluconazole 150 mg (1-time oral dose) and metronidazole gel (0.75%) intravaginally for 5 days for yeast and bacterial vaginosis, respectively.

Sixteen months after initial presentation, the patient returned for a routine visit. She had no cervical complaints, however, her cervical exam remained abnormal with redness, friability, and yellow pus. The endocervical swab (Tem-PCR Women's 15:1 Health Panel, Diatherix Eurofins Clinical Diagnostics) was repeated and was positive for *C trachomatis* only. HIV (antibody testing) and rapid plasma regain testing were negative. EBV IgM continued to be negative with a high EBV IgG. A culture for group B streptococcus (GBS) was obtained and was positive. The patient was treated with 1 g of azithromycin for *C trachomatis* and was seen 5 weeks later. The patient again complained of pain and bleeding with intercourse and tampon insertion. On examination, her cervix remained relatively unchanged; the cervix was inflamed with crypts but was not friable. Sedimentation rate, antinuclear antibody, GC, and chlamydia tests were all within normal limits, and the EBV panel remained unchanged from 16 months earlier. We determined that the patient must be treated for streptococcus species despite its inclusion among "normal vaginal flora." The patient received a course of doxycycline (which she was no longer taking for acne, 100 mg twice daily for 10 days), amoxicillin/clavulanic acid (1000 mg twice daily for 7 days), and another 1-dose course of fluconazole, per recommendation from an infectious disease specialist. She was seen in follow-up 3 months later. Her cervix appeared completely normal. She had no cervical complaints. Routine sexually transmitted infection screening (GC, chlamydia, and HIV) was negative. GBS culture was not performed at that time.

Diagnosis

We diagnosed the patient with chronic cervicitis due to GBS.

Summary and Conclusion

Although a literature review reveals GBS as a more common potential pathogen among pregnant women, neonates, elderly individuals, and those with immunocompromise, there are few reported cases of GBS serving as a true pathogen among healthy adolescents and young adults. Only 1 study involving multiple adolescents was found in the literature.[4] In that study, 13 of 18 adolescents who had vaginal bacterial cultures positive exclusively for GBS also complained of clinical symptoms consistent with vulvovaginitis; 3 of 12 who had a documented speculum exam had evidence of cervicitis.[4] We found only 1 reported case of ulcerative lesions associated with GBS similar to those described in the patient in this report; this case involved a healthy, 19-year-old male patient with urethritis and ulcerative lesions on his penis, both attributed to GBS.[5] The 2 other published case reports on GBS cervicitis in healthy young women were published in 1985[6] and 2013.[7] This review of the literature suggests that GBS might be a much more common, yet often discounted, cause of vulvovaginitis and cervicitis in healthy young people than previously thought.

Little is known regarding why a micro-organism that is usually a nonpathogen within a host might become a pathogen that causes disease. Most experts describe the pathogenic variability of an organism among various hosts as being "context-dependent pathogenicity" related to genetic and environmental factors of the host. As noted previously, environmental factors might include pregnancy, immunocompromise, or perhaps a change in the vaginal environment from a chemical or product such as nonoxynol-9, which is implicated in irritation of the vaginal mucosa and thus increased vulnerability to infection and disease. The sparse literature available on GBS infections among adolescents and young adults implies that some "routine" cases of vulvovaginitis and cervicitis might be because of GBS more frequently that previously recognized. Cultures for GBS are not routinely obtained among nonpregnant, immunocompetent women with cervicitis.

Our patient experienced chronic cervicitis on the basis of the longevity of symptoms. Although *C trachomatis* and GC are the most common causes of cervicitis, there are other infections and bacteria that have been linked to cervicitis. Bacterial vaginosis is defined as a disturbance in vaginal flora and is frequently found in conjunction with cervicitis.[3] It has been found to cause inflammation, and in some cases might be the source of chronic cervicitis.[1,3] This patient had bacterial vaginosis and *C trachomatis* at different points in her disease course; they were treated appropriately with no change noted in the patient's long-standing symptoms. Other causes of cervicitis include the presence of *M genitalium* at the cervix, trichomoniasis, or HSV.[1] This patient tested negative for these pathogens. Although *M genitalium* is a relatively newly described pathogen that can be detected in 10%-30% of women with clinical cervicitis, it is difficult to diagnose. Repeated PCR testing from a large laboratory was negative, and this patient was treated with azithromycin, the current medication of choice, as well as treatment doses of doxycycline during the course of her disease without effect. Although there are treatment failures associated with *M genitalium* with azithromycin, *M genitalium* would likely not have cleared with the doxycycline (31% cure rate) and amoxicillin/clavulanic acid regimen that eventually cleared the cervical infection for this patient.[8]

For women who have nongonococcal nonchlamydial cervicitis, it is common to experience the symptoms for longer than 1 calendar year because of the possible difficulties of finding the cause of the cervicitis.[2] Because of its generally nonpathogenic nature and frequent presence in the genital tract, GBS was not initially considered as a possible cause of this patient's cervicitis, despite a positive culture. After the patient was found to have negative initial test results for sexually transmitted infections as well as other common causes of cervicitis, and further test results were negative for viral and autoimmune causes, GBS was the only entity for which she had not yet received treatment. The last combination of antibiotics prescribed included amoxicillin/clavulanic acid after which her cervix appeared normal for the very first time since initial

presentation. The resolution of symptoms after amoxicillin/clavulanic acid treatment supports the theory that GBS was the cause of her cervicitis, because GBS is susceptible to drugs from the penicillin family. Ideally, this patient would have had a GBS culture collected after resolution of her symptoms to help confirm the diagnosis; this culture was not obtained at that time, and the patient subsequently moved with loss to follow up.

Although certain bacteria commonly present in the human body are often considered nonpathogenic, it is important not to overlook them when searching for the underlying cause of a chronic infection or condition. Test results might indicate that "normal flora" are present in the system; to find the true cause of infection, a provider might need to search specifically among usually nonpathogenic suspects.

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