Vulvodynia: An Indicator or Even an Early Symptom of Vulvar Cancer

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Vulvodynia is a symptom of chronic, painful vulvar discomfort of multicausal origin. Vulvar cancer is an underestimated cause of vulvodynia. Even early stages of vulvar neoplasia can lead to aching lesions. Three cases of vulvar carcinoma eliciting persistent pain have been diagnosed within a 2-year period. In 2 of our case studies, women had antecedent periods of vulvar pruritus of long duration (5 and 20 years, respectively). We conclude that early histologic examination of all visible vulvar lesions is necessary to exclude the presence of malignant vulvar neoplasia.

The International Society for the Study of Vulvar Disease defines vulvodynia as "chronic vulvar discomfort, especially that characterized by the patient's complaints of burning and sometimes stinging, irritation, or rawness."[1] These leading symptoms may have several nosologic classifications (Table).[2] Although vulvodynia is associated with considerable suffering, most conditions are not life threatening. However, in a 2-year period we observed 3 cases of vulvar cancer with symptomatic, persistent, localized pain. Vulvar cancer is often miscalculated and mismanaged by physicians and patients.

Case Reports

Patient 1—A 45-year-old woman experienced chronic vulvar discomfort for 5 years. Initially, she complained of pruritus vulvae, which showed no significant improvement with local estradiol therapy. Twelve months prior to admission, she experienced premenstrual burning that subsequently increased in intensity and was accompanied by a slowly growing erosion on the right labium minus. On examination, no punch biopsy was taken because all of these symptoms were thought to be caused by relapsing infections. The patient also had a brown vaginal discharge and reported that sexual intercourse was no longer possible. A fibrinous, polycyclic ulcer with a diameter of 1.5 cm was found on the right labium minus. A similar ulcer with a diameter of 5 mm was found on the left labium minus. Because pain was extreme, speculum investigations were only possible after the administration of analgesic medication. Lymph nodes with diameters of up to 1 cm were palpable at the groin. Both abdominal sonography and chest x-ray findings were normal.

Histologic examination showed squamous cell carcinoma of the vulva with moderate cell differentiation. The depth of invasion was 2 mm. The erythrocyte sedimentation rate was 20/37 mm. The remaining laboratory values, including both white and red blood cell counts, were within the normal range. Herpes simplex 1–serology values were elevated (IgG antibodies, 1197 IU/mL enzyme immunoassay; IgM antibodies, negative), and serologic parameters for herpes simplex 2, Epstein-Barr virus, and cytomegalovirus were normal. Serologic tests for syphilis and HIV infections were negative. *Escherichia coli* were cultured from an ulcer smear, but *Candida albicans*, chlamydia, herpes simplex types 1 and 2, and *Neisseria gonorrhoeae* were not detected.

Following a diagnosis of vulvar cancer, radical vulvectomy with bilateral inguinal and femoral lymph node excision was undertaken (classification: T3, N2, MX, G1).

Patient 2—A 77-year-old woman suffered painful ulceration of the vestibulum vulvae for approximately 12 months. Initially, discomfort occurred only during urination, but 4 weeks prior to hospital admission, it developed into persistent burning pain, which finally prompted her to seek medical intervention. Herpes simplex infection was suspected, but systemic treatment with acyclovir was unsuccessful. On admission, a painful, 3×3-cm polycyclic ulcer with protruding lips was found on the left labium minus. Because of the painful nature of the process, further gynecologic examination and swabs were only possible after the administration of analgesic. A hard inguinal lymph node about the size of a walnut was

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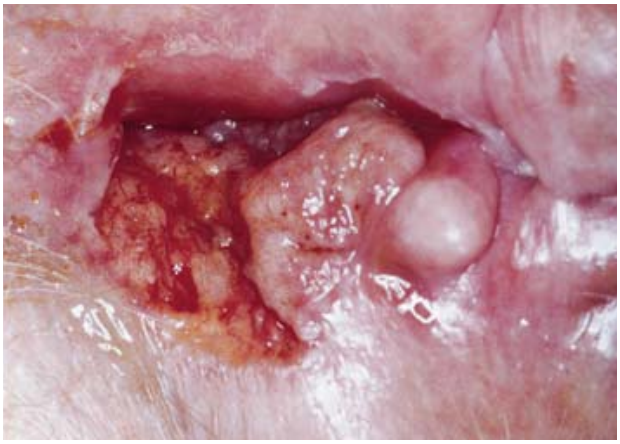
Nosologic Classification of Vulvodynia[2]

- Cyclic vulvovaginitis
- Vulvar vestibulitis syndrome
- Dysaesthetic vulvodynia
- Vulvodynia due to local dermatoses
- Vulvodynia due to other causes



Squamous cell carcinoma of the vulva in patient 2.

palpable at the left side. Chest x-rays suggested a circular focus in the left apex area, and abdominal sonography was normal. Histologic examination revealed a squamous cell carcinoma (pleomorphism and cell complexes characterized by high desmosome populations)(Figure). A test for immunofluorescence resulted in clear staining with cytokeratin LP34, MNF116, and DEK-10.

The erythrocyte sedimentation rate was 15/34 mm, and other laboratory values were within normal limits, except for slight hyperuricemia. Elevated IgG antibodies against herpes simplex 1 (1442 IU/mL enzyme immunoassay) and herpes simplex 2 (1073 IU/mL enzyme immunoassay) were measured, and IgM antibodies and serology for syphilis and HIV were negative. *Proteus mirabilis* and *E coli* were grown in cultures from the ulcer smear.

The patient underwent radical vulvectomy with bilateral inguinal and femoral lymph node excision. Of the 14 lymph nodes, 9 were involved (classification: T3, N2, M0, G2).

Patient 3—A 48-year-old woman suffered from pruritus vulvae for about 20 years. In the 4 months prior to admission, a rapidly growing, painful vulvar tumor developed, which prompted her to seek medical attention. On examination, an exophytic 1×0.7-cm tumor with a greasy yellow surface was found immediately rostral to the upper commissure in the right labium minus. No inguinal lymph nodes were palpable. Abdominal sonography and chest radiography yielded normal results, and serology for syphilis was negative. Histologic examinations disclosed a highly differentiated squamous cell carcinoma of the vulva with a depth of invasion of 1.5 mm. A slightly elevated erythrocyte sedimentation rate was the only pathologic laboratory value.

The patient underwent radical vulvectomy with bilateral inguinal and femoral lymph node excision. All lymph nodes were devoid of tumor cell infiltration (FIGO classification: I, T1, N0, M0).

Comment

In the United States, the incidence of vulvar intraepithelial neoplasia (VIN) doubled to 2.1/100,000 between 1973 and 1987.[3] In particular, VIN is becoming more prevalent in women younger than 35 years. Invasive vulvar cancer is a rare tumor that amounts to 1% of all malignant tumors in women[4] and includes squamous cell carcinomas, basal cell carcinomas, Paget disease, several forms of greater vestibular gland carcinoma, sarcomas, melanomas, and metastases.[4,5]

Pruritus vulvae is commonly the first symptom of vulvar neoplasia, although aching pain could become the leading symptom or the secondary symptom after local swelling.[4] Pain is often considered to be a late symptom of vulvar cancer, particularly in cystic adenocarcinomas of the greater vestibular gland.[6,7] However, our observations from patient 3 suggest that algesia could become symptomatic of vulvar cancer even at low depths of invasion. Fischer et al,[8] who discovered vulvar intraepithelial neoplasia in 5% of cases, supports this hypothesis on the etiology of chronic vulvar complaints. Every fifth patient with VIN (1% of the whole collective) also suffered vulvodynia. The pathogenesis of this phenomenon has not yet been clarified. Perineural invasion,[9] which detrimentally affects the intraepithelial nerve fibers of the introitus vaginae, has been suggested. An involvement of these free nerve endings may explain pain and pruritus because they can be mediated by C-fiber neurons and only differ in central neural modulation.[10,-12] This fact underlines the difficulty in distinguishing between pruritus vulvae and vulvodynia in some cases because many patients experience both symptoms. This is also described by McKay,[13] though she clearly differentiates between the 2 symptoms. In our opinion, defining the leading

CONTINUED ON PAGE 238

CONTINUED FROM PAGE 236

or major symptom, especially for cutaneous causes of chronic vulvar discomfort, might be the best idea.

It must be pointed out that vulvar cancer and VIN are known,[14,15] but not recognized, as causing these forms of vulvar complaints. Differential diagnoses of painful vulvar ulcers and erosions include infections due to herpes viruses (eg, herpes simplex, cytomegalovirus), vesiculobullous autoimmune disorders, and ulcers due to systemic lupus erythematosus or Behçet's syndrome.[15,16]

Our cases show that vulvodynia may be a leading and possible early sign of vulvar cancer. Early histologic examination in all cases of epithelial abnormalities, especially erosive or ulcerative lesions at the vulva, should be mandatory to improve the prognoses of the patients.

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