

TREATMENT OF IN SITU CARCINOMA OF THE VULVA

(Received 19 June, 1995)

A. Erk, M.D. / D. Marchetti, M.D.* / H. Çağlar, M.D.***

* Associate Professor, University of New York at Buffalo (SUNY) Department of Obstetrics and Gynecology Division of Gynecological Oncology (Gynecologic Oncology Group of Buffalo, NY USA)

** Assistant Professor, University of Texas Southwestern Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Medicine, Dallas TX USA.

ABSTRACT

We retrospectively reviewed the cases of carcinoma in situ of the vulva seen at the State University of New York at Buffalo affiliated hospitals. The frequency of carcinoma in situ of the vulva is increasing among the younger population. There is a close relationship with sexually transmitted diseases and other genital and extragenital premalignant and malignant conditions, infections, immunosuppression, previous pelvic radiation, possible synergetic action of herpes simplex type 2 and human papilloma virus. In his study we tried to compare the results of different modes of therapies. This is an updated version of the publication of Buffalo Oncology Group about this subject (Obstetrics and Gynecology; 64:4, 1986 pp 504-507).

Key Words: Carcinoma in situ of the vulva, partial skinning vulvectomy, total skinning vulvectomy, topical 5-fluorourasil treatment.

INTRODUCTION

Eventhough it is a very uncommon problem for Turkey, the incidence of carcinoma in situ of the vulva seems to be rising in developing countries especially in the US. This new group is in reproductive age. There is a close relationship with sexually transmitted diseases and other genital and extragenital premalignant and malignant conditions, infections, immunosuppression, previous pelvic radiation, possible synergetic action of herpes simplex type 2 and human papilloma virus. (1-3)

Progression of in situ carcinoma of the vulva to the invasive stage had been shown (3). Topical

treatments with 5-Fluorourasil cream and carbon dioxide laser (CO₂ laser) could have a disadvantage of potential non-recognition of an early invasive lesion (1). To avoid this diagnostic problem of the latter two procedures and the mutilating effect of vulvectomies in the last 15 years we have employed skinning vulvectomy; partial and total depending on the extend of the disease, and split thickness skin graft in the treatment of intraepithelial neoplasia of the vulva (4).

MATERIALS AND METHODS

In the first phase of the study we have studied records of 42 patients with carcinoma in situ of the vulva, who were seen in the University of Buffalo (SUNY) affiliated hospitals from 1968 to 1981. All the patients fulfilled the histological criteria defined by the International Society for the Study of Vulvar Disease (4). Carcinoma simplex, Bowen disease, and erythroplasia of Queyrat were all considered intraepithelial carcinomas. Diagnosis in all patients was based on biopsy of the symptomatic and/or asymptomatic vulvar lesions and discolorations. Toluidine blue was used frequently for targeting the biopsy site, and since 1974 colposcopic examination has been part of the diagnostic investigation.

Thirteen patients were treated with total vulvectomy. In two of these patients lower vaginectomy was necessary and one required partial vaginectomy with partial excision of the anus. One patient required pedicle graft for approximation of the vulvectomy site. Twenty - three patients were treated with wide local excision (partial vulvectomy). Three patients were treated electively with topical 5-fluorouracil cream and two with CO₂ laser. One patient received no treatment.

In the second phase therapeutic implications and surgical techniques of partial and total skinning vulvectomy in 50 patients with in situ carcinoma of the vulva, performed from 1977 to 1992 were studied.

Surgical Technique

It is preferable to obtain skin graft first. Using the buttocks has the disadvantage of the need for rotation of the patient under anesthesia from the lithotomy to supine position. Our preference is for using the anterior thigh, if cosmetic appearance is not of important factor for the patient. The donor site is shaven prior to surgery. After it has been painted with Betadine, it is lubricated with mineral oil or liquid petroleum in order to maintain a gliding surface for the cutting instrument. As for healing we find the 0.015 in. thickness graft most satisfactory when it is taken prior to skinning vulvectomy from a well stabilized donor site. Following the excision of the vulva and/or perineal anal skin, the skin thickness graft is fitted and sutured to the edges of the wound with 5.0 Dexon or Vicryl suture on a cutting edge needle, and/or staples. (Figs. 1, 2, 3)

Within three to four days after surgery fibroblasts and capillary tufts invade the graft. During that time there must be no motion between the graft and the recipient site and detachment of the graft resulting from excess serum and blood accumulation must be prevented. To accomplish this the patients were kept with the pressure dressing in place for four to five days postoperatively at complete bed rest, on clear liquids, antidiarrheatics and subcutaneously administered heparin and antibiotics. Earlier removal of the dressing may be necessitated by wound infection which one suspects when there is temperature elevation or foul odor. Following removal of the dressing frequent wound irrigation with normal saline are instituted. Urine drainage was accomplished via suprapubic catheter or using Foley catheters.

The donor site is usually more uncomfortable than the vulva. In the first eight patients it was dressed with Vaseline gauze. The dressing was changed daily and the wound was irrigated with normal saline. This, however was uncomfortable for the patients therefore, in the other patients a silk dressing was applied to the wound as a first layer and Vaseline gauze was a second layer. The next day the Vaseline gauze was removed and the wound was exposed to

the air with only the silk dressing firmly adherent to the wound. No irrigation was necessary and the silk dressing was allowed to dry on the wound. This was then easily pulled off by the patient herself within 10 to 14 days after the surgery.

Patients were fully ambulatory by the 5th postoperative day and were discharged home on the 8th or 9th day after the surgery.

RESULTS

A morphologic description was available in most of the patients. The most common clinical presentation was a white lesion (65%). The appearance varied from detectable only by colposcopy to raised regular, irregular or desquamative forms with shading ranging from opaque to brown. In five patients (10%) condylomatous lesions were typical of condyloma accuminata.

Itching was present in 43.5% of the patients, and in 35% of this group bleeding and pain accompanied the itching. Duration of itching ranged from few months to 10 years. 10 % of the patients had pain and perineal discharge with no itching. The rest of the patients were asymptomatic.

Follow-up was not available in 12 patients. The remaining 80 patients were followed-up to between two years to 15 years. There were no cancer related deaths.

There were three recurrences after topical 5% 5-fluorouracil treatment; one of the patients had persistent disease three months after the treatment and disease in the other two recurred two years later. Both underwent wide local excision and are free of disease at present. Biopsy of the third patient, four months after 5-fluorouracil treatment indicated early invasion. She subsequently had a radical vulvectomy with bilateral groin dissection in addition to microinvasive carcinoma of the vulva, showed a clinically nondetectable invasive carcinoma originating from the Bartholin gland.

Five other patients had recurrence of disease after wide local excision. In one who had positive surgical margins clinical recurrence developed within five months of a wide right vulvar excision. The same therapy was repeated and the margins were again involved. Three years later, when wide local excision

of both labia was required, the margins were still involved. The patient is however, clinically free of disease four years after the last operation. The second patient had carcinoma in situ and superimposed basal cell carcinoma of the vulva. Wide local excision was performed and eight months later both basal cell and in situ carcinoma of the vulva recurred. The same operation was performed but did not prevent recurrence five years later.

Three months later, repeat biopsy of another patient that received laser treatment for carcinoma in situ of the vulva; showed microinvasive carcinoma, and she underwent radical vulvectomy with bilateral groin dissection.

Five patients had invasive carcinoma. Two of them have been previously mentioned one had had topical 5-fluorouracil treatment. In the remaining three, biopsy showed carcinoma in situ, and therapeutic local excision showed early invasion. One of these women underwent radical vulvectomy with bilateral groin dissection. The other two had no further treatment. One was lost to follow-up and the other is free of disease for over ten years.

Of 50 patients treated with total and partial skinning, recurrence of neoplasia occurred in 6 patients. In one of these 6 patients the extent of the primary surgery necessitated not only skinning of the vulva but also that of the adjacent tissues. On frozen section positive margins were found in the anal mucosa and for technical reasons further removal of the involved tissue was postponed for eight weeks when additional removal of 3 cm of the rectal mucosa up to the dentate line, as recommended by Kaplan, with approximation of the proximal rectal mucosa to the previously placed skin graft in the anal ring was performed (5). Six months later anoscopic examination revealed two well demarcated raised white epithelial lesions 2 mm and 3 mm in the diameter which on biopsy proved to be carcinoma in situ. The area of involvement was treated with laser and the patient is presently free of disease. In the other 5 patient recurrence were detected within 2 to 6 months. All other patients were free of neoplasia 12 months to 11 years after surgery.

DISCUSSION

As the condition can occur at any age after puberty without alarming symptoms, in almost half of the

patients the diagnosis depends on the physician's careful inspection of the vulva during routine gynecologic examination. In the presence of suspicious vulvar lesions, in persistent condylomatous and other vulvar lesions, vulvar biopsy should be mandatory, and physicians should be more inclined to perform a biopsy of the vulva in patients with long-standing vulvar itching. Although the value of the toluidine blue test is controversial, it can be useful when vulvar biopsy is desired (persistent itching or abnormal cytology) in the absence of a vulvar lesion. Colposcopic evaluation is only helpful in examining white epithelium seen by the naked eye.

The standard treatment for carcinoma in situ of the vulva is wide local excision or unilateral vulvectomy for unilateral localized lesions and total simple vulvectomy for unilateral localized lesions and total simple vulvectomy for widespread multicentric disease. Topical treatment with 5-fluorouracil cream has been less successful in eradicating the neoplasia and laser treatment is another alternative therapy. In one study of 33 patients with vulvar intraepithelial neoplasia (7 Grade II 26 Grade III) 14 required more than one laser treatment.

Although progression of in situ carcinoma of the vulva to the invasive forms is thought to be rare the presence of undetected early invasion of the cancer must be considered whenever one uses 5-fluorouracil cream or laser (6).

In reviewing five patients in whom the pretreatment colposcopic evaluation was done by an expert colposcopist, the biopsy failed to reveal the nature of the disease (7). Initially one of these patients as treated with 5-fluorouracil cream and another with laser before the invasive carcinoma was recognized. In three of them invasion was an incidental finding at the time of therapeutic wide local excision. Rettenmaier described a 7.1% incidence of biopsies failing to reveal the presence of invasion (8). Crum raised the possibility of missed invasion with biopsy in patients developing invasive carcinoma of the vulva within one year of the diagnosis of vulvar carcinoma in situ (9). Presently in our institution, CO₂ laser treatment is limited to Grades I and II intraepithelial neoplasia and Bowenoid dysplasia of the vulva (10). Local excision with the primary closure is an appropriate treatment for most of the patients with unifocal in situ carcinoma of the vulva. Now that the neoplasia appears to be more common and

especially among younger women, standard simple vulvectomy in multicentric intraepithelial neoplasia is of course unacceptable.

Total skinning vulvectomy with split thickness graft was first introduced in the USA by Rutledge and Sinclair who successfully treated ten patients ages between 22 to 47 (11). This method alone or combined with skinning of involved perineum, anus or lower rectal mucosa was then used by others as well. Partial skinning vulvectomy has definite cosmetic and/or functional advantages over complete vulvar skinnectomy or partial closure of very wide vulvar excision. When the results are compared with other modes of therapies skinning vulvectomy has many advantages beside the cosmetic results; operation site heals much faster, less painful and traumatic for the patient (Figs 1, 2, 3) (12).

In this institution partial vulvar skinning with split thickness skin graft was successfully applied to two groups of patients. The first group included patients with wide spread multicentric neoplasia, sometimes extending to the adjacent perineal and anal skin but with presence of normal vulvar skin in some parts of the vulva as per colposcopic evaluation and frozen section studies of the margins.

In the second group, the intraepithelial neoplasia was localized but the surface area of the locally excised skin with free surgical margins were wide enough to threaten the cosmetic and sometimes the functional integrity of the vulva with partial approximation of the wound edges. All the patients treated with skinning vulvectomy (partial or total) had very good cosmetic results.



Fig. 1: Carcinoma in situ of the vulva. Well demarcated lesion unifocal lesion extending to the perianal mucosa.

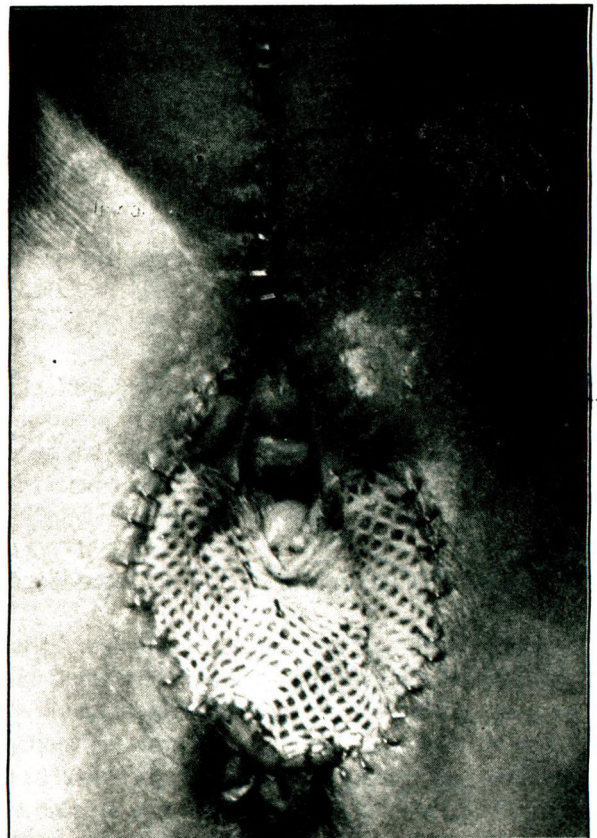


Fig. 2: Appearance of the lesion after partial skinning vulvectomy and skin thickness graft.

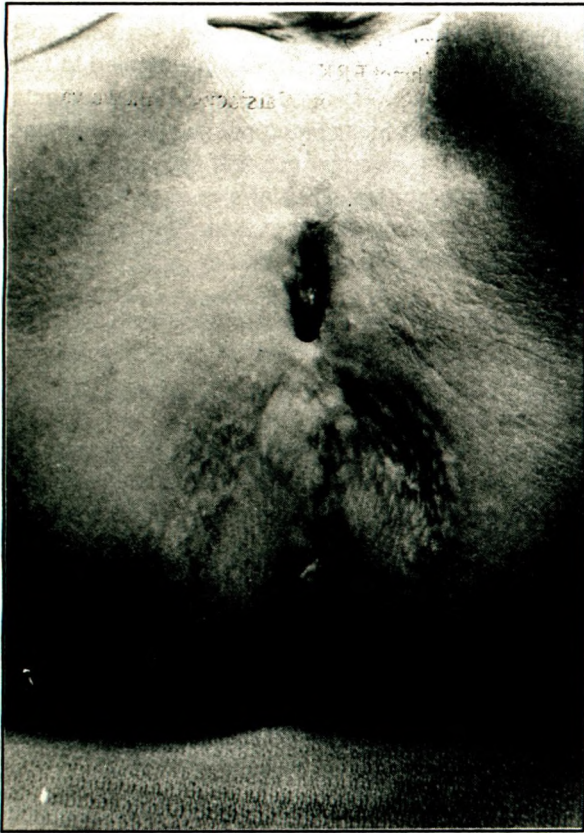


Fig. 3: Same patient 3 months after the surgery with very good cosmetic result.

REFERENCES

1. Çağlar H, Tamer S, Hreshchshyn MM. Vulvar intraepithelial neoplasia. *Obstet Gynecol* 1982; 60:346-349.
2. Reid R, Greenberg M, Jenson AB, et al. Sexually transmitted papillomaviral infections. 1. The anatomic distribution and pathologic grade of neoplastic lesions associated with different viral types. *Am J Obstet Gynecol* 1987; 156: 212-222.
3. Jones RW, McLean MR. Carcinoma in situ of the vulva. A review of 31 treated and five untreated cases. *Obstet Gynecol* 1986;68:499-503.
4. International Society for the Study of Vulvar Disease: New nomenclature for vulvar disease. *Obstet Gynecol* 1976;47:122-124.
5. Kaplan AL, Kaufman RH, Birken A. et al Intraepithelial carcinoma of the vulva with extension to the anal canal. *Obstet Gynecol* 1981;58:368-371.
6. Townsend ED, Levine RU, Richart RM, et al: Management of vulvar intraepithelial neoplasia by carbon dioxide laser. *Obstet Gynecol* 1982;60:49-52.
7. Baggish MS, Dorsey JH. CO₂ laser for the treatment of vulvar carcinoma in situ. *Obstet Gynecol* 1981;57:371-375.
8. Rettenmair AM, Berman LM, DiSaia PJ. Skinning vulvectomy for the treatment of multifocal vulvar intraepithelial neoplasia. *Obstet Gynecol* 1987;69:247-250.
9. Crum CP, Liskow A, Petras P. Vulvar intraepithelial neoplasia. A clinopathologic analysis of 41 cases. *Cancer* 1984;54:1429-1434.
10. Ulbright TM, Stehman FB, Roth LM, et al. Bowenoid dysplasia of the vulva. *Cancer* 1982;50:2910-2919.
11. Rutledge F, Sinclair M. Treatment of intraepithelial carcinoma of the vulva by skin excision and graft. *Am J Obstet Gynecol* 1968;102:806-811.
12. Çağlar H, Delgado G, Hreshchshyn MM. Partial and total skinning vulvectomy in treatment of carcinoma in situ of the vulva. *Obstet Gynecol* 1986; 68: 504 - 509.