Vulvar squamous cell carcinoma. Presentation of 28 patients

V. Parra[1], F. Flores[2], C. Sánchez de Giménez[3], P. Daguerre[4], V. García Llaver[2], F. Galdeano[2], N. Driban[5]

Abstract

Introduction. Vulvar squamous cell carcinoma constitutes from 1 to 4 percent of all female cancers, and is placed fourth among female genital tract neoplasias.
Objectives. To determine the incidence of vulvar squamous cell carcinoma and identify degree of invasion.
Material and methods. An observational retrospective study was conducted on patients consulting for vulvar pathologies in a period of 4 years and 8 months. The study included 28 patients with clinical and histopathologic diagnosis of vulvar squamous cell carcinoma.
Results. From the total of patients assessed in our hospital office, 6.17 percent (28) had squamous cell carcinoma. The average age was 62.5 years. Of the 28 patients, 64.28 percent (18) had invasive squamous cell carcinoma, and 35.7 percent (10) had vulvar intradermal neoplasia (VIN), where 4 developed from lichen sclerosus, 3 from epithelial dysplasia (differentiated VIN) and 3 from a bowenoid papulosis (usual VIN) diagnosis. All patients referred itching as dominant sign, and 60 percent of patients were smokers.
Conclusions. 28 cases of vulvar epidermoid carcinoma were studied, whereof 64.2 percent were invasive and 35.7 percent were VIN. Of the latter, 70 percent were differentiated VIN and 30 percent were usual VIN. This case material enabled us to learn about the incidence of squamous cell carcinoma in our setting, and to differentiate degrees of invasion and pathogenic factors (Dermatol Argent 2009; 15(5):344-349).

Key words: *squamous cell carcinoma, vulvar intraepidermal neoplasia, vulvar carcinoma.*

Introduction

Vulvar squamous cell carcinoma constitutes from 1 to 4 percent of female patient cancers, and is placed fourth within female genital neoplasias.[1,2]
According to clinical, pathological, and ethiological presentation, it is classified into two main categories (**Chart 1**):[3,4]

1. **Vulvar intradermal neoplasia** (VIN) or *in situ* carcinoma.
   1.1. Usual or classic VIN (associated to HPV infection).
   1.2. Differentiated VIN (associated with lichen sclerosus and epithelial dysplasias).
   1.3. Non-classified VIN.
2. **Invasive carcinoma.**

Usual VIN refers to human papilloma virus infection, especially serotypes 16 and 18, and less frequently serotypes 31, 33, 35, and 39. It appears in young women, and the incidence increases according to the age at onset of sexual intercourse, the number of sexual partners, smoking, and the use of immunosuppressive drugs.[5-10] Differenciated VIN appears in older women associated with lichen sclerosis in 15 to 40 percent of the cases.

Reception date: 17/11/08 | **Approval date:** 5/2/09

1. Head of Dermatology Department, Hospital "Luis Lagomaggiore". Adjunct professor of the Dermatology Department.
2. Attending physicians of the Dermatology Department, Hospital "Luis Lagomaggiore".
3. Staff Physician of the Gynecology Department, Hospital "Luis Lagomaggiore".
4. Staff Physician of the Gynecology Department. Adjunct professor of the Gynecology Department, Universidad Nacional de Cuyo.
5. Named Professor of the Dermatology Department, Universidad Nacional de Cuyo. Mendoza, Argentine Republic.

Correspondence
Viviana Parra: Guayaquil 115, (5519) Dorrego, Mendoza, Argentine Republic | Ph.: 0261-4315618 | vivianaparra@arnet.com.ar

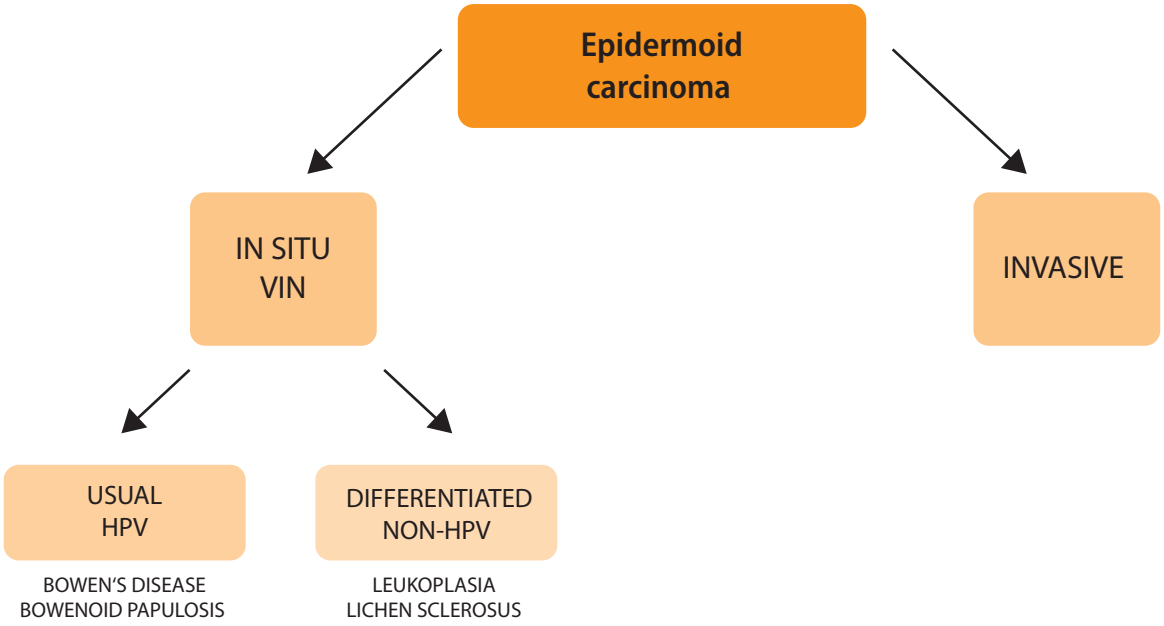

Chart 1. *Classification of vulvar squamous carcinoma.*

Invasive carcinoma penetrates the basement membrane, and it is classified into four stages according to FIGO staging (International Federation of Gynecology and Obstetrics).

Objectives

1. To determine incidence of vulvar squamous carcinoma in our setting.
2. To detect average age and predominant signs and symptoms.
3. To obtain objective clinical and pathological invasion degree of lesions.
4. To identify dominant risk factors.
5. To determine types of therapy performed.

Material and methods (Chart 2)

A retrospective, observational study was performed, including 454 patients from the vulvar pathology consulting office of Hospital "Luis Lagomaggiore" between January 2003 and August 2008. It must be highlighted that dermatologists and gynecologists work jointly in this consulting office, which receives referred patients exclusively; therefore, consulting patients present themselves with pathologies not resolved at primary health centers.

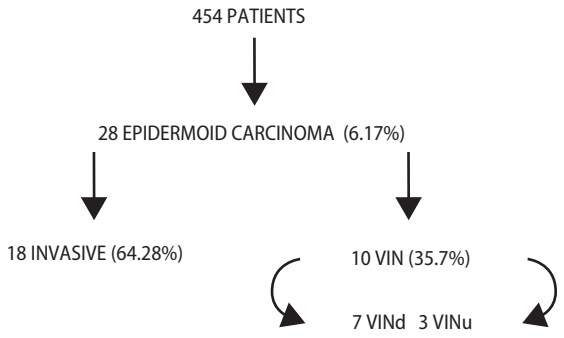

Chart 2. *Material and methods.*

The study enrolled 28 patients with clinical and pathological diagnosis of vulvar squamous cell carcinoma. Clinical record and pathological and iconographic data archives were reviewed.

Results

Between January 2003 and August 2008, 454 patients of a 15 to 90-years age range consulted our office (mean 51.5 years). Diagnosis of squamous cell carcinoma was established in 28 patients, constituting 6.17 percent of our population. From the total of genital carcinomas, vulvar squamous cell carcinoma appeared in 5 percent of genital tract tumors, preceded by cervical, endometrium, and ovary carcinomas.

Average age of squamous cell carcinoma incidence, including epitelial neoplasia and invasive carcinoma, was 62.5 years with the following age distribution: 20 to 30 years: 10.7 percent, 31 to 40 years: 7.14 percent, 41 to 50 years: 3.57 percent, 51 to 60 years: 22 percent, 61 to 70 years: 22 percent, 71 to 80 years: 19 percent, and 81 to 90 years: 15 percent.

From the 28 squamous cell carcinomas, 18 invasive carcinomas (64.28 percent) (**Figures 1**, **2,** and **3**), and 10 VIN (35.7 percent) (**Figures 4** and **5**) were detected.

TABLE 1. LESION STAGING.

STAGE	N	%
S0	10	35.7%
S1	2	7.14%
S2	8	28.5%
S3	4	14.2%
S4	4	14.2%

Predominant symptom was itching in 85.7 percent of the cases, followed by pain in 42.8 percent of the cases. Most outstanding signs were tumor in 32 percent, and bleeding in 40 percent. Location coincided with the one described in the literature: dominant in labia (57 percent), followed by diffuse involvement forms (28 percent), clitoris (10.7 percent), and perineum in one patient (3.57 percent).

Staging at the time of diagnosis was stage II or higher in 58 percent in invasive carcinomas, and stage 0 in VIN (**Table 1**).

Lapse from onset of lesions to consulting was greater than 8 months in more than 80 percent of the cases.

From the total of squamous cell neoplasias, 10 patients had diagnosis of VIN (35.7 percent), four developed from lichen sclerosus, three from epitelial dysplasia (differentiated VIN), and three had diagnosis of bowenoid papulosis (usual VIN).

Topic treatment with imiquimod cream was used in 3 patients (10.7 percent), partial resection in 7 (25 percent), simple vulvectomy in 4 (14.2 percent), radical vulvectomy plus lymphadenectomy in 10 patients (35.7 percent), and palliative in 4 (14.2 percent).

Smoking was reported in 60 percent of the patients.

Discussion

According to statistics, vulvar squamous carcinoma accounts for 1 to 4 percent of female tumors. Incidence shows an exponential progressive increase related to human papilloma virus infection, especially associated to serotypes 16, 18, 31, and 33.[8]

Predisposing factors are mainly age at onset of sexual intercourse, number of partners, the presence of acuminated condiloma, immunosuppression, lichen sclerosus, bad hygiene, and smoking.[9,10]

The number of vulvar squamous carcinomas (5 percent of genital tract carcinomas) found at Hospital

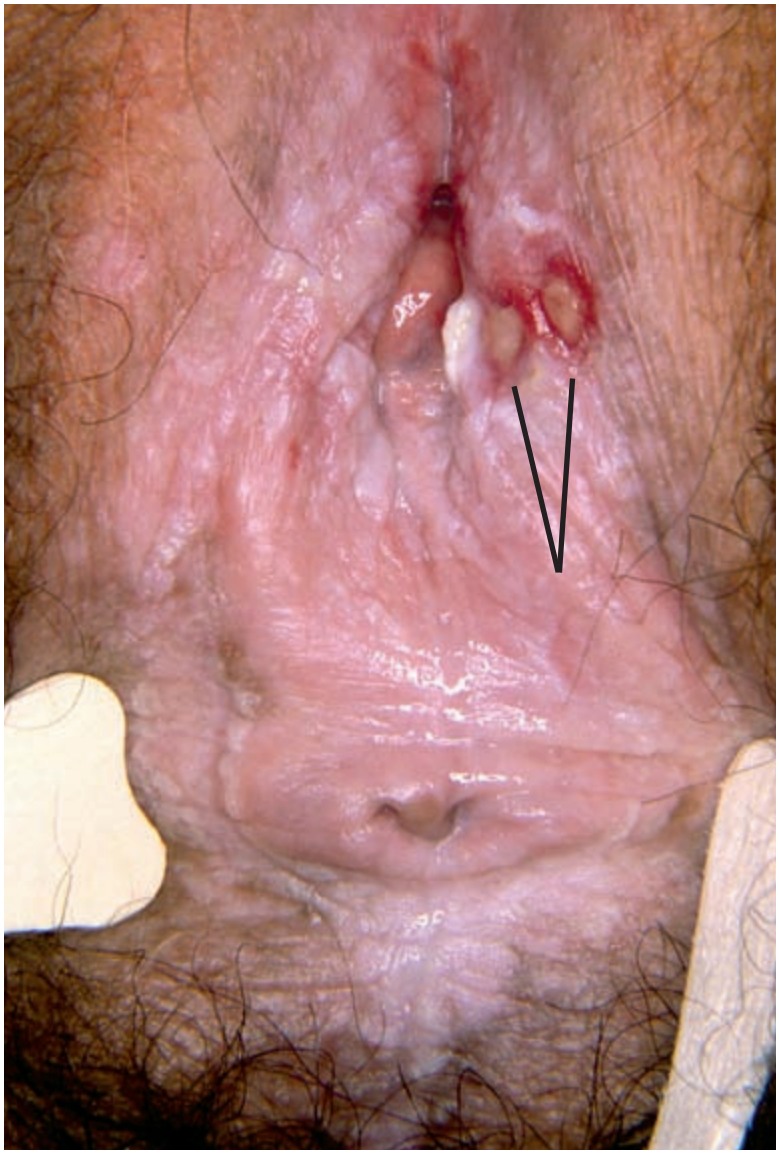

Figure 1. *Epidermoid carcinoma on lichen sclerosus.*

"Luis Lagomaggiore" exceeds the percentage referred to in the literature, probably because it is a province reference center with higher number of patients with rare pathologies.[1,2]

Average age of detected incidence was 62.5 years, which is expected to decrease with time, due to the exponential increase of human papilloma virus infection mainly affecting young women.

Lesion location and dominant signs and symptoms coincide with those published in the international literature; noteworthy is the delayed patient consultation, with higher incidence of lesions in stage II or higher.[11]

Therapy varied according to type of lesion and degree of invasion.[12-14]

In the cases of usual type of intraepidermal vulvar neoplasia (bowenoid papulosis), imiquimod therapy was instituted three times a week for 14 or 16 weeks, with good response.[15,16] Differentiated VIN lesions, both from lichen sclerosus and severe epitelial dysplasia, were mainly treated by local resection, except where lesions were clinically multicentric, which were more extensively excised by surgery (simple vulvectomy).[17,18]

With time, the trend is to reduce the size of vulvar excisions, because they cause great morbidity without survival improvement. Radical vulvectomy has been replaced by broad local excision with at least 1 cm margins; it was found that in T1 (size lesion < 2 cm) there were no increase in recurrences, and statistical data is lacking in T2 (size tumor > 2 cm) or higher.

Montones et al. found 50 percent recurrences with less than 8 mm margins, while De Hullu reported 0 percent recurrences with larger than 8 mm margins, and 22.5 percent with less than 8 mm margins.[18]

Current standard therapy is broad local excision with 2 cm margins and unilateral or bilateral inguinofemoral lymphadenectomy by the triple incision technique (preferably preserving fascia lata and saphenous vein) after detecting sentinel lymph node.[19-23]

The purpose of this work was to determine vulvar carcinoma incidence in our setting; noteworthy is the delayed patient consultation, probably due to lack of information.

Highlighted is the need of intensifying vulvar carcinoma prevention through extended information diffusion, both among the general population and health personnel, because only the thorough examination of the vulvar area, and the joint work of dermatologists and gynecologists may enable early detection of pre-neoplastic and neoplastic lesions.

Figure 2. *Epidermoid carcinoma on clitoris.*

Figure 3. *Invasive epidermoid carcinoma.*

References

1. Wagner W, Prott FJ, Weissmann J, Niewöhner-Desbordes U, Ostkamp K, Alfrink M. Vulvar carcinoma: a retrospective analysis of 80 patients. Arch Gynecol Obstet 1999; 262:99-104.
2. van de Nieuwenhof HP, van der Avoort IA, de Hullu JA. Review of squamous premalignant vulvar lesions. Crit Rev Oncol Hematol 2008; 68:131-156.
3. Sideri M, Jones RW, Wilkinson EJ, Preti M, et al. Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med. 2005; 50:807-810.
4. Bergeron C. New histological terminology of vulvar intraepithelial neoplasia. Gynecol Obstet Fertil 2008; 36:74-78.
5. Jones RW, Rowan DM, Stewart AW. Vulvar intraepithelial neoplasia: aspects of the natural history and outcome in 405 women. Obstet Gynecol 2005; 106:1319-1326.
6. van Seters M, ten Kate FJ, van Beurden M. In the absence of (early) invasive carcinoma, vulvar intraepithelial neoplasia associated with lichen sclerosus is mainly of undifferentiated type: new insights in histology and aetiology. J Clin Pathol 2007; 60:504-509.
7. Leroy JL, Vinatier D, Collier F, Thomas P. Diagnosis of vulvar intraepithelial neoplasias (VIN). Gynecol Obstet Fertil 2008; 36:190-199.

Figure 4. *Multicentric VIN.*

Figure 5. *VIN on lichen sclerosus.*

8. Hillemanns P, Wang X. Integration of HPV-16 and HPV18 DNA in vulvar intraepithelial neoplasia. Gynecol Oncol 2006; 100:276-282.
9. Wassila S, Leila S, Noureddine H, Sihem H, et al. Prognostic factors in squamous cell carcinoma of the vulva. About 35 cases Tunis Med 2005; 83:612-616.
10. Hussain SK, Madeleine MM, Johnson LG. Cervical and vulvar cancer risk in relation to the joint effects of cigarette smoking and genetic variation in interleukin 2. Cancer Epidemiol Biomarkers Prev 2008; 17:1790-1799.
11. Preti M, Rouzier R, Mariani L, Wilkinson EJ. Superficially invasive carcinoma of the vulva: diagnosis and treatment. Clin Obstet Gynecol 2005; 48:862-868.
12. Masak L, Hudakova G. Comparison of the treatment results in the vulvar and clitoris squamous cell carcinoma. Neoplasma 1998; 45:377-379.
13. Chiesa-Vottero A, Dvoretsky PM, Hart WR. Histopathologic study of thin vulvar squamous cell carcinomas and associated cutaneous lesions: a correlative study of 48 tumors in 44 patients with analysis of adjacent vulvar intraepithelial neoplasia types and lichen sclerosus. Am J Surg Pathol 2006; 30:310-318.
14. Bousema MT, Romppanen U, Geiger JM, Baudin M, et al. Acitretin in the treatment of severe Echen sclerosus et atrophicus of the vulvae: a double-blind, placebo-controlled study. J Am Acad Dermatol 1994; 30:225-231.
15. Moore A, Edwards J, Hopwood J, Hicks D. Imiquimod for the treatment of genital warts: a quantitative systematic review. BMC Infectious Diseases 2001; 1:3.
16. Le T, Hicks W, Menard C, Hopkins L. Preliminary results of 5% imiquimod cream in the primary treatment of vulva intraepithelial neoplasia grade 2/3. J Obstet Gynecol 2006; 194:377-380.
17. Rouzier R, Haddad B, Atallah D, Dubois P, Paniel BJ. Surgery for vulvar cancer. Clin Obstet Gynecol. 2005; 48:869-878. -
18. van der Avoort IA, Shirango H, Hoevenaars BM, Grefte JM, et al. Vulvar squamous cell carcinoma is a multifactorial disease following two separate and independent pathways. Int J Gynecol Pathol 2006; 25:22-29.
19. Balega J, Van Trappen PO. The sentinel node in gynaecological malignancies. Cancer Imaging 2006; 28;6:7-15.
20. Wydra D, Sawicki S, Emerich J, Romanowicz G. Evaluation of sentinel node detection in vulvar cancer. Nucl Med Rev Cent East Eur 2005; 8:128-130.
21. Douay-Hauser N, Akerman G, Tulpin L, et al. Sentinel node biopsy in vulvar cancer. Bull Cancer 2008; 95:701-706.
22. Johann S, Klaeser B, Krause T, Mueller MD. Comparison of outcome and recurrence-free survival after sentinel lymph node biopsy and lymphadenectomy in vulvar cancer. Gynecol Oncol 2008; 110:324-328.
23. Beriwal S, Heron DE, Kim H, King G, et al. Intensity-modulated radiotherapy for the treatment of vulvar carcinoma: a comparative dosimetric study with early clinical outcome. Int J Radiat Oncol Biol Phys 2006; 64:1395-1400.