Published in final edited form as:

J Low Genit Tract Dis. 2013 January ; 17(1): 88–91. doi:10.1097/LGT.0b013e3182656991.

Vaginal Toxic Shock Reaction Triggering Desquamative Inflammatory Vaginitis

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Abstract

Objective—To report two cases of desquamative inflammatory vaginitis (DIV) associated with toxic shock syndrome toxin-1 (TSST-1)-producing *Staphylococcus aureus* strains.

Materials and Methods—Case report of two patients, one with an acute and one with a chronic presentation, diagnosed with DIV on the basis of clinical findings and wet mount microscopy. Pre- and posttreatment vaginal bacterial and yeast cultures were obtained.

Results—Pretreatment vaginal bacterial cultures from both patients grew TSST-1-producing *S. aureus*. Subsequent vaginal bacterial cultures following oral antibiotic therapy were negative.

Conclusions—DIV may be triggered through TSST-1-mediated vaginal toxic shock reaction.

Keywords

Desquamative inflammatory vaginitis; Vaginitis; toxic shock syndrome; toxic shock syndrome toxin

Desquamative inflammatory vaginitis (DIV) is a well-described chronic clinical condition of unknown cause characterized by a copious purulent discharge, diffuse inflammation, and vaginal pruritus, burning, or dyspareunia [1–3]. Although DIV is recognized in up to 8% of patients with chronic vaginitis, it remains frequently undiagnosed [4]. Because most cases are diagnosed in women with chronic symptoms, very little is known about acute triggers of DIV. We searched MEDLINE (1990–2011) using PubMed for English-language articles with search terms including “DIV,” “vaginitis,” “vaginal infections,” “toxic shock syndrome,” and “toxic shock syndrome toxin” and found no description of acute DIV specifically caused by a toxin-producing infectious agent. Here, we present two patients, one

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Conflicts of Interest: For the remaining authors none were declared.

with an acute and one with a chronic presentation, in whom DIV may have been caused by toxic shock syndrome toxin-1 (TSST-1)-producing *Staphylococcus aureus* strains.

CASE REPORTS

Case 1

A 27-year-old nulligravid white woman was referred to our specialty clinic with a 1-month history of profuse vaginal discharge, vulvar erythema, and pruritus. Prior to the onset of symptoms, the patient engaged in receptive oral and digital sexual intercourse with a new partner, followed 2 days later by menses and use of tampons. The patient had tried multiple treatment modalities including vaginal miconazole, oral doxycycline, and oral fluconazole. Although she obtained temporary relief from these medications, symptoms recurred within a few weeks.

Physical examination revealed an erythematous, swollen vulva with desquamation of the labia majora. The vaginal sidewalls were erythematous and tender with a purulent discharge at the introitus (Fig. 1). In addition, the vestibule was erythematous with a small fissure in the posterior vestibule. She met criteria for DIV based on an elevated vaginal pH (5.5), and saline microscopy revealed numerous parabasal cells, polymorphonuclear leukocytes (PMNs), and altered vaginal flora. Whiff and rapid trichomonal antigen tests were negative. Because the initial diagnosis was DIV and because the findings were severe, we started the patient on oral clindamycin, 300 mg three times daily, along with prophylactic oral fluconazole, 200 mg twice weekly. Vaginal yeast culture was negative; bacterial cultures were positive for group B streptococci and *S. aureus*, resistant to clindamycin. Subsequent testing revealed that one strain of *S. aureus* produced both TSST-1 and staphylococcal enterotoxin C (SEC), while the group B streptococci were non-toxin producing.

The patient returned 1 week later and reported an 80% improvement in her symptoms. However, she now reported desquamation on her palms and nose. Physical examination showed markedly improved vulvovaginal inflammation, but mild scaling on the vulva (Fig. 2), as well as the desquamation on her palms. The vaginal pH was within normal limits and saline microscopy revealed no abnormalities. Because of the resistance profile of the initial *S. aureus* culture and to minimize the chance of recurrence, the antibiotic was changed to oral trimethoprim-sulfamethoxazole, 800/160 mg twice daily. She was also advised to apply 2% mupirocin to her nares twice daily for 5 days. Testing of the patient's antibody status revealed low titers of antibodies to both TSST-1 (<1:10) and SEC (1:40), where titer is the reciprocal of the last twofold dilution to give a positive absorbance at 450-nm wavelength by enzyme-linked immunosorbent assay; intravenous immunoglobulin typically has antibody titers to both TSST-1 and SEC of 1:160 to 1:320. Vaginal yeast and bacterial cultures were negative.

Two weeks later, the patient reported complete resolution of her vulvovaginal symptoms. Mild vulvar scaling, however, persisted, and she was referred to a dermatologist, who performed a vulvar biopsy, which revealed nonspecific spongiotic changes. On follow-up, 1 month after initial presentation, the patient was completely symptom-free.

Case 2

A 50-year-old white woman, gravida 2, para 2, presented to our specialty clinic with a 2-year on-and-off history of vaginal discharge, vulvar burning, pruritus, and erythema. The patient had been diagnosed 4 years previously with recurrent bacterial vaginosis, which was treated with oral metronidazole, vaginal metronidazole gel, and boric acid suppositories, after which her symptoms resolved completely. However, 2 years later, her symptoms recurred, and despite treatment with multiple courses of oral and vaginal metronidazole, the

patient had only temporary relief. Her last menstrual period was 2 weeks previously, during which she used tampons. She had been in a monogamous relationship for the past 30 years.

On physical examination, the vestibule and vulva were moderately erythematous. The vagina walls were markedly erythematous with spots of contact bleeding and profuse yellow discharge. The vaginal pH was 5.5, and saline microscopy revealed numerous parabasal cells, a PMN-to-epithelial-cell ratio of greater than 1, and many cocci. Clue cells and trichomonads were absent, and whiff and rapid trichomonal antigen tests were negative. Bacterial and yeast cultures were obtained, and the patient was advised to use 2% clindamycin cream intravaginally once daily for 14 days.

She returned 1 month later and reported complete resolution of all symptoms. Although the yeast cultures were negative, bacterial cultures were positive for *S. aureus*, sensitive to clindamycin. The *S. aureus* strains were tested for toxin production and showed TSST-1 and SEC production. Repeat bacterial and yeast cultures obtained following treatment were negative.

Discussion

The first case of DIV was described almost 50 years ago, and since then our understanding of this clinical condition has slowly increased. In 1994, Sobel [1] proposed diagnostic criteria for DIV that included purulent vaginitis, signs of epithelial cell exfoliation (increased parabasal cells), a complete or relative absence of gram-positive bacilli and replacement by gram-positive cocci, a leukocyte-to-epithelial-cell ratio greater than 1:1, and vaginal pH greater than 4.5, as well as exclusion of bacterial vaginosis and *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* infection [1–3]. Studies have evaluated a myriad of historical risk factors as well as medications, infectious agents, and allergens causing DIV, but there is no consensus about a single causal mechanism [2]. Current evidence, however, suggests that DIV occurs primarily in perimenopausal white women who may have specific personal triggers including diarrhea, medication exposure, excessive sweating, or even hormone replacement therapy [2]. Many other medical conditions may have dermatologic findings similar to DIV. Hence, the differential diagnosis of DIV is extensive and should include atrophic vaginitis, contact dermatitis, vulvovaginal fixed drug eruptions, estrogen hypersensitivity vulvovaginitis, erosive lichen planus, pemphigus vulgaris, bullous pemphigoid, and graft-versus-host disease [2,3].

Little is known about the microbiology of DIV. Sobel [1] found that in 34 patients with DIV in whom vaginal cultures were obtained, 15 patients (44%) had group B streptococci, 1 patient (3%) had group A streptococci, and 2 patients (6%) had *S. aureus*. In a recent study of 101 patients with DIV, Bradford and Fischer [2] showed that of all vaginal cultures obtained, 13 patients (13%) had group B streptococci and 2 patients (2%) had *S. aureus*. In neither case was it clear whether these microorganisms were causative or merely incidental colonizers. Not only did our patients have vaginal cultures positive for *S. aureus*, but we were also able to demonstrate that they were TSST-1-producing strains. We hypothesize that a local toxic shock reaction may have triggered DIV in these patients.

Toxic shock syndrome is an acute systemic disease characterized by fever, hypotension, multiorgan failure, and late desquamation of hands and feet. It can be menstrual (mTSS) or non-menstrual related, with more than 99% of cases of mTSS associated with tampon use. Factors required for mTSS to develop in a patient include vaginal colonization with a toxigenic strain of *S. aureus*, production of TSST-1, penetration of a sufficient quantity of TSST-1 across the vaginal epithelium, and absent or low titers of TSST-1-neutralizing antibodies [5]. In human vaginal epithelial cells, TSST-1 was shown to increase the

production of proinflammatory cytokines and chemokines, which suggested an initial inflammatory response that acts to disrupt the mucosal barrier and increase TSST-1 penetration [6]. Because of our first patient's acute presentation and later systemic symptoms of mild toxic shock syndrome, we think that this patient had a form of vaginitis identical in appearance to DIV that was caused by a toxin-producing strain of *S. aureus*. This local response may have been insufficient to cause significant vaginal mucosal disruption and penetration of TSST-1 systemically, as supported by the patient's limited systemic symptoms and the absence of multiorgan involvement. We were subsequently able to find a TSST-1-producing strain of *S. aureus* in the second patient, who had a chronic form of DIV.

Although we hypothesize that both our patients had a local vaginal toxic shock reaction causing DIV, our hypothesis is limited by a few aspects. Because DIV is a condition that generally affects the vestibule and vagina, it is possible that some of the more extensive vulvar findings and the desquamation on patient #1's hands were caused by some other skin abnormality, such as reactive psoriasis. Although we were able to show that the *S. aureus* strains were toxin producing, we did not obtain vaginal levels of TSST-1, which would have further supported our hypothesis. Given the low percentage of patients with positive *S. aureus* cultures in other studies, our findings may not be applicable to other women with DIV. However, in some patients with DIV and negative vaginal cultures for *S. aureus*, a local toxic shock reaction with subsequent clearing of the offending organism may have triggered an uncontrollable inflammatory cascade, and the trigger may have been another, as yet uncharacterized toxin.

Acknowledgments

Source of Funding: Patrick M. Schlievert was funded by USPHS research grants AI-74283 and AI57153 from the NIH-supported Great Lakes Regional Center for Excellence in Biodefense and Emerging Diseases where he is a member.

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Figure 1.
Vulvovaginal findings showing erythematous and swollen vulva with purulent discharge at the introitus (case 1).

Figure 2.
Vulvovaginal findings following 1 week of oral clindamycin therapy (case 1).