Vulvar and Vaginal Cancer

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KEYWORDS

- Vulvar cancer • Vaginal cancer • Epidemiology • Pathology • Treatment
- Prognosis

KEY POINTS

- The incidence of vulvar dysplasia is increasing, particularly in women aged 20 to 35 years, many of whom have a history of genital dysplasia at other sites.
- Vulvar cancer is primarily a disease of the elderly. Most can be cured with surgery and adjuvant radiotherapy. Sentinel lymph node sampling is becoming the new standard of care for women with early stage vulvar cancer.
- Vaginal cancer a is rare cancer affecting elderly women. Treatment involves a combination of external beam radiotherapy and brachytherapy with surgical resection in a small subset of patients. Despite these treatments, prognosis is poor.

This article describes epidemiology, diagnosis, staging, pathology, management, and prognosis for vulvar and vaginal cancers.

VULVAR CANCER

The vulva consists of the external female genital organs that include the mons pubis, labia minora, labia majora, clitoris, vaginal vestibule containing the Skene and Bartholin glands, and the urethral meatus. Squamous cell carcinomas (SCC) make up 85% to 95% of invasive vulvar carcinomas. The remaining 5% to 15% are adenocarcinoma, basal cell carcinoma, sarcoma, melanoma, and undifferentiated carcinoma.[1]

Epidemiology

In the United States, invasive vulvar cancer will be diagnosed in an estimated 4340 women in 2011, making up 4% of female genital tract cancers and .6% of all cancers in women.[2] Most cases occur in white postmenopausal women, and the incidence has risen steadily by 20% over the last 40 years.[3]

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The etiologic factor responsible for invasive vulvar cancer is not clear, because it is associated with both chronic vulvar inflammatory lesions and vulvar intraepithelial neoplasia (VIN). SCC is associated with adjacent VIN in up to 85%, and lichen sclerosis in 15% to 40% of cases.[4] Human papillomavirus (HPV) DNA has been isolated in 20% to 60% of invasive vulvar carcinoma, and its role in pathogenesis, or the natural history of infection, may be different from cervical cancer.[5,6] HPV type 16 is the most commonly isolated HPV type in vulvar cancer. HPV 16 or 33 is reported in 71% of warty carcinomas, in 100% of basaloid carcinomas, and in only 4% of invasive differentiated (keratinizing) type vulvar carcinoma.[7] HPV-associated vulvar cancer is more common in women younger than 45 years and more often diagnosed at an earlier stage, compared with that associated with vulvar inflammatory disease, which is seen more commonly in older women and often diagnosed at a later stage.[8] The differentiated (keratinizing) type is usually HPV-negative and frequently associated with p53 mutations.[9] This association supports the theory that there are two different causes for vulvar carcinoma.

Noninvasive Vulvar Disease

Benign vulvar diseases are defined by the International Society for the Study on Vulvar Disease (ISSVD) and have gone through changes of terminology over the years. In 1976, the ISSVD classified benign vulvar disease into categories including vulvar dystrophies (including hyperplastic dystrophy, lichen sclerosis, and mixed dystrophy), vulvar atypia, Paget disease, and squamous cell carcinoma in situ.[10] The classification system was revised in 1989 when the term *vulvar dystrophy* was replaced with *nonneoplastic epithelial disorders of skin and mucosa* (including lichen sclerosis, squamous cell hyperplasia, and other dermatoses), and the terms *atypia* and *in situ lesions* were replaced with *vulvar intraepithelial neoplasia*. VIN was graded 1 to 3 for mild, moderate, or severe/in situ dysplasia, respectively.[11] In 2004, the category of VIN I was removed because of low interobserver reliability, and the differentiation between types of VIN was included,[12] listed as follows:

I. VIN, usual type
   a. VIN, warty type
   b. VIN, basaloid type
   c. VIN, mixed (warty/basaloid) type
II. VIN, differentiated type
III. VIN, unclassified type.

Vulvar intraepithelial neoplasia

The incidence of vulvar dysplasia is drastically increasing with a rate of .56 to 2.86 per 100,000 women,[3] and it is becoming more common in younger women aged 20 to 35 years.[13] Approximately 50% of women with vulvar dysplasia have dysplasia at other sites involving the genital tract, most commonly the cervix. Usual type is associated with HPV infection (particularly HPV16) and cigarette smoking, is often multifocal, and has a pathogenesis similar to cervical dysplasia. Differentiated VIN is generally not associated with HPV infection and is morphologically similar to invasive squamous cell carcinoma in appearance.

Most women with vulvar dysplasia are asymptomatic, and the diagnosis is made with a high index of suspicion. When symptomatic, pruritus is common. Other symptoms include burning, dyspareunia, erythema, edema, and pain. Lesions have a raised surface and are pigmented in 25% of cases.[14] Half of VIN lesions become acetowhite after the application of 5% acetic acid, which should be applied for at least 5 minutes before examination. Thorough examination with the colposcope