

Vulvar cancer: prognostic significance of the clinicopathological characteristics

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Summary

Vulvar cancer is a relatively uncommon neoplasm of the female reproductive system. The aim of this retrospective study was the analysis of the pathologic and clinical characteristics of vulvar cancer and their prognostic significance. During the period January 1996 to December 2005, 82 patients were treated for a vulvar malignancy. The management was surgical.

Key words: Vulva; Cancer; Carcinoma; Melanoma; Sarcoma.

Introduction

Primary vulvar carcinoma is an uncommon disease which usually presents in elderly women with comorbidity such as hypertension, diabetes or obesity. Vulvar carcinoma is a skin tumor presenting with different histological types. The vast majority of vulvar carcinomas are of squamous cell type and more rare histological types such as melanoma (5%), basal cell carcinoma (1-2%), adenocarcinoma or sarcoma. The incidence of such tumors accounts for 3-5% of all gynecological cancers [1]. Its detection is possible in an early stage due to the characteristic signs and symptoms. Biopsy in an outpatient clinic is very important for the diagnosis. Decreased survival rates have been reported according to tumor size, localization of the primary tumor and lymph node involvement. The major prognostic factors of overall and disease-free survival are the stage, grade of differentiation, tumor diameter, node involvement, depth of invasion and tumor-free surgical margins.

Method

This was a retrospective analysis of women diagnosed with vulvar carcinoma treated between January 1996 and December 2005 in the 2nd Department of Obstetrics and Gynecology, University of Athens, Aretaieion Hospital, Athens, Greece. The necessary data were collected by reviewing patients records or hospital electronic bases and contacting the physicians and patients regarding the age at diagnosis, stage, histological type of the tumor, treatment, relapse rate and 5-year survival. The staging of disease was performed according to FIGO criteria. Ethical review approval was achieved by the ethical committee of our hospital. Statistical analysis was made by using SPSS with statistical significance in all cases defined as $p < 0.05$.

Management

The first diagnosis is usually made by vulvar biopsy. Further investigation following the diagnosis includes chest X-ray,

abdominal computed tomography (CT) scan and bone scanning. The management is the same regardless of tumor type, but different according to the stage of the disease. All patients were operated within 15 days after diagnosis. Radical wide excision, radical vulvectomy, radical vulvectomy with unilateral lymphadenectomy and radical vulvectomy with bilateral lymphadenectomy were the surgical options. A redovac slow suction drain was used for ten days. Foley's catheter was used to avoid wound soiling. Twice daily dressing of the wound was necessary and the stitches were usually removed on the tenth postoperative day. Radiotherapy was given when inguino-femoral lymph nodes were involved. Follow-up was scheduled for every three months the first year and then every six months for five years. The postoperative radiotherapy was directed at the bilateral groin nodes and the perineum. Patients with Stage III or IV were additionally irradiated at the pelvic nodes. The doses ranged from 32.4 Gy to 54 Gy (median 50 Gy) with a 6-mega electron volt linear accelerator and 1.8 Gy daily tumor dose.

Results

Eighty-two patients were included in our retrospective study. The mean age of them was 72.33 years (range 52-84 years). The mean body mass index (BMI) was 26.3 ± 3.2 (range 20.5-34.2). Regarding obstetric history 6/82, 12/82, 64/82 patients were nulliparas, primiparas and multiparas, respectively. There was no significant relationship with smoking. HPV infection, low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) in the Pap smear were detected in 14/82, 3/82 and 1/82 patients, respectively. Of the patients 12/82 and 7/82 had a previous diagnosis of VIN I and VIN II or III, respectively. The main initial symptom in 59/82 patients was pruritus, followed by presence of the tumor 48/82, pain 7/82 and bleeding 6/82. Eight of 82 patients reported no symptoms. The vast majority of vulvar carcinoma were squamous cell carcinoma (74/82), then basal cell carcinoma 4/82, melanomas (3/82) and sarcoma (1/82). Preoperatively 19/82, 10/82, 46/82 and 7/82 had Stage I, II, III and IV, respectively. Clitoral involvement was found in 20/82 patients. The mean tumor size was 47.2 ± 12.7 mm

Revised manuscript accepted for publication February 8, 2010

Fig. 1

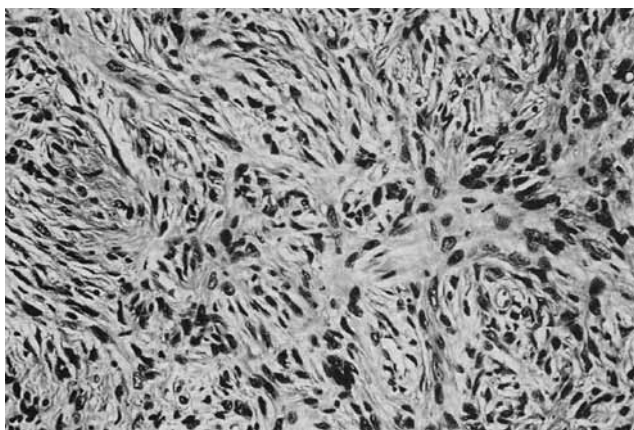


Fig. 2

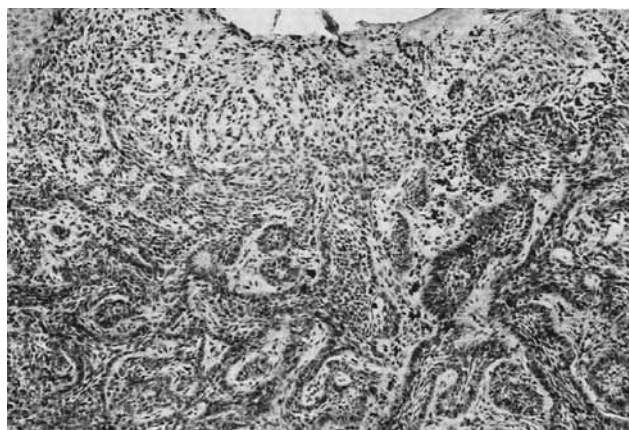


Fig. 3

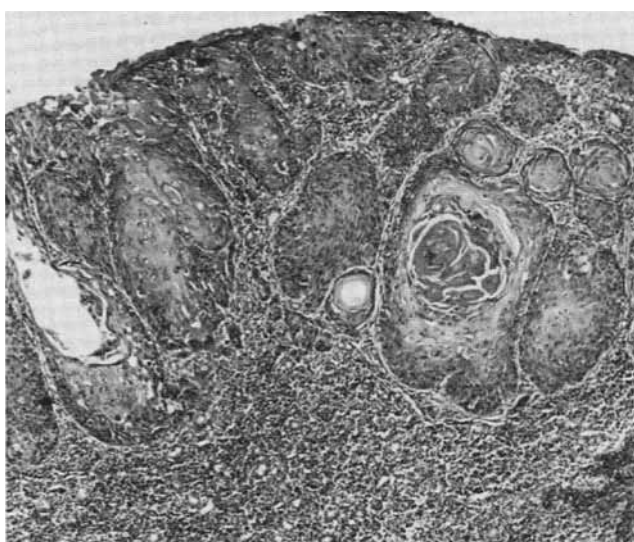


Figure 1. — Histological section of malignant fibrous histiocytoma of the vulva (hematoxylin-eosin x 250).

Figure 2. — Histological section of basal cell carcinoma of the vulva (hematoxylin-eosin x 120).

Figure 3. — Histological section of squamous cell vulvar carcinoma well differentiated with deep invasion of the vulvar wall (hematoxylin-eosin x 250).

(range 17-58 mm). Surgical treatment consisted of radical wide excision in 15/82, radical vulvectomy in 10/82, radical vulvectomy with unilateral lymphadenectomy in 14/82 and radical vulvectomy with bilateral lymphadenectomy in 43/82 patients. The most common complication was wound breakdown (19/82) followed by lymphedema (12/82). Thirty-eight of 82 patients received adjuvant chemotherapy and 57/82 patients received adjuvant radiotherapy. The mean follow-up was 48 months (range 36-60 months). All patients had tumor recurrence from three months up to 54 months (median, 20.4 months). Of the patients 31/82, 11/82, and 40/82 had a groin recurrence, a recurrence in the former location of the vulva, and a distant metastasis, respectively.

Overall five-year survival was 27/82. The five-year survival was 12/19, 6/10, 9/53 for Stage I, II (III and IV), respectively. Patients with recurrences 12 months or less after surgery had a significantly decreased median overall survival compared with those with a later recurrence.

Discussion

Although vulvar cancer yields early symptoms, its prognosis can not be characterized as favorable. Signifi-

cant prognostic factors include tumor size and location, lymph node involvement, location of recurrence, and disease-free survival. Smoking and obesity seem to increase the risk of vulvar carcinoma. Nola *et al.* revealed that the depth of tumor invasion represents the most important prognostic parameter in the group of patients with invasive squamous vulvar carcinoma [2]. Lymph node status is an important prognostic factor and for this reason, complete inguinofemoral lymph node dissection is proposed. Stage and nodal involvement are predictors of survival, and stage is a predictor of disease-free survival [3]. Clinical significance of DNA ploidy and proliferative activity has not been found [2]. Moreover, bilateral involvement of the inguinal lymph nodes carries a worse prognosis [4]. Narayansingh *et al.* showed a 20-fold higher recurrence rate in patients with lymph node micrometastases [5]. HPV is proposed to be a possible risk factor in the etiology of vulvar carcinoma. Epithelial disorders are found adjacent to vulvar carcinoma in 70-80% of patients and could serve to separate patients that differ in prognosis [6]. According to Eva *et al.* vulvar carcinoma arising in a background of differentiated VIN appears more likely to recur than vulvar carcinoma arising from undifferentiated VIN [7].

Landrum *et al.* found a mean age of 59.9 years in a similar study to ours with Stage I 51%, Stage II 30%, Stage III 17% and Stage IV 4.2% [8]. According to Cheng *et al.* age and lymph node metastasis were the most significant prognostic factors of disease-free survival [9]. In the same study, recurrence was mentioned locally (58.8%), in the groins (5.9%) and distant metastases (14.7%) [9]. de Giorgi *et al.* in a retrospective study showed the different characteristics of vulvar basal cell carcinoma (average size was 2.1 cm and 28% were ulcerated at presentation) and proposed that basal cell carcinoma should be suspected whenever inflammatory vulvar lesions do not respond to usual treatment [10].

The excision margins also have an important role in the prognosis of women with vulvar cancer. Heaps *et al.* have already reported a sharp rise of local recurrence when the resection margins were less than 10 mm [11]. Gonzalez Bosquet *et al.* in a large retrospective study found that ipsilateral lymphadenectomy is suitable for patients with unilateral lesions distant from the midline, and either negative ipsilateral lymph nodes or positive ipsilateral lymph nodes with lesions smaller than two cm [12]. Landrum *et al.* compared the outcome in patients with advanced squamous vulvar carcinoma treated with surgery or primary chemoradiation and found no differences regarding overall survival, progression-free survival or recurrence rates (2 = 19). However, older patients with smaller lesions and positive lymph nodes tend to be surgically managed whereas younger patients with larger volume disease and fewer lymph node metastases are treated with primary chemoradiation [13]. Radiotherapy and conservative surgery could be an alternative to radical surgery with less morbidity in elderly patients [14]. According to Katz *et al.* radiotherapy alone or in combination with lymph node dissection is highly effective in preventing disease recurrence in patients with vulvar carcinoma [15]. Woolderink *et al.* showed that wide local excision and superficial inguinal lymphadenectomy with separate incisions result in a high groin recurrence rate. For this reason, deep inguinofemoral lymphadenectomy is proposed [16].

Gaavenstroom *et al.* [17] found that the main complications after vulvectomy and inguinofemoral lymphadenectomy using separable groin incisions are wound breakdown (17%) and/or infection (39%) of the groin, lymphocyst formation (40%) and lymphedema (28%). In a similar study of Hanprasertpong *et al.* the most common complication was wound infection, wound dehiscence, lymphosis and leg edema [3]. Magrina *et al.* showed that modified radical vulvar surgery is associated with decreased complications and five-year overall and disease-free survival and recurrence rates similar to those of radical vulvar surgery [18, 19]. Woolderink *et al.* showed that the 5-year local relapse-free survival is 70% [20]. After a local recurrence, 72% of the patients developed a second local recurrence [20].

Gonzalez Bosquet *et al.* stated that most recurrences usually occur within the first two years of follow-up, while 35% of their patients showed a recurrence five

years or more after diagnosis [21]. Thus, long-term follow-up is proposed.

Landrum *et al.* compared data from 1990-2005 with data of the Gynecologic Oncology Group from 1977-1984 and found that the survival rates are similar in the minimal and low risk groups in spite of less radical surgery [22]. Furthermore, they found that five year survival rates for intermediate- and high-risk groups have improved due to the advancement in adjuvant chemoradiation and a younger patient population that presents with less advanced disease [22].

Conclusion

Vulvar carcinoma is a disease of elderly women. As life expectancy increases, more women are going to face this a problem in the near future. Clinicians should be aware of such an entity as early diagnosis and treatment are critical for the patient. Individualization of the treatment is proposed. A close follow-up is necessary.

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