Nontrichomonal Purulent Vaginitis: Clinical Approach

Jack D. Sobel, MD

Address
Division of Infectious Diseases, Harper Hospital, 4 Brush, Room 4811 3990 John R, Detroit, MI 48201, USA.
E-mail: jsobel@intmed.wayne.edu

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Although trichomonal vaginitis and cervicitis are responsible for most presentations of a frankly purulent vaginal discharge, nontrichomonal vaginitis and purulent exudate are being seen in an increasing number of cases. Purulent vaginitis remains poorly defined and largely ignored, with little increase in the amount of knowledge we have of this not infrequent entity. Accordingly, a variety of empirical therapies, often including multiple simultaneous measures, are prescribed. Considerable numbers of causes are now identified, and this review describes a step-by-step approach to diagnosis and management.

Introduction

A purulent vaginal discharge is one that is yellowish-green, when viewed macroscopically at the introitus or upon further vaginal speculum examination. Not always copious, the purulence reflects a marked increase in inflammatory cells, *ie*, polymorphonuclear (PMN) and mononuclear cells, resulting in a purulent exudate.

Mucopurulent cervicitis—characterized by a friable cervix, easy bleeding on touch, and macroscopic purulence of the endocervical discharge—is also defined, microscopically, by the detection of more than 30 PMNs per high-power field (HPF). A similar definition, applied to the number of PMNs in pooled vaginal secretions, has not been validated. Many clinicians define a leukocyte increase as a ratio of PMNs to squamous epithelial cells in excess of one, as visualized in several HPFs.

Unfortunately, the common standard of clinical practice neither requires nor demands quantitative or semi-quantitative measurement of inflammatory cells observed on saline microscopy; hence, the physiologic and pathologic causes of increased PMNs in vaginal secretions are poorly documented and poorly understood. This represents a major obstacle to understanding the pathophysiology of vaginal disease.

Further, determining the origin of the purulent discharge is often an extremely difficult and frustrating process. Clearly in some cases, overt inflammation of the vagina (erythema, rawness, ulceration, erosion, hemorrhage, rash) or the cervix (friability, hemorrhage, edema, ulceration of an overt purulent discharge visible at the endocervix) allows ready identification of the source of the purulent discharge. However, it is frequently impossible to make this distinction, especially in the presence of cervical ectopy or dilatation of the cervical canal in multiparous women. In the management of a purulent discharge, identifying the source is paramount.

The symptoms of a purulent discharge relate to the origin of the discharge and site of inflammation. Cervical or supracervical origin usually results in the sole primary complaint of a purulent discharge, with a variable accompanying odor. Deep dyspareunia may be present, but is more common is women with frank vaginitis who also present with a purulent discharge, vaginal pain, soreness, and pruritus. Tampon use is not tolerated. Vulvovestibular signs and symptoms are variable, depending on the pathology (*eg*, prominent with erosive lichen planus; absent in cervicitis). In addition, variable vestibulitis is evident in purulent vaginitis when the vulvovestibular manifestations reflect a secondary local inflammatory reaction to so-called toxic or proinflammatory components of the discharge; this condition resolves when the vaginitis is appropriately treated. This latter phenomenon is best exemplified by trichomonal vaginitis, which is also characterized by a high rate of asymptomatic carriage.

Purulent vaginitis due to *Trichomonas vaginalis* is extremely common and well known in both the industrialized and non-industrialized world, and its importance has recently been emphasized by its potential role in HIV transmission in men and women [1•].

Trichomonal vaginitis (*ie*, trichomoniasis) is the most common cause of purulent vaginitis, and culturing for *T. vaginalis* is an essential part of the clinical investigation of any woman found to have a purulent vaginal discharge and elevated vaginal pH; culturing is required to exclude this entity, even in so called low risk women, regardless of age.

Approach to Nontrichomonal Purulent Vaginitis

In the clinical investigation of possible purulent vaginitis, it is vital to obtain a detailed patient history when considering a differential diagnosis. For example, a history of the recent use of chemical irritants, such as fluorouracil for

genital warts, suggests a chemical rather than infectious etiology. Similarly, recent vaginal surgery, such as rectocele repair, might suggest a rectovaginal fistula.

In HIV-positive women, unusual opportunistic pathogens, such as cytomegalovirus (CMV), or unusual manifestations of common pathogens, such as herpes simplex virus (HSV), may cause cervicitis or even vaginitis. Idiopathic vulvar, vestibular, or vaginal ulcers are often giant, and are well described in advanced HIV-associated immunodeficiency; they respond to steroids and thalidomide therapy [2].

Following allogeneic bone-marrow transplantation (for example, in the treatment of leukemia) a woman might develop purulent vaginitis secondary to graft-versus-host disease (GVHD); thus, the clinician should investigate other manifestations of GVHD in such cases. Another important area to explore is hormonal status, because recent hormone therapy (*eg*, therapy for endometriosis or infertility) and manipulation (*eg*, recent prolonged lactation or breast-feeding) are associated with desquamative inflammatory vaginitis (DIV) [3••].

Once trichomoniasis is excluded, the clinician should attempt to localize the site of pathology, according to a differential diagnosis (*see* Table 1). In the majority of cases, elevated vaginal pH is observed. A normal pH level indicates focal inflammation or disease, localized to the cervix (*see* Table 2), invariably excludes diffuse vaginitis, and implies at least normal or near-normal vaginal flora, as well as adequate lactobacilli, which can be verified on saline microscopy or Gram stain. Malodor of the discharge implies a major disruption of the vaginal flora, as evident in trichomoniasis, foreign-body presence, or rectovaginal fistula.

Clinical examination offers important diagnostic clues. One of these is the appearance of the vestibule; secondary vulvovestibulitis is often common in the presence of a copious purulent vaginal discharge, but an erosive appearance should generate suspicion of erosive lichen planus. Other important clues include evidence of vestibular atrophy and telangiectasia, often indicating estrogen deficiency or DIV [3••].

Speculum examination of the vagina is crucial, but often fails to provide a diagnosis. The observer should attempt to identify, for example, a foreign body, ulcerations, focal or localized mucosal erosions, rawness, atrophy, vascular changes (telangiectasia), or macular rash. Similarly, evaluation of the cervix, without colposcopy, is critical, to investigate the presence of ectropion, friability, the tendency to hemorrhage, ulceration, dilatation of the cervix, and the nature of the endocervical discharge.

The appearance of the cervix is essential to the differential diagnosis, but excluding the cervix as a source of the inflammatory exudate is difficult. It is often valuable to use two separate cotton swabs to obtain different specimens, one from the middle third of the vaginal wall, directly (*ie*, not from the pooled secretions in the lower blade of the speculum) and one from the cervical os. If the pH of the vaginal-swab sample is normal or nearly normal and if it contains significantly fewer PMN per HPF than does either the cervical-swab sample or the pooled-secretion sample, then purulent vaginitis is unlikely.

Table 1. Differential diagnosis: purulent vaginal discharge

Purulent vaginitis
Trichomoniasis
Foreign body
Desquamative inflammatory vaginitis
Erosive lichen planus
Bacterial vaginitis
Group A *Streptococcus*
Atrophic vaginitis and secondary infection
Group B *Streptococcus* (?)
Rectovaginal fistula
HIV-related ulcer
Pemphigus
Pemphigoid
Linear immunoglobulin A disease
Graft-versus-host disease
Chemical etiology
Idiopathic etiology
Cervicitis
Mucopurulent cervicitis
Neisseria gonorrhoeae
Chlamydia trachomatis
Herpes simplex virus
Cytomegalovirus
Idiopathic etiology
Inflammatory ectropion (?)
Endometritis

Microscopic Examination

If the patient has purulent vaginitis and an elevated vaginal pH level, saline microscopy is the next step to take. Once an increased number of inflammatory cells has been established, the investigator should look for mononuclear inflammatory cells, because their presence suggests both chronicity and a non-bacterial cause, particularly erosive lichen planus (ELP) or immune-mediated inflammation. An increase in parabasal cells suggests estrogen deficiency or an exfoliative inflammatory process typical of DIV [3••].

Perhaps the most critical finding pertains to an element that is often overlooked, likely because of regrettable ignorance; it is vital to evaluate the resident vaginal flora by saline microscopy or Gram stain. The presence of a large number of lactobacilli (morphotype) usually excludes diffuse vaginitis; thus, the presence of *Lactobacillus* is a sensitive marker of good vaginal health.

Regardless of whether the cause of the patient's purulent vaginitis is immunologic or infectious, her flora is rarely normal, typically demonstrating large numbers of gram-positive cocci, gram-negative rods, or various combinations of these organisms. The most common observation is mixed flora; the bacterial culture of vaginal

Table 2. Investigation of patient with purulent vaginal discharge

Obtain a comprehensive history
Perform wet mount to assess increased PMNs, elevated pH level
Perform culture to exclude *Trichomonas* vaginitis
Differentiate purulent vaginitis from purulent (mucopurulent) cervicitis
Assess appearance of cervix/discharge
Assess cervix
Perform culture/DNA probe of cervix for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Herpes simplex virus
Use two-swab technique for pH level, white blood-cell count
Assess appearance of vaginal epithelial surface
Perform saline microscopy
Compare polymorphonuclear and mononuclear cell
Assess parabasal cells
Assess bacterial flora
Obtain gram stain of vaginal secretions
Perform selective bacterial cultures
(Perform colposcopy)
Selectively perform vaginal biopsy
Perform specific studies, as needed
Rectovaginal fistula (gastrografin enema, etc.)
Initiate trial of therapy
Clindamycin (2% vaginal cream)
Hydrocortisone (10% vaginal cream)
Systemic anti-inflammatory agents, steroids
Antibiotic therapy

secretions inevitably reveals multiple species. Moreover, the significance of these isolates is entirely unclear, and usually leads to the prescription of unnecessary antibiotics, which further alter vaginal flora and predispose the patient to superimposed *Candida* vaginitis.

Bacterial Vaginitis?

In bacterial vaginosis a causal relationship has been established between abnormal bacterial flora and clinical disease. In contrast, no such relationship is evident in purulent vaginitis, with rare exception.

Group A *Streptococcus* (*Streptococcus pyogenes*) is a proven cause of acute purulent vaginitis, which is usually seen in young women, frequently mothers of children with streptococcal pharyngitis or proctitis [4]. Patients present with a copious purulent discharge, frequent vulvovestibulitis, and diffuse inflammation of the vagina. The Gram stain of the high-pH vaginal secretions reveals sheets of gram-positive cocci. A prompt response to conventional oral penicillin therapy can be anticipated. Overgrowth of gram-negative anaerobes, such as *Prevotella* and *Bacteroides* species, often indicates an unrecognized foreign body or rectovaginal fistula.

The vagina is never sterile; inevitably, the vaginal culture of any patient with purulent vaginitis shows various species of microorganisms. Even if a single species or pure cultures of large numbers of the microorganism were reported, this would in no way establish a cause-effect relationship. We know considerably less about the bacterial pathogens responsible for vaginal disease than we do about those responsible for gastrointestinal-tract disease. We have virtually no information, from studies of premenopausal women, about enterococcal vaginitis or vaginitis caused, for example, by *Pseudomonas* species, *Escherichia coli*, or *Klebsiella* species.

In this context, no single species is more controversial than Group B *Streptococcus* (GBS; *Streptococcus agalactiae*), which is found in the vagina of 15% to 20% of symptomatic, healthy, non-pregnant women. Numerous case reports have described a causal relationship between *S. agalactiae* and sporadic purulent vaginitis [5]; description of the resolution of signs and symptoms of vaginitis following penicillin therapy has even been reported [6]. Unfortunately, virtually all of these reports lack one or more components of evidence necessary to fulfill all of Koch's postulates to prove a cause-effect relationship.

Therefore, even though Sobel [3••] reported the presence of *S. agalactiae* in 60% to 70% of postmenopausal women with DIV and a prompt response to clindamycin (three times higher than the predicted rate), no control studies or patients were included in the report [3••]. DIV has been shown not to respond to metronidazole therapy, and GBS is resistant to metronidazole and sensitive to clindamycin. Nevertheless the equation is complicated by the fact that clindamycin is not only antibacterial—active against gram-positive cocci, gram-positive bacilli, and anaerobic gram-negative rods—but was recently shown to have potent anti-inflammatory properties, blocking the effects of the pro-inflammatory cytokines tumor necrosis factor-α and interleukin-1β [7•]. Thus, proof that GBS causes purulent vaginitis remains inconclusive.

Given the current epidemic of the general abuse of antibiotics in the treatment of vaginitis, we must be cautious before concluding that the detection of microorganisms commonly found in the vagina—even in symptomatic women and in high numbers—necessitates antimicrobial therapy. Clearly, additional data are necessary in such cases and, even in women with idiopathic vaginitis, the results of bacterial cultures should interpreted together with Gram-stain results.

Although frequently reported in the literature, atrophic vaginitis with secondary bacterial infection is poorly described. Most women with atrophic vaginitis are asymptomatic or complain only of vaginal dryness.; even when the atrophy is severe—as it is in many elderly women—atrophic vaginitis remains asymptomatic in the absence of vaginal sexual activity. In the latter scenario, in which patients complain of severe dyspareunia and vaginal dryness, secondary bacterial infections are rare.

More advanced atrophic vaginitis is associated with a high level of pH, a moderate increase in PMNs, and the finding of few squamous cells, mostly basal and parabasal

cells and scant mixed flora (not lactobacilli). Rarely is a profuse purulent discharge apparent. Moreover, the usual macroscopic findings in these symptomatic cases are severe atrophy with marked thinning of the vaginal walls and vestibule. Thus, the distinction and recognition of atrophic vaginitis is not difficult.

In the rare cases of atrophic vaginitis and true bacterial secondary infection, Gram stain reveals large numbers of gram-negative rods, usually coliforms. Finally, the cardinal characteristic of atrophic vaginitis—with or without secondary bacterial infection—is rapid response to topical, locally applied, estrogen analogues. The issue of estrogen deficiency contributing to, but not wholly responsible for, purulent vaginitis in postmenopausal women deserves attention and often mandates a trial of topical estrogen therapy in these cases.

Colposcopy and Histopathology

In this investigator's opinion, colposcopy—vulvar or cervical—has little, if any, role in the differential diagnosis of purulent vaginitis. Similarly, cervical biopsy has little to contribute.

On the other hand, in the investigation of vaginal lesions, especially localized or focal ones, vaginal biopsy can be used to diagnose pemphigus, pemphigoid, cicatrical pemphigus, or ELP of the vagina or vestibule. Each of these conditions requires specific anti-inflammatory therapy with topical or systemic steroids and immunosuppressive therapy.

Further Diagnostic Considerations

ELP of the vagina is easily diagnosed in the presence of dermatologic and oral lesions of lichen planus, or—when merited by erosive vestibular changes—by biopsy [8]. When clinical manifestations are confined to the vagina, diagnosis is often delayed, but this entity is increasingly recognized [9,10]. Differentiation from DIV may be difficult, in the absence of specific diagnostic testing [11,12].

Both conditions present with a purulent vaginal discharge, pain and dyspareunia, elevated pH, increased inflammatory cells, and abnormal flora on saline microscopy. Subtle differences between DIV and ELP do exist. DIV is characterized by the presence of an increased number of parabasal cells and polymorphonuclear cells, as well as a more consistent finding of gram-positive cocci. In contrast, ELP is characterized by fewer parabasal cells, a greater number of mononuclear cells, and a more variable bacterial flora.

Vaginal biopsy and histopathological findings may be helpful in differentiation, but few data about this have been published. Whereas DIV presents as a diffuse vaginitis, often with a rash, ELP is more likely to present as localized disease, with a distinct border or demarcation between normal and eroded vaginal areas.

Therapy

Therapy should be directed at the specific etiologic mechanism. Vaginal 2% clindamycin has been reported to be extremely valuable against DIV; however, no prospective randomized control studies have been performed, and published information is minimal [3••]. The optimal duration of clindamycin therapy is unknown, but the typical initial course of therapy is 14 days, which is often sufficient to achieve a cure. However, approximately one third of patients relapse and require a repeat course, as well as a maintenance regimen of suppressive clindamycin [3••].

To date, no other antimicrobial regimen has shown comparable results. Repeated relapse on cessation of clindamycin or an incomplete response to this regimen justifies a change to topical corticosteroid therapy and may identify a subgroup of patients in whom the etiology is not microbial.

ELP usually responds to topical hydrocortisone acetate therapy (one 25-mg suppository, daily), but a higher-dose regimen of hydrocortisone (best administered as 100 mg/gm vaginal cream; one 5-g application, nightly) is frequently required,. Prolonged vaginal steroid therapy is necessary, and care must be exercised to avoid the formation of vaginal synechiae and obliteration of the vagina.

Not infrequently, distinguishing between DIV and ELP is difficult, and the patient's response to clindamycin or cortisone may establish the final diagnosis. If a high-dose topical-steroid regimen fails to control vaginal ELP, the clinician should be aware that treatments using other topical immunosuppressives (*ie*, tacrolimus and cyclosporine) [13,14] and systemic thalidomide [15] have been reported to be successful. Topical and systemic steroids are necessary for the treatment of pemphigoid vaginal involvement [16].

Conclusions

Most cases of frankly purulent vaginal discharge are due to trichomoniasis or cervicitis; however, nontrichomonal vaginitis and purulent exudate are increasingly common. Despite its increasing incidence, purulent vaginitis remains poorly defined and largely ignored; thus, numerous empirical therapies are used in these cases.

The intent of the step-by-step approach to the diagnosis and clinical management of nontrichomonal purulent vaginitis presented here is to provide the clinician with practical guidelines based on a review of the currently available knowledge.

Particularly considering the potential for the prescription of unnecessary antibiotics, further research into all aspects of nontrichomonal purulent vaginitis is vital to both clinicians and their patients.

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