Problems in Family Practice

Lesions of the Vulva

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Lesions of the vulva are common and are often associated with unnecessary and sometimes harmful delays in diagnosis and definitive therapy. Simple office biopsies, performed prior to treatment, permit histologic classification of the lesion and provide a basis for therapeutic recommendations.

A majority of patients having vulvar intraepithelial neoplasia are in their forties or fifties. Recently there appears to be an increase in the number of cases reported in patients of reproductive age, possibly resulting from an apparent predisposition among those who have had certain sexually transmitted diseases, other genital or extragenital neoplasias, or immunosuppressive therapy. Intraepithelial neoplasias of the vulva are commonly multifocal in origin, and although vulvar pruritus is the most common primary complaint, many patients are totally asymptomatic.

The patient who discovers a lesion on her vulva is likely to observe it for an indefinite period of time and to treat it with "home remedies." When her efforts have failed, she may then consult a physician. The primary care physician is likely to be the first to detect lesions of the vulva or to hear the patient's initial complaint regarding them. Unfortunately, studies have shown that there is frequently an unnecessary delay in correctly diagnosing and treating lesions of the vulva by the first physician to encounter them. These delays are probably the result of three factors: confusing terminology, nonspecific therapy, and reluctance to perform a biopsy of the lesion. The primary purpose of this article is to encourage all physicians to take a biopsy of every suspicious lesion of the vulva, and then, using the current histologic classification for vulvar neoplasia, to recommend a specific therapeutic approach.

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Biopsy

Neoplastic lesions of the vulva may be single or multiple, localized or diffuse, unilateral or bilateral. Some lesions may be more apparent than others. The toluidine blue test has proven helpful in the selection of areas to be biopsied.[1] A 1 percent aqueous solution of toluidine blue should be applied liberally to a clean area of the vulva and allowed to dry for several minutes. The area bearing the dye should then be decolorized by washing lightly with a 1 percent solution of acetic acid.

Since toluidine blue is a nuclear stain, it will be retained by surface tissues containing nuclear material. Normally the keratin layer of the epidermis does not contain nuclear material; however, since the keratin layer of neoplastic tissues may contain large amounts of nuclear material, it will retain the blue stain. Benign epithelial ulcerations and areas of benign parakeratosis may also remain blue. Selective biopsy of the areas that remain stained is indicated.

Biopsy procedures should be kept simple.

Usually these procedures can be performed without difficulty in an office setting.[2] Shaving the vulva or even the biopsy site is not necessary, though clipping a portion of the pubic hair with scissors may be helpful. An antiseptic solution should be used to cleanse the area. Subcutaneous injections of the biopsy site with a small amount of a local anesthetic solution (ie, 1 percent lidocaine hydrochloride, with or without epinephrine) using a 25-gauge needle usually provides satisfactory relief from pain.[3]

The Keyes dermatologic punch (4 mm diameter) is useful for obtaining biopsies of the vulva and is available as a disposable instrument. After the punch biopsy is taken, the skin edges should be approximated and hemostasis secured with one or two stitches of fine absorbable suture material.

Conventional incisional or excisional biopsies may be performed after a local anesthetic is administered. Incisional biopsies may be performed on any lesion; excisional biopsies are best reserved for isolated, small, and well-defined lesions. In excisional biopsies the incisions should be in normal skin 2 to 3 mm outside the margins of the lesion. In general, biopsies are best performed using a No. 15 scalpel blade. It should be held perpendicular to the skin's surface and used to circumscribe an ellipse of tissue three times as long as the ellipse is wide. The long axis of the ellipse should follow the natural lines of tension of the skin (Langer's lines). The tissue removed should include both epidermis and dermis. The skin edges may be approximated and hemostasis secured with fine absorbable suture material. Multiple, small, well-selected biopsies improve diagnostic accuracy.

Vulvar Dystrophy

Older classifications of the epithelial changes of the vulva are nonspecific and are of little prognostic value: They depend too much upon descriptions of clinical appearance and too little upon pathologic features, and they are burdened with dermatologic jargon.

In 1975 the International Society for the Study of Vulvar Diseases recommended an improved classification of the vulvar dystrophies.[4] Based upon histopathological findings, this classification describes three basic entities, two of which are subdivided according to the presence or absence of cellular atypia (Table 1).

Table 1. Classification of Vulvar Dystrophies

Hyperplastic dystrophy
Without atypia
With atypia
Lichen sclerosis
Mixed dystrophy (lichen sclerosis with foci of epithelial hyperplasia)
Without atypia
With atypia
From the International Society for the Study of Vulvar Diseases[4]

Lichen Sclerosis

Classically lichen sclerosis appears on its surface as pale, thin, wrinkled skin that has the consistency of parchment. It tends to involve the vulva, perineum, and perianal areas in a bilaterally symmetrical manner. Extreme atrophy of affected tissues causes them to lose their shape and to blend one with another. Shrinkage about the introitus causes dyspareunia. Fissures may develop about the posterior fourchette and anus. Subepithelial ecchymoses are not uncommon.[5]

Histopathologically lichen sclerosis is characterized by thinning of the squamous epithelium and flattening of the rete pegs. The dermis is a relatively acellular, homogenous layer with a chronic inflammatory infiltrate along its base.

Hyperplastic Dystrophy Without Atypia

Hyperplastic lesions may be found anywhere on the vulva, perineum, or about the perianal region. They vary tremendously in size, are often multiple, and may be bilateral. Since all of these lesions have hyperkeratosis and thickening of the epithelium, they often appear as slightly elevated white plaques. For that reason some hyperplastic lesions have been referred to as "leukoplakia." Color

alone cannot be used to diagnose hyperplastic lesions because there are those that are not so typically white.

Histopathologically hyperplastic dystrophy without atypia is characterized by thickening of the keratin layer (hyperkeratosis); thickening, lengthening, and blunting of the rete pegs; and an inflammatory infiltrate and edema within the dermis.[6] There is no cellular atypia. Such lesions are benign and without significant malignant potential.

Hyperplastic Dystrophy With Atypia

Gross appearance and location do not distinguish hyperplastic dystrophies without atypia from those with atypia.[6] Although increasing atypia is likely to be associated with a reddish-brown discoloration, this discoloration cannot be used as a basis for diagnosis. Biopsy is the only means of diagnosing vulvar dystrophy and determining the presence or absence of cellular atypia.

The basic histologic pattern of hyperplastic dystrophy without atypia and with atypia is similar, except that the atypical variety has an increased number of immature squamous cells. These cells have abnormal nuclei, increased mitotic activity, a discrepancy in their nuclear-cytoplasmic ratio, and a disorderly arrangement as a result of loss of polarity as they approach the surface. It is important to estimate the degree of atypia as mild, moderate, or severe. Increasing degrees of atypia are felt to be associated with an increase in malignant potential.

Mixed Dystrophy

Mixed dystrophy consists of areas of hyperplastic dystrophy as described above that usually exist within a field of lichen sclerosis. The areas of epithelial hyperplasia should be further characterized as "without atypia" or "with atypia."

The pathogenesis of the vulvar dystrophies remains unclear. Their gross appearance is the result of variations in the thickness of their epithelium and its keratin layer, the loss of skin pigment, and changes in superficial vascularity. In general, younger patients are more likely to have hyperplastic dystrophy and older patients are more likely to have lichen sclerosis.

The chief complaint of the majority of patients with vulvar dystrophy is pruritus. It is more severe with the hyperplastic dystrophies than it is with lichen sclerosis. Pruritus often initiates a vicious itch-scratch cycle, which leads to fissuring and excoriation. The lesions become increasingly symptomatic and may become infected. Dyspareunia is also a frequent complaint. Skin changes about the introitus may preclude intercourse.

Hygienic measures that keep the vulva clean and dry should be encouraged. Wearing underwear of 100 percent cotton and loose-fitting clothing will permit evaporation in this normally moist area. Strong soaps and deodorants should not be applied to the vulva. Vaginal infections should be treated, and the perianal area should be kept clean. The application of disposable compresses (eg, sanitary napkins) soaked in dilute (1:40) Burow's solution for 30 minutes three or four times a day offers symptomatic relief. Antibiotic ointments may benefit superficial infections.

Lichen sclerosis improves if treated with topical testosterone. It is recommended that the pharmacist prepare an ointment of 2 percent testosterone proprionate in white petrolatum, which should be massaged into the affected areas two or three times a day for at least three or four months. Patients should be warned that pruritus and burning may intensify soon after therapy is initiated, but that these reactions should subside with time. When pruritus has been eliminated, application of the ointment may be gradually decreased to once or twice weekly.

Hyperplastic dystrophy without atypia should be treated by application of a corticosteroid two or three times daily for four to six weeks. Suggested preparations include 0.01 percent fluocinolone acetonide, 1 percent hydrocortisone cream, or 0.1 percent triamcinolone. In general, once pruritus is controlled and scratching eliminated, hyperplastic lesions will regress. They may not, however, completely disappear.

Hyperplastic dystrophy with atypia of mild or moderate degree may be treated as hyperplastic dystrophy without atypia. Hyperplastic dystrophy with atypia of severe degree should be treated as if it were carcinoma in situ of the vulva. Since all vulvar dystrophies with atypia are considered as having some malignant potential, the

patient should have re-examinations at least every six months. Repeat biopsies may be necessary.

Carcinoma in Situ

Clinically squamous cell carcinoma in situ of the vulva is indistinguishable from the vulvar dystrophies and may appear as single or multiple, localized or diffuse, unilateral or bilateral lesions. Squamous cell carcinoma has greater variation in skin color in the area of the lesion,[7] and biopsy is essential for diagnosis.

Histologic sections of the epithelium in squamous cell carcinoma in situ reveal a full-thickness abnormality manifested by a loss of normal stratification and orientation of cells, nuclear atypia, and an increase in mitotic activity. Such abnormalities are, by definition, limited to the epithelium and do not affect the underlying dermis. Histologically there may be difficulty in differentiating hyperplastic dystrophy with severe atypia from carcinoma in situ. Therefore, some authors recommend grouping all of the hyperplastic dystrophies with atypia and squamous cell carcinoma in situ under the category of vulvar intraepithelial neoplasia (VIN).[8] This concept may be important in understanding the relationship of preinvasive and invasive squamous cell carcinoma of the vulva.[9,10]

Many therapeutic modalities have been recommended as treatment for squamous cell carcinoma in situ of the vulva. Wide excision of the lesions permits histological analysis of all lesions. If there is evidence of microinvasion, further surgery may be indicated. Lesser forms of therapy such as the application of topical chemotherapy (eg, 5-fluorouracil), cryotherapy, and laser therapy are best left to trained oncologists.

Paget's Disease

Paget's disease of the vulva is a distinct entity, both clinically and pathologically.[11] The skin lesions are usually well-defined, elevated white or reddish areas often with a scaly surface. Pruritus is a common complaint.

The histogenesis of Paget's disease of the vulva is unclear. It appears to be the result of an abnormal differentiation of stem cells within the epidermis. Paget's disease is often associated with another invasive carcinoma within the same patient, an adenocarcinoma; however, it may be a squamous cell carcinoma of the vulva, vagina, or cervix.

Histologically the epithelium will contain large neoplastic cells with clear, vacuolated cytoplasm. These cells contain large amounts of the mucopolysaccharides and are referred to as Paget's cells. The underlying dermis will contain an inflammatory infiltrate. Lymph node metastasis has been reported.

Biopsy-proven Paget's disease of the vulva requires an exhaustive search for an associated malignancy. If none is found, the patient should have a bilateral vulvectomy. Consideration should be given to a superficial node dissection. Histologic evidence of an invasive malignancy may indicate the need for additional surgery. If there is an associated malignancy of another organ, therapy will depend upon the origin of the malignancy.

Carcinoma of the Vulva

Carcinoma of the vulva accounts for approximately 4 percent of all female genital cancers and approximately 1 percent of all cancers in women. Although there are many histologic types, 90 percent are of the squamous cell variety. Squamous cell carcinoma of the vulva is primarily a disease of the postmenopausal female. The average age at diagnosis is 65 years. Some of the patients have previously had one or more of the venereal diseases, but the etiologic role of those diseases is unclear as far as the development of carcinoma is concerned. The progress of hyperplastic dystrophy with atypia to squamous cell carcinoma is better accepted. Fifteen percent of women with vulvar carcinoma will have an associated vaginal neoplasia.

Vulvar carcinoma usually presents with pruritus, pain, bleeding, or the presence of a mass. Pruritus is more likely the result of an associated dystrophy than from the invasive lesion itself. Dysuria may result from urine irritating the lesion. Only a rare patient will have an asymptomatic carcinoma of the vulva.

The majority of squamous cell carcinomas of

the vulva will be seen on the labium majus, the labium minus, or the clitoris. The lesion may be clean or infected, dry or wet, and painless or tender; it may appear white, pink, red, or brown in color. Squamous cell carcinomas are usually unifocal, but may vary in size from less than 1 cm to lesions that entirely replace the vulva. They may be exophytic, ulcerative, or infiltrative in nature. The inguinal lymph nodes should be evaluated for metastasis. A biopsy is required to make the diagnosis of invasive carcinoma of the vulva, as treatment without an established histologic diagnosis is a frequent source of clinical error. Condyloma acuminatum, vulvar dystrophy, and a variety of infections may mimic vulvar carcinoma.

The preferred treatment of invasive carcinoma of the vulva is radical vulvectomy with bilateral groin lymph node dissection. This standard of therapy has produced the best cure rate.[12] The radical operation is tolerated remarkably well by the older patient. If medical conditions dictate, it may be done in separate stages. Lesser surgical procedures are rarely indicated as such lesions are more prone to recurrence. If treated appropriately, one third of those women aged 70 years and older can be expected to survive five years.

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