Acta Radiologica Oncology 21 (1982) Fasc. 1

FROM THE INSTITUTE OF RADIOLOGY, UNIVERSITY OF FLORENCE, I-50134 FLORENCE, ITALY.

RESULTS OF RADIATION THERAPY FOR VULVAR CARCINOMA

L. PIRTOLI and M. L. ROTTOLI

The poor results of radiation therapy for vulvar carcinoma that have been reported (ELLIS 1949, TOD 1949) have given rise to the widespread opinion that surgery is the therapy of choice; irradiation is considered indicated only for palliation or in patients with contraindication for operation.

An analysis of some factors with possible influence on results of irradiation, i. e. dose-time parameters, presence or absence of residual tumor at end of treatment, inclusion of the inguinal nodes in the irradiated volume, was made in a series of patients in an attempt to elucidate the value of radiation therapy.

Materials and Methods

From January 1958 to December 1976, 53 patients with proven vulvar carcinoma were referred to this Institute. No treatment had been given to 36, and these constitute the evaluated series. Surgery was considered contraindicated in all these patients due to poor medical condition or too advanced disease. The age distribution ranged from 57 to 90 years, with a maximum incidence in the eighth decade.

Each patient underwent clinical examination and chest radiography. Urography, barium enema and radiography of the pelvis were performed only if involvement of bladder, rectum or pubic bone was possible. Lymphangiography was not routinely performed, due to the advanced age of most patients. The series was retrospectively subdivided according to the TNM classification system (UICC 1978, Table 1). No patient had evidence of hematogenous spread.

Depending on the extension of the disease and the gradation of the patient, radical irradiation was given to 19 cases and palliative to 17. The series covers a rather long period, which implies that the patients were treated by different radiation modalities.

In radically irradiated patients, the primary tumor was usually given external irradiation with a betatron electron beam or a 200 kV roentgen beam through a perineal port. In 5 cases a 50 kV beam was used and in 3 interstitial radium or iridium implant. Except for these last 8 cases the entire vulva was included in the treatment field. Treatment of inguinal nodes was preformed with radical purpose in 8 of the 19 patients (2 with a T1N0, 3 with a T2N0, 1 with a T1N1, 1 with a T2N2, 1 with a T2N3 tumor). Both inguinal regions were irradiated through anterior fields, usually with telecobalt or betatron electrons. The doses ranged from 45 to 85 Gy to the primary tumor, and from 45 to 55 Gy (3 cm depth) to the inguinal nodes. Fractionation schedules and total time of treatment varied, according to the radiation source and the tolerance of the patients.

In the 17 patients receiving palliative treatment, irradiation of the primary tumor was performed with the same techniques as described. In 2 of these patients, inguinal irradiation of the involved side only was performed (1 with a T2N1 and 1 with a T2N3 tumor). The dose never exceeded 45 Gy, neither to the primary tumor nor to the inguinal nodes.

All patients underwent periodical follow-up; only

Accepted for publication 19 January 1982.

5 were lost shortly after end of treatment (all in the group given palliative irradiation).

The results have been expressed as local regression of the primary tumor and the metastatic nodes, as evaluated at the first follow-up one month after end of treatment (36 evaluable patients), and as 5-year survival (31 patients).

Local regression has been analyzed according to the T and N categories and dose-time parameters of the treatment. A multivariate analysis (linear discriminating function) was carried out, according to the method described by ARMITAGE (1975), to identify dose-time values corresponding to an equal probability of complete regression and persistence.

The 5-year survival was analyzed according to the aim of the treatment (i.e. cure or palliation). For the radically irradiated patients a further analysis was carried out according to complete or incomplete regression of the tumor one month after end of treatment, T and N categories and inclusion of the inguinal nodes in the irradiated volume.

The adverse effects were divided into 3 groups, mild: erythema, epitheliolysis, subsequent skin or mucosal atrophy and telangiectasis; medium: stenosis of vaginal ostium, ulcers that healed with medical care, leg oedema; and severe: necrosis.

Results

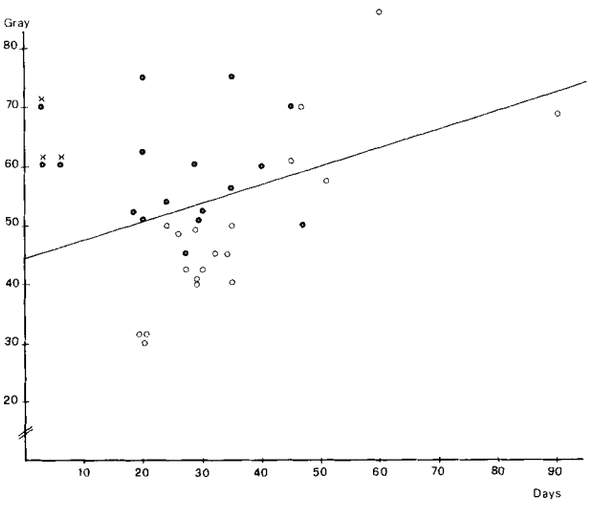
Local regression. Of the 36 patients, a complete regression of the primary tumor was achieved in 17 (47%), an incomplete in 17 (47%); no regression occurred in 2 (6%). The analysis according to T categories appears in Table 2.

Complete regression of the primary tumor was analyzed according to dose-time parameters and the results are shown in the Figure.

Of 5 patients with palpable inguinal nodes, complete regression was achieved only in one case, incomplete regression in 3 cases, and no regression in one case. An analysis of regression of the inguinal nodes according to N categories appears in Table 3.

Five-year survival. All deaths but one were caused by the tumor, one patient died of heart failure 8 years after irradiation, without evidence of malignancy.

Eight patients of the 19 given radical irradiation were alive 5 years or more after end of treatment (Tables 4, 5). Of these, 5 never relapsed (follow-up ranging from 6 to 14 years). In one a relapse of the primary tumor occurred 2 years after the treatment



Complete regression and persistence of the primary tumor, analyzed according to dose-time relationship. The curve has been obtained according to the method described by ARMITAGE (1975) (multivariate analysis, linear discriminating function). Complete regression of 80 per cent is obtained for dose-time values corresponding to the upper area of the graph; the same percentage of persistence is obtained for values corresponding to the lower area. Patients with complete regression (o). Patients with persistence (o). Patients with interstitial implants (x).

Table 1

TNM classification of vulvar carcinoma in 36 patients given irradiation as primary treatment

	T1	T2	T3	T4	Total
N0	10	8	6	1	25
N1	1	2	2	–	5
N2	–	2	–	2	4
N3	–	1	1	–	2
Total	11	13	9	3	36

Table 2

Local regression of the primary tumor, analyzed according to T categories (figures in parentheses indicate patients given radical irradiation)

	Complete regression	Incomplete regression	No response or progression
T1	7/11 (6/9)	4/11 (3/9)	0/11 (0/9)
T2	6/13 (4/7)	6/13 (3/7)	1/13 (0/7)
T3	4/9 (2/3)	5/9 (1/3)	0/9 (0/3)
T4	0/3 (0/0)	2/3 (0/0)	1/3 (0/0)
Total	17/36 (12/19)	17/36 (7/19)	2/36 (0/19)
Per cent	47 (63)	47 (37)	6 (0)

Table 3

Local regression of clinically palpable inguinal node metastases, analyzed according to N categories (figures in parentheses indicate patients given radical irradiation)

	Complete regression	Incomplete regression	No response or progression
N1	1/2 (1/1)	1/2 (0/1)	0/2 (0/1)
N2	0/1 (0/1)	1/1 (1/1)	0/1 (0/1)
N3	0/2 (0/1)	1/2 (0/1)	1/2 (1/1)
Total	1/5 (1/3)	3/5 (1/3)	1/5 (1/3)

Table 4

Five-year survival for radically irradiated patients, analyzed according to T and N categories

	T1	T2	T3	T4	Total
N0	5/8	2/5	1/3	–	8/16
N1	0/1	–	–	–	0/1
N2	–	0/1	–	–	0/1
N3	–	0/1	–	–	0/1
Total	5/9	2/7	1/3	–	8/19

Table 5

Five-year survival for patients with the inguinal nodes radically irradiated, analyzed according to T and N categories

	T1	T2	T3	T4	Total
N0	2/2	2/3	–	–	4/5
N1	0/1	–	–	–	0/1
N2	–	0/1	–	–	0/1
N3	–	0/1	–	–	0/1
Total	2/3	2/5	–	–	4/8

(cured by surgery) and in 2 after 5 years (both dead with recurrence of the tumor in the vulva and the inguinal nodes, at 7 and 11 years).

In all patients surviving 5 years or more complete regression of the tumor was found at the end of the treatment.

Survival values, for radically irradiated patients, were analyzed according to T and N categories (Table 4) and separately for patients with inguinal irradiation (Table 5).

Adverse effects. Mild effects were recorded in all patients, medium in 2 cases in which ulcers developed, which healed with medical care; stenosis of the vaginal ostium and leg oedema were not recorded; a severe effect (necrosis) developed in one case.

Discussion

Only a few reports on radiation therapy of vulvar carcinoma have appeared, each consisting of small series and usually collected over many years. Sometimes patients with squamous cell carcinoma are grouped together with other types of tumor, and the results of irradiation alone are reported together with those of pre- and postoperative treatment (JAFARI & MAGALOTTI 1981). An analysis of the therapeutic results carried out according to the same items that have been adopted in the present report has not been found.

The local response to irradiation of the primary tumor in the present series (47% complete regression) can be compared with the results reported by ACOSTA et coll. (1978). In the surgical specimen of 13 patients operated upon after receiving 35 to 55 Gy in 4 to 6 weeks to the vulvar region they found no macroscopic residual tumor. The present percentage of complete regression does not greatly differ in T1, T2 and T3 categories but the small number of patients in each T category prevents certain evaluation. Dose-time relationship correlated with the probability of complete regression or persistence shows that most complete regressions occur when high doses are administered in a limited time: the discriminating function in the Figure corresponds to Nominal Single Doses (ELLIS 1967) between 1600 and 2200 ret, according to the fractionation schedule (3 to 5 weekly sessions), in the time range of 15 to 50 days.

The local result following irradiation of palpable metastatic inguinal nodes was poor. In only one of 5 patients (with a T1N1 tumor) was complete regression achieved after administration of 55 Gy in 6 weeks both to the vulva and the inguinal nodes. Inguinal recurrence occurred one year after the primary treatment and the patient died 8 months later.

The 5-year survival was 8 of 31 patients (26%). A similar result was reported by ELLIS (1949, 35%), TOD (21%) and KUIPERS (1975, 25%). If only patients given radical irradiation are considered, a survival of 8/19 patients was obtained (42%). This last result, analyzed according to T and N categories, shows that a satisfactory survival rate can be obtained (8/16), provided that no palpable metastatic node is present. In radically treated N0 patients whose inguinal regions were included in the irradiated volume, a good result was demonstrated: 4 of 5 patients were alive at 5 years, which is comparable with the results reported by FRISHBIER & THOMSEN

(1971). They obtained in 33 N0 patients a survival of 70 per cent after radiation therapy extended to the inguinal nodes. These results are similar to the figures in most surgical series (TAUSSIG 1940, WAY 1959, RUTLEDGE et coll. 1970, JAPAZE et coll. 1977).

A severe adverse radiation effect occurred in one patient only, who developed necrosis; previously reported data vary from 4.5 (FRISHBIER & THOMSEN) to 30 per cent (TOD).

Conclusions

The small number of patients in the present series does not allow any definite conclusion on the value of irradiation as primary treatment for vulvar carcinoma. However, some conclusions may be drawn: Complete regression of the primary tumor can be achieved, provided that high doses are administered (up to 85 Gy, NSD ranging from 1 600 to 2 200 ret, at least, in the different fractionation schedules); only patients with complete regression of the tumor shortly after treatment may be definitely cured; survival results are satisfactory in N0 tumors, similar to those obtained by surgery, when prophylactic irradiation of inguinal nodes is performed; no definitive cure can usually be obtained if palpable metastatic lymph nodes are present; in such cases surgery is the only effective therapeutic means.

SUMMARY

Radical radiation therapy was given to 19 patients with vulvar squamous cell carcinoma, and as a palliative to 17. Complete regression of the tumor was achieved in 17 patients (47%), The 5-year survival rate was 8/31 patients (26%) in the overall series and 8/19 patients (42%) in the radically irradiated group.

ACKNOWLEDGEMENT

The authors wish to thank Dr Marta Bucciolini (Medical Physics, Institute of Radiology, University of Florence) for mathematical assistance.

Request for reprints: Dr Luigi Pirtoli, Istituto di Radiologia, Viale Morgagni, Policlinico Careggi, I-50134 Firenze, Italy.

REFERENCES

ACOSTA A. A., GIVEN F. T., FRAZIER A. B., CORDOBA R. B. and LUMINARI A.: Preoperative radiation therapy in the management of squamous cell carcinoma of the vulva. Preliminary report. Amer. J. Obstet. Gynec. 132 (1978), 198.

ARMITAGE P.: Statistica medica, p. 325. Feltrinelli, Milano 1975.

ELLIS F.: Cancer of the vulva treated by radiation. An analysis of 127 cases. Brit. J. Radiol. 22 (1949), 513.

— Fractionation in radiotherapy. *In*: Modern trends in radiotherapy. Volume 1, p. 34. Edited by T. J. Deeley and C. A. P. Wood. Butterworths, London 1967.

FRISHBIER H. J. and THOMSEN K.: Treatment of cancer of the vulva with high energy electrons. Amer. J. Obstet. Gynec. 111 (1971), 431.

JAFARI K. and MAGALOTTI M.: Radiation therapy in carcinoma of the vulva. Cancer 47 (1981), 686.

JAPAZE H., GARCIA-BUNUEL R. and WOODRUFF J. D.: Primary vulvar neoplasia. A review of in situ and invasive carcinoma. 1932–1972. Obstet. and Gynec. 49 (1977), 404.

KUIPERS T.: Carcinoma of the vulva. Radiol. clin. 44 (1975), 475.

RUTLEDGE F., SMITH J. P. and FRANKLIN E. W.: Carcinoma of the vulva. Amer. J. Obstet. Gynec. 106 (1970), 1117.

TAUSSIG F. J.: Cancer of the vulva. An analysis of 155 cases (1911–1940). Amer. J. Obstet. Gynec. 40 (1940), 764.

TOD M.: Radium implantation treatment of carcinoma of the vulva. Brit. J. Radiol. 22 (1949), 508.

WAY S.: Carcinoma of the vulva. Amer. J. Obstet. Gynec. 79 (1959), 692.