Complex Vaginitis Cases: Applying New Diagnostic Methods to Enhance Patient Outcomes

Announcer:
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Dr. Schwebke:
Okay, welcome everybody. I'm Dr. Jane Schwebke. I'm a Professor of Medicine and Infectious
Diseases at the University of Alabama at Birmingham. And today, we’re going to go over some complex vaginitis clinical cases using NAATs technology to help us solve them.

Our learning objectives are to demonstrate an increased ability to manage patients with vaginitis and to integrate NAATs testing into clinical practice to improve diagnostic accuracy and drive management decisions. And I should mention that, for those of you who don’t know, who I can’t imagine, NAATs testing stands for nucleic acid amplification testing.

So, we all know that vaginitis is very common. It can be symptomatic, including vaginal discharge, vulvar itching, irritation, or odor, and many women seek over-the-counter alternative therapies before seeking professional care. And in addition to that, where they could be wrong, even if they do seek professional care, the providers can often pursue empiric diagnosis and testing and can be wrong themselves. Inaccurate diagnosis and improper treatment increase the risk of serious complications such as late-term miscarriage, preterm or low-birthweight babies, HIV infection, and pelvic inflammatory disease.

Common etiologies of vaginitis include bacterial vaginosis, or BV, which accounts for 40 to 45% of total cases and is detected in up to 50% of symptomatic women. Vulvovaginal candidiasis is thought to occur in about 20 to 25% of the total cases and is detected in 17 to 39% of symptomatic women. Trichomoniasis, 15 to 20% of total cases, and is detected in 4 to 35% of symptomatic women. And then there is a small proportion of women who actually have mixed diagnoses. So, for example, in my clinic I fairly frequently see mixed diagnosis with bacterial vaginosis and candidiasis.

We’re all familiar, I think, with sort of the classical way of trying to determine what the infectious etiology is by using vaginal pH, characteristics of the discharge, the whiff test, and the microscopic appearance of the wet prep to look for things such as clue cells, trichomonads and pseudohyphae of yeast. And within these different diseases, the pH can be a helpful differential. So, for example, the normal pH is 3.8 to 4.2. In bacterial vaginosis it’s going to be greater than 4.5. In trich it’s usually greater than 4.5 but can be normal. And in candida it’s usually normal unless there’s mixed infection. And then, I think we’re all familiar with looking under the microscope to look for motile trichomonads, the pseudohyphae or budding yeast, and clue cells.

There are cultures available for some of these options, and the advantage of that is that you can use those to test antibiotic sensitivities, if the need arises. However, they have not been recommended for Gardnerella or the diagnosis of BV, per se. There are non-amplified DNA detection tests. They’re better than antigen detection, more stable than culture, but still they lack sensitivity. And so now we have the new NAATs testing, which are amplified detection of organism-specific DNA or RNA sequencing, resulting in a very sensitive and specific result.
So, there are NAAT panels that are out there now that provide for detection of the various etiologies of vaginosis and cervicitis. So, for bacterial vaginosis it's usually a combination of different targets that they look at, BV-associated bacteria, sometimes also in association with lactobacillus. For vulvovaginal candidiasis, of course, they're looking for Candida albicans, which is the main cause of disease, but also other species, and that's a nice plus with some of these tests is that they can differentiate the species of Candida. Trichomonas, of course, is Trichomonas vaginalis. And for cervicitis we're looking for chlamydia, chlamydia trachomatis, and gonorrhea, Neisseria gonorrhoea. And as I said, the NAATs tests are really the new gold standard for sensitivity and specificity.

So, now we're going to go over some clinical cases. First case: Jan, who's 26 years old, is a new patient of yours complaining of frequent yeast infections. She says she gets these symptoms with vaginal discharge frequently over the last 2 years. She's used over-the-counter antifungal creams, she's been previously prescribed oral fluconazole, but she keeps having this problem. And on exam you see a clumpy vaginal discharge with moderate erythema.

So, what's next? And here we have some options. You could treat her with oral voriconazole, tell Jan to avoid thong underwear and to change her soap, obtain a vaginal sample for NAATs vaginal panel testing, or treat her with intravaginal Monistat and oral fluconazole simultaneously. Well, the right answer would be to go ahead and get the NAATs vaginal panel because this will support the correct diagnosis and treatment approach for Jan. And in fact, the panel not only detects that she does have yeast, but the type of yeast she has is Candida glabrata. And Candida glabrata can often be resistant to azoles and very difficult to treat, so that’s probably what’s been going on with Jan. A possible option is intravaginal boric acid suppositories or intravaginal flucytosine, but sometimes these cases are resistant to most therapies, and this can be a real problem. It’s also important to note that the NAATs panel could also detect Candida krusei, which could be another instance of something that may be more difficult to treat and require different treatment options.

Okay, case 2: Elizabeth, who’s 35, is in follow-up for recurrent vaginal discharge and odor. Your office, unfortunately, does not perform microscopy. Based on Elizabeth’s symptoms, she received both metronidazole for 7 days and intravaginal metronidazole for 5 days and intravaginal clindamycin cream at some point in time. She says her symptoms typically abate for a few days and then they recur. She is sexually active with 1 male and 1 female partner.

So, what can we do for Elizabeth? Well, we could treat Elizabeth’s BV with vaginal metronidazole and oral secnidazole; we could treat empirically for all causes of vaginitis using fluconazole and oral metronidazole; we could suggest that she sees a specialist to confirm the current diagnosis, or none of the above. So, here we get back to the point that empirical diagnosis of vaginitis is notoriously
inaccurate, results in the wrong treatment, and frustration on the part of the patient and clinician. And in fact, in the more recent CDC treatment guidelines, they note that nucleic acid testing is an appropriate first-line method for evaluating women with vaginal symptoms. Use of a highly specific NAAT vaginal panel, in this case, confirms BV. A vaginal swab specimen is easy to obtain, either clinician-collected or self-collected, and, as I said before, looks at different algorithms of BV-associated bacteria to determine the diagnosis of BV.

Now, BV is not proven to be sexually transmitted; however, there is a high concordance of BV between lesbian couples, and condoms have been shown to be protective in heterosexual couples. So, based on that, it’s recommended that you evaluate and treat the female partner and counsel on the use of condoms with the male partner, so that would be important for Elizabeth. And then you need to go back and get creative. Some possible options for Elizabeth with her difficult-to-treat recurrent BV are: re-treatment of the index case with metronidazole, just treat her again; high-dose intravaginal metronidazole, which can be obtained through a compounding pharmacy where you ask them to put 750 to 1000 mg of metronidazole into an intravaginal vehicle, and she uses this once a day for 1-2 weeks. Some people have used oral metronidazole plus intravaginal boric acid suppositories for 2-3 week, and some people use suppressive therapy with intravaginal metronidazole gel twice a week, indefinitely. So, those are some options for Elizabeth, and it can be a difficult problem.

Case 3, which is our last case, involves Michelle, who’s 28 years old, complains of a vaginal discharge, irritation, and dysuria. She was recently treated empirically for a UTI with no improvement in her symptoms. On exam she has moderate vaginal discharge and some erythema.

What should we do for her? We could recommend that she use Monistat for likely yeast infection, we could re-treat her supposed UTI with a different antibiotic, we could get a vaginal sample for BV, yeast, and trichomonas using NAAT testing, or we could do both A and C, recommend she use Monistat and get a vaginal sample. So, you do send a NAATs test, and you’re surprised because NAATs comes back positive for trichomonas, and you realize that failure to have done a specific test would have resulted in continued inappropriate antimicrobial therapy and continued infection with this sexually transmitted infection.

So, you treat Michelle and her sexual partner, and the treatment right now that’s recommended is metronidazole 2 g stat dose p.o. However, there is data, recent data, that suggests that 500 mg p.o. b.i.d. for 7 days may be superior to the stat dose. About 5% of cases of trichomonas are resistant to metronidazole. So, if you have a patient who has recurrent disease, the first thing to do is to rule out reinfection, and if you’re convinced that that’s not the case, then you can go to tinidazole, which has some superior pharmacokinetics than metronidazole against trich, usually around 2 g per day for 5-7
days orally. But if that fails, I’ve found useful, although cumbersome, the combination of high-dose oral tinidazole, 2-3 g a day, plus intravaginal paromomycin vaginal cream for 2 weeks.

So, in summary, misdiagnosis of vaginal infections is common and leads to inappropriate treatment, prolonged symptoms, and increased risk of developing serious complications. Traditional assessment methods: symptoms, physical exam, pH, microscopy, and whiff, lack sensitivity and specificity. NAATs is currently recommended by the CDC as an appropriate first-line method of evaluating women with vaginal symptoms, and the NAATs panels require a single collection and test, reducing the burden on clinicians and improving diagnostic coverage.

Thank you so much for your attention.

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