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CARCINOMA OF THE VULVA

Results of an individualized treatment schedule

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Carcinoma of the vulva is a relatively rare malignant condition and constitutes about four per cent of all gynaecologic carcinomas and one per cent of all new malignant growths in women (Cancer Registry of Sweden 1971). As the vulva and the lymph nodes of the groin are accessible for early diagnosis and radical treatment, good prognosis might be expected in this disease. However, carcinoma of the vulva mostly affects women over sixty years of age, less prone to be so worried by the symptoms such as pruritus or ulceration and the condition is therefore often in a relatively advanced stage when the patient comes under treatment.

Radical vulvectomy, including bilateral dissection of the inguinal lymph nodes, has many advocates. The mortality of the operation in an unselected material has been reported however to be as high as 19 per cent (WAY 1960). Various modifications of the operation have been proposed in order to diminish this rate and improve the results. Individualized treatment in which the extension of the operation is determined by the clinical stage of the growth and the physical state of the patient seems to give good results (RUTLEDGE et coll. 1970). The widespread precancerous lesions often present in the vulva together with the latent

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condition usually suggest, however, total vulvectomy in most cases (LUNDWALL 1961).

Electrocoagulation of the vulva was introduced about 1922 (BERVEN 1941) and is still used in some centres. It is as radical a procedure as total vulvectomy and may be applied in patients in poor physical condition. Inguinal lymph node dissection may be combined with electrocoagulation of the primary growth but is then usually postponed until the coagulation wound has healed.

Radiation treatment of the primary growth has been described by several authors (BERVEN 1941, JOHNSSON 1964, ALMENDRAL 1972). General experience has been that the vulvar tissues are relatively sensitive to irradiation, resulting in a fairly large number of complications, mainly necrosis. No doubt exists that high energy photons or electrons from supervoltage machines have increased the possibilities of adequate radiation treatment of carcinoma of the vulva. Irradiation is especially valuable in advanced neoplasms in which total vulvectomy or electrocoagulation may be impossible or attended by too great risks of complications. Some authors (SCHUBERT et coll. 1960) have even used radiation treatment in early operable cases, but surgical methods in this group are generally preferred.

The treatment of the regional lymph nodes presents a complicated problem. The frequency of lymph node metastases varies in different materials from 45 to 57 per cent (TAUSSIG 1940, WAY 1951, EDSMYR 1962, BOUTSELIS 1972). Clinically manifest lymph node metastases may be treated by surgical dissection, irradiation or a combination of both. In cases without clinically established lymph node metastases, some authors use so-called prophylactic bilateral dissection of the lymph nodes of the groin (inguinal nodes, femoral nodes and sometimes iliac nodes) or radiation treatment of the inguinal regions for eradication of subclinical metastases. As the frequency of lymph node involvement is largely dependent upon the size and site of the primary tumour (EDSMYR 1962, BOUTSELIS 1972) and on the degree of tumour differentiation (WAY 1951), some centres have a more individualized approach. For example, when the primary tumour is situated laterally in the vulva, the frequency of metastases in the contralateral nodes is much lower than in the homolateral nodes. Radiumhemmet, Stockholm, which has largely influenced the treatment of carcinoma of the vulva, has employed the following method (BERVEN 1941.) After electrocoagulation of the vulva, both groins receive radiation treatment, followed by lymph node dissection in which clinically manifest metastases are present; so-called prophylactic dissection is not performed. A detailed report of 560 cases treated in this way was published by EDSMYR (1962).

An individualized treatment schedule has been used since 1959 in our department, the stage of the condition and the physical state of the patient

Table 1

Treatment method and clinical staging in patients with squamous cell carcinoma of the vulva

Primary tumour	Inguinal lymph modes	No. of cases	Stage				Lymph node metastases (microscopically verified)		
			I	II	III	IV	None	Unilat.	Bilat.
Electrocoagulation		16	9	5	2	—	13	3	—
"	+homolateral inguinal radiation treatment	12	—	6	3	3	6	6	—
"	+bilateral inguinal radiation treatment	11	—	1	10	—	8	2	1
Radical excision		5	3	2	—	—	5	—	—
" "	+homolateral inguinal radiation treatment	1	—	—	—	1	—	5	—
" "	+bilateral inguinal radiation treatment	—	—	—	—	—	—	—	—
Radiation		4	3	—	—	1	4	—	—
"	+homolateral inguinal radiation treatment	2	—	—	1	1	1	1	—
"	+bilateral inguinal radiation treatment	4	—	—	1	3	1	—	3
No treatment		2	—	—	—	2	—	—	2
Total		57	15	14	17	11	38	13	6

having determined the type. The purpose of the present investigation was to assess the results of this schedule of treatment.

Material. The Department of Radiation therapy serves a population of about 650 000. During the period 1959 to 1971 a total of 73 patients with malignancy of the vulva were admitted. The department was consulted regarding 3 additional patients who were not admitted. (Two of these had basal cell carcinomas and one had a malignant melanoma.) Eight of the patients admitted had been treated elsewhere for the primary growth and had a recurrence. Of the 65 primary patients 57 had squamous cell carcinomas, 4 had malignant melanomas, 2 had basal cell carcinomas, one had morbus Bowen, and one a malignant apocrine neoplasm.

This report deals mainly with 57 patients with squamous cell carcinomas, 55 of whom were treated. The mean age of the group was 64 years; the youngest patient was 28 and the oldest 91 years old. Twenty-two of these patients (38.6 per cent) had palpable inguinal nodes probably containing metastases from the

Table 2

Time elapsed from the onset of the symptoms until admission. Data from 54 patients

Duration of history, years	No. of patients
> 0 −0.5	20
> 0.5−1	19
> 1 −1.5	3
> 1.5−2	4
> 2 −2.5	1
> 2.5−3	3
> 3 −3.5	—
> 3.5−4	1
> 4 −4.5	—
> 4.5−5	1
> 5	2

vulva. The presence of metastases was verified in 19 of these patients, either by cytology after fine needle biopsy or by histology after removal. In 35 patients no inguinal nodes could be palpated or they were classified as normal (Table 1).

Length of history. Only signs and symptoms that could possibly be connected with the condition were taken into account. Fifty-four patients could give an adequate history. Pruritus was the most frequent symptom and was complained of by 18 of 54 patients; some however had had pruritus for many years and had been examined on repeated occasions with negative results before diagnosis of the tumour; pruritus was therefore not included in determining the duration of the history (Table 2).

Other malignant conditions. Five of the 57 patients with epidermoid carcinoma had been — or were later on — treated for another malignant condition; 2 had cervical carcinoma, one carcinoma of the uterine body and one carcinoma of the breast. Another patient was treated for a growth of the buccal mucosa some years after treatment of her vulvar carcinoma. Further, one patient who was treated for morbus Bowen of the vulva had earlier been treated for carcinoma of the cervix uteri.

Classification. A retrospective classification of the patients with squamous cell carcinoma has been according to the TNM system proposed by UICC 1967,

Table 3

Complications of the treatment that required intervention

Treatment	Total No. of patients treated	Type of complication	No. of patients
Electrocoagulation	39	Adhesion of introitus vaginae	2
		Postoperative hemorrhage	3
		Edema of the vulva	1
		Vulvar infection	1
Irradiation	10	Severe radiation reaction	3
Radical excision	6		0
Total	55		10

from which EDSMYR & KOTTMEIER (1971) have developed a method of clinical staging. The material has been grouped into 4 stages; the neoplasms were also classified microscopically as highly differentiated (40), fairly well differentiated (11) and poorly differentiated (6).

Treatment. This was individualized according to the extension and type of the primary tumour and the age and state of the patient. The primary tumour was usually treated by electrocoagulation of the whole vulva (BERVEN 1941). However, in younger patients and especially in those with more limited growths, wide local excision or hemivulvectomy was sometimes preferred; those cases regarded as inoperable received radiation treatment. The total tumour doses varied between 6 000 and 6 500 rad over 40 to 60 days with daily treatments five days per week usually with a ^{60}Co kilocurie unit or with high energy electrons from a betatron (15 to 30 MeV).

Clinical lymph node metastases were treated mostly by dissection, often combined with pre- or postoperative radiation treatment; with no clinical metastases, prophylactic radiation treatment was withheld if the primary tumour was small and highly or fairly well differentiated. Patients with medium-sized or large primary tumours and all those with poorly differentiated tumours received prophylactic radiation treatment to the groins; in well lateralized tumours, however, this treatment was confined to the homolateral side. The total dose of radiation administered to the inguinal regions varied between 3 000 and 6 000 rad over 15 to 55 days in daily treatments of 5 days per week.

Twelve patients had unilateral (10) or bilateral (2) lymph node dissections of the groin, in 9 of these in close connection with the primary treatment, while

Table 4

Three- and five-year results

	Three years	Five years
No. of patients referred	44	39
No. of patients treated	44	39
Alive without signs of carcinoma	24 (55 %)	21 (54 %)
Alive with carcinoma	0	0
Died with carcinoma	14	11
Died of intercurrent disease, probably without carcinoma	8	7

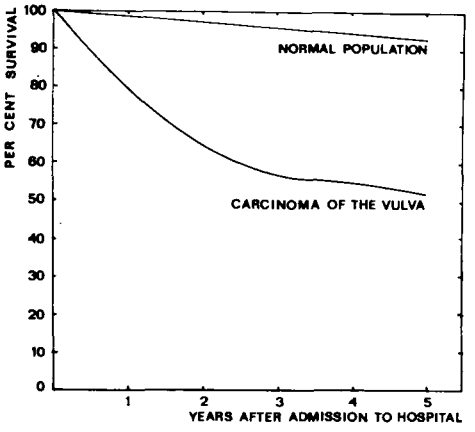
Table 5

Survival rates in different clinical stages

Stage	3-year survival rate		5-year survival rate	
	Alive/observed	%	Alive/observed	%
I	9/11	82	8/9	89
II	8/11	73	7/10	70
III	4/14	29	4/12	33
IV	3/8	38	2/8	25
Total	24/44	55	21/39	54
Without lymph node metastases	17/29	59	15/26	58
With lymph node metastases	7/15	47	6/13	46

in the remaining 3 patients later on due to the appearance of lymph node metastases not demonstrable on admission. Eight patients received preoperative radiation treatment shortly after the electrocoagulation of the primary tumour which was regarded as especially necessary as the dissection was postponed until the coagulation wound was healed. Three patients operated on later and not prophylactically irradiated received postoperative radiation treatment.

Complications. Only complications severe enough to require treatment were included, for example a radiation reaction necessitating admission to hospital: 10 complications in all in 55 patients were registered. The treatment produced no deaths (Table 3).



Survival curves for patients with carcinoma of the vulva and for a female population of Sweden 1965—1970 of the same average age.

Survival. Fifty-five patients with squamous cell carcinomata received treatment of some kind; 2 patients with advanced conditions were not treated. The three- and five-year results appear in Table 4. The absolute five-year survival rate and cure rate was 54 per cent. As could be expected a close correlation existed between the clinical stage and the prognosis (Table 5). A survival curve for the patients from calculations with the actuarial method and a survival curve for a Swedish female population of the same average age (BERKSON & GAGE 1950) is presented in the figure. Six of the 13 patients with verified inguinal node metastases on admission were alive at five years (46 per cent). Fifteen of 26 patients without demonstrable lymph node metastases on admission were alive at five years (58 per cent).

Radiation treatment of lymph node regions. Twelve patients observed for more than three years without palpable inguinal nodes considered to be metastases received radiation treatment to the homolateral (5) or to both inguinal regions (7). These may be compared with 17 patients without clinical metastases, also observed for more than three years, who received no radiation treatment to the inguinal regions. In the first group no inguinal metastases were registered in the subsequent course, but in the second group 3 patients developed metastases. It should be noted that those patients who received inguinal irradiation were on an average in a more advanced clinical stage than the others. The difference observed thus supports the opinion that adequate radiation treatment can sterilize subclinical lymph node metastases.

Table 6

Squamous cell carcinoma of the vulva. Results from the literature

Authors	No. of cases	5-year survival rate %
WAY (1960)	79	61
WAY (1960)	96	49
EDSMYR (1962)	657	35.5
COLLINS et coll. (1963)	74	54
MCKELVEY & ADCOCK (1965)	111	56.7
GOPLERUD & KEETTEL (1968)	156	36
RUTLEDGE et coll. (1970)	164	55.7
BOUTSELIS (1972)	90	52.5
FRANKENDAL et coll. (1972)	57	54

Discussion

The mean duration of history has been reported to be 8 to 10 months (EDSMYR 1962, GOPLERUD & KEETTEL 1968). GUSBERG & FRICK (1970) observed in some cases a history of several years, and similar observations were made in the present series. Reduction of this delay of diagnosis should certainly improve the prognosis.

There are different ways of treating carcinoma of the vulva. Some surgeons prefer extensive surgery as standard treatment, including radical vulvectomy and bilateral groin node dissection, sometimes including deep iliac nodes; some patients are however too old or in too poor physical condition for this extensive treatment. The patients who are treated surgically are thus selected which influences the mortality rate for the operation; in some reports this is about 6 per cent (MCKELVEY & ADCOCK 1965, GOPLERUD & KEETTEL 1968). Extensive surgery of this type is attended by a high incidence of complications. One possible way to lower this risk is to adapt the extension of the operation to the stage of the tumour and the physical state of the patient. Another possibility is to carry out the operation in stages. This is in fact done with many patients treated by the method of Radiumhemmet. Combining surgery with irradiation of the inguinal regions does not seem to influence the frequency of complications. The results attained in this way expressed in three- and five-year survival rates and five-year cure rates are as good as those reported by authors with more extensive surgical treatment. The results expressed in five-year survival rates presented by some authors since 1960 are collected in Table 6. The report of EDSMYR (1962) included 30 cases without confirmation by histology. COLLINS et coll. (1963)

included 9 patients with intraepithelial carcinomas who survived five years. Eighty-seven per cent of the patients reported by GOPLERUD & KEETTEL (1968) had epidermoid carcinomas. Finally RUTLEDGE et coll. (1970) excluded 17 patients who either refused treatment or appeared only at consultations. Most of the patients reported had some sort of surgical treatment.

The mean duration of stay in hospital of patients treated only with electrocoagulation was 23 days. BYRON (1965) reported a mean of 23.8 days for 10 patients treated by conventional surgery. GOPLERUD & KEETTEL (1968) on the other hand reported a mean hospital stay of 51 days for patients in whom radical vulvectomy and groin dissection were performed.

WAY (1951) has convincingly demonstrated that palpation is a poor method of diagnosing inguinal metastases. TAUSSIG (1940) reported that the superficial nodes were involved in 50 per cent of the cases. EDSMYR (1962) stated that histologic verification was evident in only 210 of 260 patients with nodes diagnosed as containing metastases by palpation. BOUTSELIS (1972) recorded 74 per cent accuracy in positive and 87 per cent in negative examinations. So-called prophylactic radiation treatment where no nodes can be palpated seems well grounded. Although the present material is too small to permit any definitive conclusions, the mere fact that no metastases appeared in the irradiated group compared with three in the nonirradiated group suggests that the inguinal regions should be irradiated at least when the probability of subclinical lymph node metastases seems to be large.

SUMMARY

Individualized treatment was given to 57 patients with squamous cell carcinoma of the vulva according to the stage of the disease and their physical states. The absolute five-year survival rate of 54 per cent was comparable to that reported with extensive surgery.

ZUSAMMENFASSUNG

Siebenundfünfzig Patienten mit einem Schuppenzellkarzinom der Vulva wurde eine individuelle Behandlung entsprechend dem Stadium der Erkrankung und dem körperlichen Zustand der Patienten gegeben. Die absolute Fünfjahres-Überlebensrate von 54 % war vergleichbar mit der, wie sie für extensive Chirurgie beschrieben ist.

RÉSUMÉ

Cinquante-sept malades atteintes d'épithélioma pavimenteux de la vulve ont subi un traitement individualisé d'après le stade de leur maladie et d'après leur état physique. Le taux de survie absolue à cinq ans était de 54 pour cent et était comparable à celui donné par une chirurgie étendue.

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