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Review article

Infectious disorders of the vulva

Somaye Y. Zare*

Department of Pathology, University of California San Diego, La Jolla, CA, USA

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ABSTRACT

The vulva can be affected by a variety of sexually transmitted infections as well as other common infections that are not typically related to sexual transmission. Vulvar infections may adversely affect the quality of life of the patients by causing discomfort and pain. Some of these infections, especially the ulcerative ones, may also increase the risk of transmission of other infectious diseases, including HIV. Due to the recently increasing number of sexually transmitted infections and atypical presentations of these infections in immunocompromised patients, it is important for pathologists to be familiar with histopathologic features of the infectious diseases of the vulva, so that accurate diagnoses can be rendered as promptly as possible. This review discusses the clinicopathologic presentations of the non-HPV related infections of the vulva.

Introduction

A multitude of bacterial, viral, fungal, and parasitic organisms can infect vulva that are commonly, but not exclusively, transmitted by sexual contact. Some of these infections, such as Candida vulvitis, are extremely common and usually do not cause serious complications, whereas others such as human papilloma virus (HPV) can result in precancerous lesion. Sexually transmitted infections (STI) are a global public health issue, and in the recent years the Centers for Disease Control and Prevention (CDC) has reported an increasing numbers of STIs. Many of these infections present with vulvar ulcerations, which may increase the risk of HIV transmission and acquisition of other STIs. A summary of clinicopathological characteristics of the common ulcerative STIs of the vulva are reviewed in Table 1.

Infections of the vulva are commonly diagnosed clinically and by laboratory tests such as serology, antigen detection methods, microbiology culture, and increasingly nucleic acid amplification methods such as polymerase chain reaction (PCR). Tissue biopsies are uncommonly performed for confirmation of diagnosis. However, in some instances, especially those with atypical clinical presentations, cases that are refractory to treatment, or less common conditions, tissue biopsies have an important diagnostic role.

Viral infections

Herpes simplex virus

Clinical features. Genital herpes is caused by the human *herpes simplex virus* (HSV), a double-stranded DNA virus that belongs to Herpesviridae family. HSV is the most common infections cause of genital ulcers in the United States.[1] The virus has two different types, HSV-1 and HSV-2, and both can result in genital herpes. HSV-2 is the main cause of genital herpes; although, increasing numbers of cases that are caused by HSV-1 have been reported.[2, 3] Peak transmission of the virus is through direct contact with ulcers or exposure to mucosal secretions during periods of viral shedding. Although the active herpetic lesions are more contagious, the infection can be acquired when lesions are not identified clinically.[4, 5] Vertical transmission of HSV from mother to baby during pregnancy is uncommon and most cases are acquired at the time of passing through birth canal. Therefore, in the presence of active lesions, a cesarean section is indicated. If new HSV infection is acquired late in pregnancy, there is a high risk of transmission to the newborn.[6] HSV infection is very common among human immunodeficiency virus (HIV) infected patients, with reported frequencies that range from 50% to 90%, depending on the specific populations. Furthermore, similar to other ulcerative genital disease, patients with HSV infection are at higher risk of HIV infection.[7]

In primary herpes, the vulva is red and edematous with numerous vesicles. The vesicles then rupture and result in painful ulcers, which heal without leaving any substantial scarring. The virus remains latent in the sacral ganglion for the life of the host. Periodically, the virus reactivates, manifesting as mucocutaneous lesions.[8] HSV-1 infections recur 1 to 2 times a year, compared with HSV-2 infections, which cause 4 to 6 episodes of recurrence per year.[3, 6] Immunodeficient individuals have a higher risk for extensive and recurrent lesions, and atypical

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* Corresponding author.
E-mail address: syekezare@health.ucsd.edu.

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Table 1
Clinicopathologic features of common ulcerative sexually transmitted infections of the vulva.

Disease	Etiology	Characteristics of the ulcers	Regional adenopathy	Histology of vulvar lesions	Diagnosis/Ancillary methods
Herpes Simplex Virus	HSV-1 and HSV-2	Painful multiple small vesicles that evolves into ulcers	Occasional tender adenopathy	Ballooning degeneration of keratinocytes and epidermal vesicles. "3 Ms": multinucleation, molding, and margination of chromatin.	Detection of viral DNA by PCR or viral culture
Primary Syphilis/ Chancre	*Treponema pallidum*	Painless usually single non-purulent ulcer with well-defined elevated borders	Non-tender adenopathy	Endothelial swelling and proliferation with dense lympho-plasmocytic inflammation. Endarteritis obliterans may be present.	Dark field microscopy, serologic testing, PCR. Silver stain or immunohistochemistry of fixed tissue
Chancroid	*Haemophilus ducreyi*	Painful coalescent purulent ulcers with ragged poorly-defined borders	Tender, usually unilateral adenopathy, may suppurate	Ulcer with fibrino-purulent material, lympho-plasmocytic inflammation and granulation tissue. "School of fish" refers to the parallel chains of bacteria seen on cytology.	Culture of lesions. Giemsa or Gram stain detects the bacteria.
Granuloma inguinale	Klebsiella granulomatis	Painless usually single hypervascular ulcer with elevated borders and a friable bleeding base	None. Pseudobuboes may be present	Pseudoepitheliomatous hyperplasia, granulation tissue with prominent vascularization and dense mixed inflammatory cell infiltrate	Warthin–Starry or Giemsa stains depict Donovan bodies
Lymphogranuloma venereum	*Chlamydia trachomatis* (serotype L1–3)	Painless papule becoming an ulcer, that usually goes unnoticed	Tender usually bilateral adenopathy, may suppurate	Lympho-plasmocytic infiltrate, small foci of necrosis, and granulation tissue. Lymph nodes reveal stellate abscesses surrounded by epithelioid cells and histiocytes	Culture, direct immunofluorescence, or nucleic acid detection

presentations, including persistent ulcers and verrucous lesions, are more common in this population.[6, 7] A less common presentation of HSV infection in immunocompromised patients, known as "knife-cut sign", appears as linear ulcers and fissures in intertriginous areas, such as vulva and folds in inguinal region.[9]

Pathologic features. Genital herpes lesions initially present with vesicles followed by ulceration. The keratinocytes in epithelium demonstrates ballooning degeneration resulting in intraepidermal and subepidermal vesicles. The keratinocytes show ground-glass appearance of the nuclei with peripheral condensation of chromatin. Multinucleated cells with nuclear inclusions and nuclear "molding" can be identified at the viable interface of the ulcer. Mixed inflammation and leukocytoclastic vasculitis may be present in the dermis. Vesicles then rupture and cause epithelial ulceration with crust formation.[10] On histologic sections, exophytic masses of genital area that are an atypical manifestation of the virus in immunocompromised patients, demonstrate pseudoepitheliomatous hyperplasia and can potentially mimic cancer.[11] On cytology smears, the classic "3 Ms": multinucleation, molding, and margination of chromatin are the cytopathic effects associated with HSV. Eosinophilic intranuclear inclusions surrounded with a clear halo (Cowdry A) are variably present (Fig. 1) .[12]

Molluscum contagiosum

Clinical background. Molluscum contagiosum is a viral infection caused by *Molluscum contagiosum virus* (MCV), a double-stranded DNA virus of the Poxviridae group of viruses. Four genotypes of MCV exist; type 1 is the most common type that cause infection in healthy humans and type 2 has been reported to be more common in HIV infected patients.[13] Transmission is through direct contact with an infected individual. In healthy young adults, the virus is often transmitted sexually and lesions appear in the genital area; however, casual contact or self-inoculation may be the method of transmission in some cases. Among HIV positive patients, MCV infection is more common compared to the general population, and may present with widespread lesions.[14-15] The lesions primarily affect skin and follicular epithelium, manifesting as flesh-colored, raised, umbilicated papules or nodules. Diagnosis is usually made clinically by recognizing the characteristic lesions in most cases. Atypical presentations such as giant lesions (>1 cm), verrucous papules, or clusters of numerous small papules may be seen in immunocompromised patients.[15, 16]

Pathologic features. On histologic sections, the molluscum lesions are characterized by lobulated epithelial hyperplasia of the epithelium with cup shaped configuration. The lesion is composed of multiple layers of proliferated squamous epithelium which mature toward the center, shed keratin debris and produce the characteristic white-yellow core. The typical eosinophilic intracytoplasmic inclusions (molluscum bodies or Henderson-Patterson bodies) are due to virus replication in the cytoplasm that appear several layers above the basal layer. As these inclusions enlarge, they compress the nucleus to the periphery of the infected cell and become basophilic (Fig. 2) .[17] The surrounding dermis is relatively unremarkable with little or no inflammatory reaction; unless the lesion ruptures in dermis and triggers an inflammatory response.

Epstein-Barr virus

Primary *Epstein-Barr virus* (EBV) infection of the vulva is a rare a cause of genital ulceration, known as Lipschütz's ulcer. This infection is a non-sexually transmitted disease and primarily affects adolescent females.[18] The lesions usually manifest as one or multiple painful ulcers involving labia minora, with purple-red irregular edges and clean or fibrinous base. Lymphadenopathy distant from the site of ulceration is common. Preceding fatigue, headache, and low-grade fever are common and most patients develop clinical symptoms of

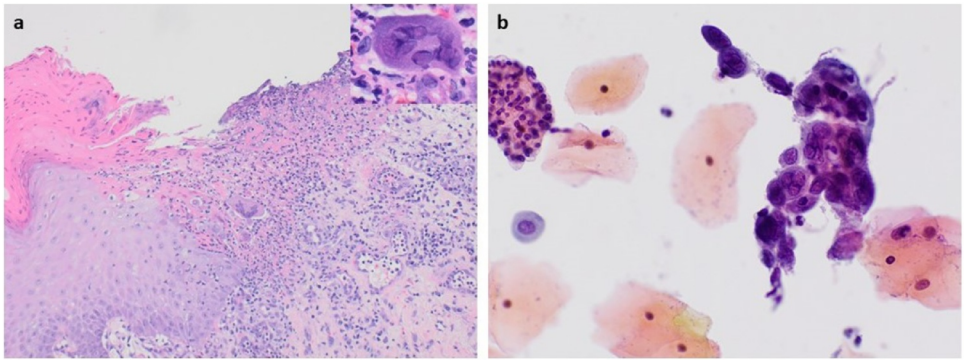

Fig. 1. Herpes simplex virus infection. (a) Epithelial ulceration with multinucleated keratinocytes. Characteristic intranuclear Cowdry A type inclusions (inset). (b) Papanicolaou-stained smear portrays keratinocytes with the classic "3 Ms" herpes cytopathic effect and ground glass chromatin.

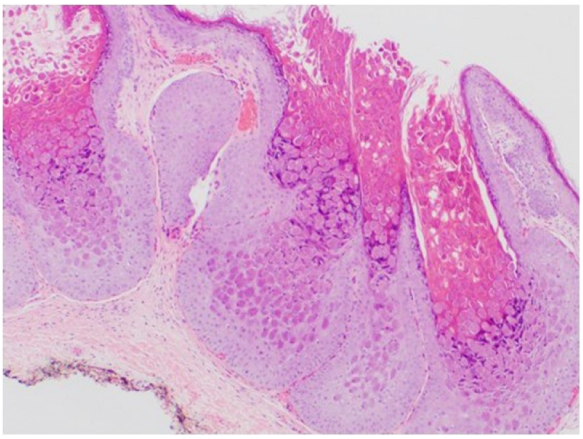

Fig. 2. Molluscum contagiosum lesions are show lobulated, crater shaped hyperplasia of the epithelium and characteristic inclusions of Molluscum contagiosum virus. The eosinophilic intracytoplasmic inclusions (Henderson-Patterson bodies) displace the nucleus to the periphery.

mononucleosis.[19]

Diagnosis is mainly clinical and is made based on ruling out other causes of genital ulcers. The diagnosis can be confirmed by detecting EBV-DNA by PCR on vulvar swabs or serologic tests showing acute EBV infection. The histologic findings are nonspecific and include epithelial ulceration with underlying vasculitis and extensive mixed inflammation in the dermis. This condition is self-limiting and ulcers usually heal without leaving a scar within 2 to 6 weeks.[18]

Varicella zoster

Varicella zoster virus (VZV) is double-stranded DNA from the Herpesviridae family. Chicken pox is the primary form of VZV infection, a self-limited childhood disease that presents with fever and disseminated vesicular rashes. The virus then establishes a dormant state in nerve ganglia after primary infection and shingles or herpes zoster is triggered by reactivation of latent VZV.[20] Isolated herpes zoster of the vulva is a rare cause of genital ulcers.[21, 22] A prodrome of pain or burning sensation is common. Lesions present as clusters of painful vesicles, pustules, and erosions in a dermatomal distribution. The lesions may be confused with genital herpes, but VZV ulcers do not recur in the same site and show dermatomal distribution which does not cross the midline. Post-herpetic neuralgia, is a common complication of VZV and should be considered in patients with vulvodynia.[23] The diagnosis can be made by detection of VZV from the lesions by applying viral culture, PCR, or direct Immunofluorescence assays (DFA). Biopsy samples are rarely taken which histologically are similar to HSV infection. On histologic sections, VZV and HSV be can be differentiated by immunohistochemical staining.[23]

Cytomegalovirus

Cytomegalovirus (CMV) is a member of Herpesviridae family that affects most of the world population. Symptomatic CMV infections of female genital tract are very rare. Few cases of anogenital ulcers and erosions caused by CMV have been reported in both healthy and immunodeficient patients.[24, 25] On histologic sections, characteristic viral cytopathic changes of enlarged cells with large eosinophilic nuclear inclusions surrounded by a clear halo (owl's eye) and intracytoplasmic granulations are diagnostic of CMV (Fig. 3). Immunohistochemical staining can be used for confirmation. CMV inclusions are mainly found in epithelial cells as well as in endothelial and mesenchymal cells of the vulva and cervix.[25]

Bacterial infections

Syphilis

Clinical background. Syphilis is a sexually transmitted infectious disease caused by spirochete *Treponema pallidum*. The incidence of syphilis decreased after penicillin became available; however, a recent increase in the number of cases have been reported worldwide.[26] The rate of infection varies in different populations and is more common among people with limited access to health care as well as individuals with high risk sexual behavior. *T. pallidum* transmission is through contact with secretions of infected individual, primarily by sexual contact followed by transmission from infected mother to child.[26] Clinical presentations of syphilis, if untreated, are divisible into 4 stages: primary, secondary, latent, and tertiary; each with different clinical manifestations. Syphilis is acquired by direct penetration of *T. pallidum*

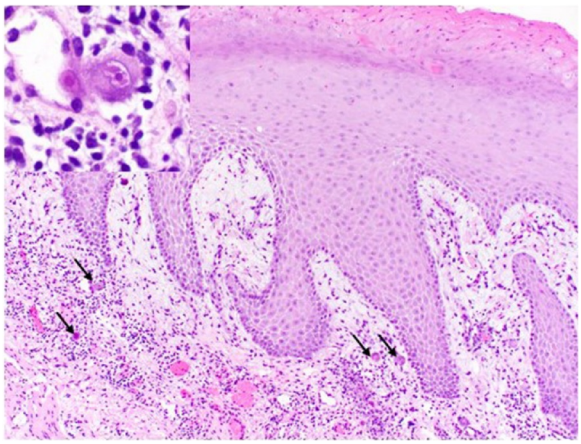

Fig. 3. Cytomegalovirus infection of the vulva in an immunosuppressed patient showing epidermal hyperplasia, hyperkeratosis, and acanthosis. Scattered interstitial and endothelial cells show CMV inclusions (arrow). Endothelial cell with typical "owl's eye" inclusions (insert).

to the mucosa or skin during sexual contact.[27] The initial manifestation of the disease in primary stage is a single chancre that occurs after 10 to 90 days at the site of exposure. The chancre is a painless lesion that typically becomes indurated and progresses to a non-purulent ulcer which heals spontaneously within 4 to 6 weeks. In women, primary lesions are most often limited to the vulva and commonly accompanied by painless regional lymphadenopathy.[28, 29]

If untreated, syphilis will progress to a secondary stage. *T. pallidum* disseminates throughout the body by hematogenous spread and may involve any organ. Presentation is heterogeneous but disseminated mucocutaneous rashes are common. Secondary stage genital lesions are more common in women and range from macules and ulcerations to condylomata lata.[28] In untreated patients, the lesions resolve over several weeks and the infection enters an asymptomatic 'latent' stage. Latent phase is when the patient is clinically asymptomatic, but is seropositive. Almost one third of patients with latent infection develop tertiary syphilis. Clinical manifestations may present with cardiovascular syphilis, neurosyphilis, and involvement of the skin, bones, or viscera with gumma. Lesions of tertiary syphilis usually result is extensive scarring in the tissue.[30] Syphilis and HIV co-infection is common, and the two diseases have a synergistic effect on each other in several ways.[31]

Pathologic features. Most primary lesions are characterized by marked dermal mixed inflammation, perivascular lymphoplasmacytic infiltration, and epidermal hyperplasia. Vessels show prominent endothelial swelling and proliferation that can result in endarteritis obliterans and subsequent ulceration.[29, 32] A variety of histologic findings are associated with secondary syphilis. The epidermis shows changes such as parakeratosis, acanthosis, and psoriasiform epidermal hyperplasia. Most cases demonstrate endarteritis, endothelial swelling, and interstitial and perivascular mixed inflammatory infiltrate in the dermis that is mainly composed of lymphocytes, plasma cells, macrophages, and some neutrophils (Fig. 4). .[32, 33] Condylomata lata show pronounced epithelial hyperplasia with parakeratosis, elongated rete ridges, and perivascular lymphoplasmacytic inflammation.[34] Tertiary syphilis lesions are mostly granulomatous, often accompanied by dense lymphocytic and plasma cell infiltration of the dermis and endarteritis obliterans.[34] Spirochetes can be visualized by using Warthin-Starry stain or immunohistochemical studies, highlighting the organism within and around dermis vessels and in the dermal-epidermal junction in primary and secondary stage lesions, and less commonly tertiary lesions. Non-treponemal spirochetes can cause false positive results on the stains.[35]

The biopsy findings in syphilis are not specific and histologic features can mimic any forms of dermatitis. Therefore, performing immunohistochemical or spirochete stains and correlation with serologic testing is required for confirmation. The differential diagnosis for vulvar lesions with a significant plasmacytic component include Zoon vulvitis (plasmacytosis mucosae), a rare chronic inflammatory disease of unknown origin that demonstrates a band-like, dense mucosal infiltration of plasma cells admixed with lymphocytes and dilated dermal vessels.[10] The absence of pronounced superficial and deep perivascular inflammation and vascular endothelial proliferation is helpful in differentiating these entities. In addition, as mentioned above, spirochete stains and correlation with serologic testing is helpful. Other conditions to consider in the differential diagnosis of early stages of syphilis include other ulcerative infectious disease of the vulva (Table 1).

Chancroid

Clinical background. Chancroid is a STI caused by a fastidious gram-negative coccobacillus called *Haemophilus ducreyi*. The prevalence of chancroid has declined in the United States, but is still common in developing countries. Clinically, the lesions present as groups of erythematous papules and pustules that rupture and form single or multiple small painful ulcers. The ulcers are tender, friable, and soft with ragged borders. They can be associated with tender, usually unilateral, inguinal lymphadenopathy. If untreated, lymph nodes become suppurative (buboes) with a fistula that drains exudate.[36, 37]

Pathologic findings. Microscopically the ulcers have three distinct zones. The surface of the ulcer shows necrosis intermixed with neutrophils, erythrocytes, and fibrin. Under the surface exudate, there is granulation tissue associated with degeneration and thrombosis of vessels. The

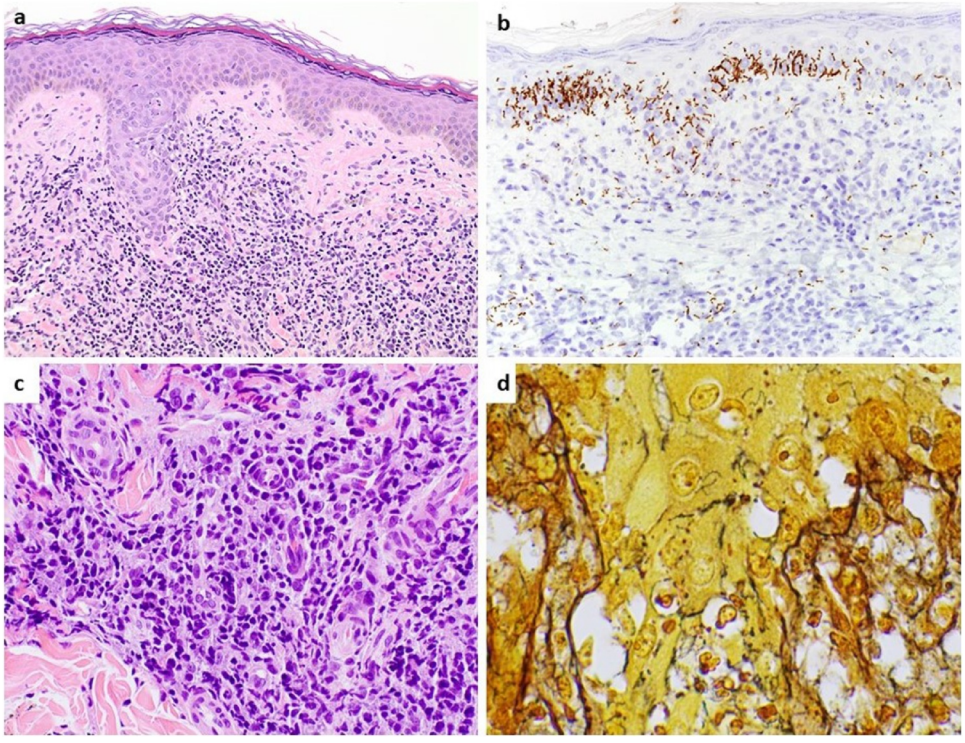

Fig. 4. Secondary syphilis: (a) Epidermis shows hyperplasia and acanthosis and dermis demonstrates lymphoplasmacytic infiltrate. (b) IHC stain for Treponema highlights spirochetes (courtesy of Dr. Brian Hinds). (c) Dermis demonstrates interstitial and perivascular lymphoplasmacytic infiltrate and vessels show endothelial swelling and proliferation. (d) Warthin–Starry stain highlights spirochetes.

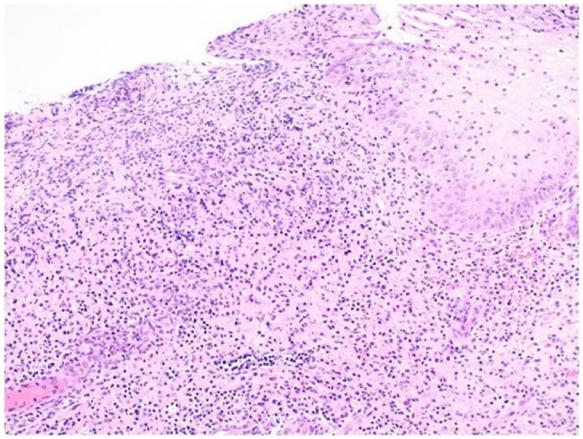

Fig. 5. Chancroid: (a) Findings are non-specific, showing ulcer with necro-inflammatory exudate and debris and underlying acute and chronic inflammation in dermis.

deepest zone is composed of dense lymphoplasmacytic infiltrate in the dermis (Fig. 5). Giemsa or gram stains are not reliable, rarely may identify the bacteria at the surface of the lesion.[36, 38]

Granuloma inguinale (Donovanosis)

Clinical background. Granuloma inguinale (also called donovanosis) is caused by *Klebsiella granulomatis* (also known as *Calymmatobacterium granulomatis*), an intracellular gram-negative bacillus.[39] The disease presents as papules or nodules that form painless ulcers on the vulva, vagina, or cervix. The ulcers have a beefy red appearance with rolled borders, and a friable base that bleeds easily. Regional inguinal adenopathy is usually associated with superimposed infections. The lesions can expand and cause disfiguration of the genitalia in severe cases.[36, 38]

Pathologic findings. These lesions are charcaterized by an ulcer with an exuberant necro-inflammatory exudate and underlying granulation tissue with prominent vascularization and dense mixed inflammatory cell infiltrate. The epidermis at the edge of biopsy may show pseudoepitheliomatous hyperplasia. The macrophages have cytoplasmic vacuoles that contain the organisms (Donovan bodies). Warthin–Starry or Giemsa stains can identify the organisms in histiocytes or extracellularly.[36, 38, 40]

Lymphogranuloma venereum

Clinical background. Lymphogranuloma venereum (LGV) or lymphogranuloma inguinale is caused by the serotypes L1, L2 and L3 of *Chlamydia trachomatis*, an obligatory intracellular gram-negative bacterium.[41] This sexually transmitted disease is more common in men and has a triphasic clinical presentation. The primary infection usually manifests with self-limiting small genital ulcers at the site of exposure that frequently goes unnoticed. The secondary stage presents with tender regional lymphadenopathy that is commonly unilateral and can cause the classic “groove sign” due to involvement of nodes along the inguinal ligament. The third phase is more common in women, consists of chronic pelvic lymphangitis with fibrosis and stricture of the genital tract and deep tissue abscess formation.[41-43]

Pathologic findings. The ulcers are rarely biopsied, demonstrating mixed lymphoplasmacytic infiltrate and granulomatous inflammation, with underlying granulation tissue. The involved lymph nodes develop stellate abscesses surrounded by granulomatous and chronic inflammation. In later lesions, tissue shows variable fibrosis.[36, 43]

Folliculitis and other bacterial infections of skin and soft tissue

Folliculitis is a common condition affecting the hair bearing skin of the vulva. The hair follicle can become inflamed due to trauma caused by removing hair or chemical irritation. The most common pathogen associated with folliculitis is *Staphylococcus aureus*.[44] Other less common pathogens include *Pseudomonas aeruginosa* (hot tub folliculitis), *Malassezia,* and dermatophytes.[45, 46] The clinical and histologic appearance are similar to folliculitis from other body sites, presenting with papules, pustules, and granulomatous inflammation (Fig. 6). Exfoliative toxins of *S. aureus* can result in formation of vesicles and blisters in genital area.[44]

Vulvar cellulitis is bacterial infection of the dermis, most commonly caused by Streptococci group A and *S. aureus*. Vulvar cellulitis affects high risk individuals including women with diabetes mellitus, obesity, pregnancy; presenting with fever, malaise, chills and nausea. Vulvar abscesses often occur as a result of progression of skin and hair follicle infections. These infections are mostly polymicrobial and Methicillin-resistant *Staphylococcus aureus* (MRSA) is the most common pathogen, that has been isolated in the majority of cultures from vulvar abscesses.[44-47] Necrotizing fasciitis (or Fournier's gangrene) is a life-threatening progression of vulvar cellulitis that causes extensive necrosis of the subcutaneous tissue and underlying fascia. Histopathologic examination can show acute suppurative inflammation, abscess formation, and extensive necrosis of the fascia, with vasculitis and microvascular thrombosis (Fig. 6) .[48, 49]

Periclitoral abscess is a rare condition and most reported cases have occurred after local procedures or female circumcision.[50-52] Spontaneous periclitoral abscess formation without any previous surgery has also been reported. Due to rarity of this condition, association with specific pathogens is unknown.[51] Histologic findings are non-specific, showing various degrees of acute inflammation, abscess formation and granulomatous inflammation.

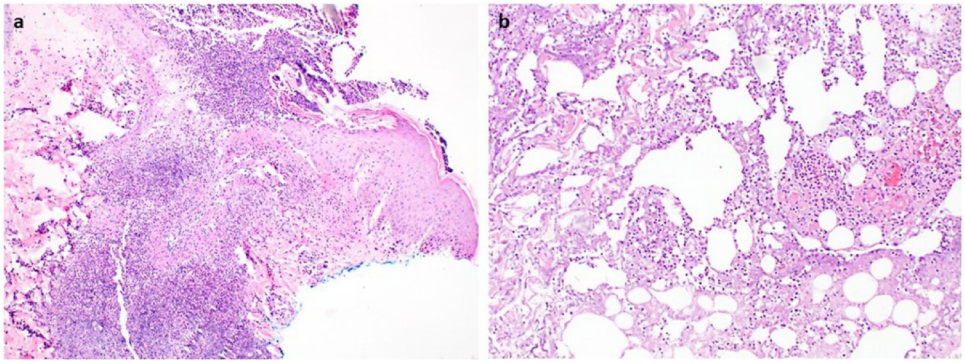

Fig. 6. Folliculitis: (a) Mixed acute and chronic inflammation surrounding hair follicle and associated epidermal ulceration. (b) Necrotizing fasciitis: sections show extensive necrosis, acute inflammation, and abscess formation that involves subcutaneous tissue, as well as vasculitis, and microvascular thrombosis.

Fungal infections

Candida

Clinical background. Vulvovaginal Candidiasis (VC) is a common infection of female genital tract. Vulvar infection in the absence of vaginal involvement is rare. *Candida albicans* which is an opportunistic yeast and a part of gastrointestinal tract and mucosal flora, is responsible for up to 90% of VCs.[53] The cases that are caused by non-albicans such as *C. glabrata, C. tropicalis* and *C. lipolytica* can be more resistant to common treatments. In North America, up to 75% of women experience VVC at least once during their lives and nearly 5–8% of women of reproductive age have recurrent vulvovaginal candidiasis.[54] *Candida* spp. are commensal organisms that can be part of normal mucosal flora. Approximately 20–30% of asymptomatic women are carriers of candida in their lower genital tract. Predisposing factors for VC include pregnancy, diabetes mellitus, immunosuppression (e.g. HIV disease), steroid use and broad-spectrum antibiotic use.[54, 55] The most common clinical presentation is intense vulvar pruritus, erythema, edema, and abnormal "cheese-like" or watery vaginal discharge.[54]

Pathologic features. Histologic examination of vulva may show epidermal hyperkeratosis or parakeratosis, spongiosis, acanthosis, and neutrophilic infiltration of squamous epithelium with subcorneal pustules (Fig. 7). The dermis is not affected in the majority of cases. Candida pseudohyphae and yeasts can be highlighted in the epidermis by silver stain or periodic acid–Schiff (PAS) .[10] The various species of *Candida* cannot be differentiated by light microscopy, the only exception is C. galbrata which is seen in yeast forms only and lacks pseudohyphae formation.[56] On cytology preparations, *Candida* organisms appear as eosinophilic yeast and pseudohyphae. Spearing of squamous cells, as if skewered by the pseudohyphae, is a frequent finding.[12] How frequently, or under what conditions histochemical studies for fungi should be performed in vulvar biopsies is not entirely clear. However, the presence of neutrophils infiltration of the epidermis and/or superficial microabscess within the surface keratinocytes, especially when accompanied by parakeratosis, should prompt a search for the organism and histochemical studies. In addition, in assessment of cases with eczematous dermatitis, psoriasiform dermatitis, intertriginous dermatitis, or lichen simplex chronicus, PAS or silver stain should be performed to exclude *Candida* infections.

Dermatophytosis

Tinea cruris (jock itch) is a superficial dermatophyte infection involving groin, pubic area, and rarely vulva. *Trichophyton rubrum* is the most common organism causing this infection. The infection is acquired by contact.[57] Clinical presentation is with pruritic, sharply demarcated rashes with erythematous scaly borders.[58] Microscopic features are usually non-specific, and include psoriasiform pattern epidermal hyperplasia, parakeratosis, spongiosis, subcorneal neutrophilic microabscess and fungal yeast and hyphae[10] (Fig. 8).

Deep dermatophytosis of the vulva is a rare infection, mainly caused by *T. mentagrophytes* and *Microsporum canis*. The infection usually involves individuals that use topical steroids. In deep dermatophytosis, the infection evolves into scaly and erythematous plaques in vulva. This condition may result in complications such as kerion or nodular granulomatous perifolliculitis (Majocchi's granuloma). Histologic sections show granulomatous perifolliculitis, or cellulitis and abscess formation with or without fungal hyphae.[59, 60]

Infestations

Pediculosis pubis

Pediculosis pubis or crab lice is caused by parasite *Phthirus pubis*. The disease is highly contagious and transmission is through intimate contact. Patients present with pruritus in pubic area. The crab louse is not a vector for systemic disease and commonly causes local symptoms by infesting pubic hair.[61] All patients with crab lice should be investigated for other STIs, because coinfection is common in this patient population.[62] On physical examination, lice or nits (eggs) are usually seen attached to hair shafts. Skin can show red papules at the site of lice bites. In established cases, blue macules (maculae ceruleae) due to deep dermal hemosiderin deposition may be identified. At the site of scratching, secondary superimposed infection may occur. The diagnosis is clinical and made by detecting the lice and nits attached to the hair shaft in genital area.[61, 63]

Scabies

Scabies is a skin infestation caused by a human mite, *Sarcoptes scabiei* var. *hominis*. The mode of transmission is usually by direct skin-to-skin contact, but can also occur by infested bedding or cloths. The mite burrows into skin and lives in the stratum corneum. The burrows can be identified in finger webs, wrists, and other skin folds such as genitalia. The most common complaint is of itchy rashes and papules in the involved area that is more intense at night. In cases with genital involvement, physical examination may reveal pruritic papular rashes or eczematous lesions can in genitalia. The diagnosis of scabies can sometimes be confirmed by microscopic examination. Mites, eggs, or fecal material may be identified in skin biopsy or preparations from scraping. Microscopic examination of skin usually demonstrates features of hypersensitivity dermatitis. Epidermis reveals parakeratosis, acanthosis, spongiosis as well as exocytosis and dermis shows superficial and deep perivascular inflammation, composed of lymphocytes, eosinophils, and histiocytes. (Fig. 9) .[63, 64] Crusted scabies (Norwegian scabies) sometimes involves vulvar region. It is a florid form of infestation that is usually seen in immunocompromised patients and presents with generalized hyperkeratotic lesions that could mimic psoriasis, drug eruptions, and eczemas.[64]

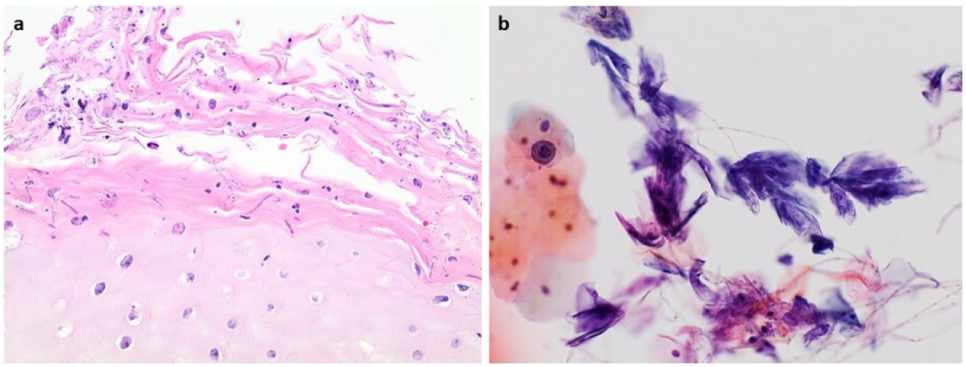

Fig. 7. Vulvovaginal candidiasis: (a) Epidermal spongiosis, mild dermal edema and neutrophilic exocytosis in epidermis. Candida organisms are readily identified on H&E stain. (b) Cervical pap smear shows Candida pseudohyphae (arrow) with spearing of squamous cells.

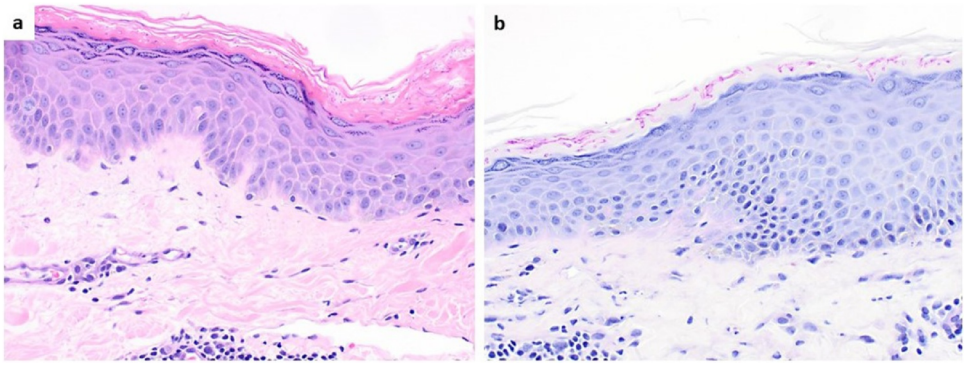

Fig. 8. Dermatophytosis: Epidermis demonstrated hyperkeratosis, parakeratosis. Keratin layer contains fugal organisms, seen on hematoxylin & eosin (a) and periodic acid-Schiff (b) stains.

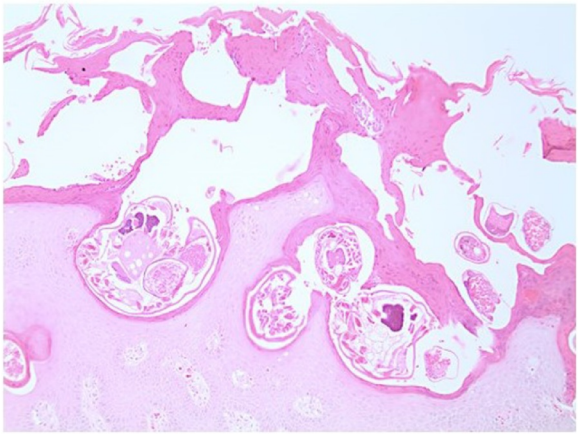

Fig. 9. Scabies: Hyperparakeratotic and acanthotic epidermis with scabies mites underneath stratum corneum.

Conclusion

A variety of bacterial, viral, fungal, and parasitic organisms can infect vulva. In biopsy samples, the histologic findings are similar across many pathogens, showing various degrees of mixed inflammation with or without ulceration, but some organisms have characteristic features that allow for their specific identification. In assessment of vulvar samples with features of dermatitis or ulceration, infectious causes should be considered in the differential diagnosis. In some cases the organisms or cytopathic effects that are specific to an organism can be detected on histologic sections and through histochemical or immunohistochemical staining, whereas correlation with laboratory tests and microbiology results are needed for confirmation of infections in many cases. Although anatomic pathologists uncommonly encounter biopsies for vulvar infections, it is important to be familiar with histopathologic features of these entities to avoid misdiagnosis of these rather common diseases.

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