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Residual carcinoma of the uterine cervix after low-dose preoperative intracavitary irradiation

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There is an increasing evidence questioning the efficacy of post-operative irradiation in the cases of cervical carcinoma with metastatic pelvic lymph nodes or in the cases where more than a half of the cervix has been invaded by carcinoma. As there is no objective test for the evaluation of radiosensibility of cervical carcinoma, preoperative brachytherapy should be an aid of response of carcinoma of irradiation. With analysing the survival of malignant cells after preoperative brachytherapy we have tried to asses the radiosensibility of the tumor as a prognostic factor in order to make a decision on further treatment.

From 1979 to 1991 a non-randomized group of 109 patients with cervical cancer of stages IB, IIA and IIB underwent radical surgery, 71 of them after preoperative intracavitary brachytherapy. Forty Gy were delivered to point A with 226-Ra or 137-Cs sources. The time interval from irradiation to surgery ranged from 5 to 46 days.

The histopathological examination of surgical specimen revealed no residual disease in 14 patients; most of them underwent surgery between the 20th and the 30th day after brachytherapy. All stages and histopathological types were included. Only in one case positive pelvic lymphatic metastases were present. This patient was post-operatively irradiated. All survived three and more years.

Fifty-seven patients have had residual disease with positive (33,3 %) or negative (66,6 %) pelvic lymph nodes. Patients with positive lymph nodes were postoperatively irradiated. In this group 9 patients died (47,3 %), in the group with negative nodes 7 died (18,4 %) within the first three years.

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Key words: cervix neoplasms-surgery; brachytherapy; prognosis

Introduction

Several attempts were made to find prognostic factors in cervical carcinoma. The first studies were published already in 1912, and in 1959 Wentz and Reagan proposed pathohistological classification with the aim to help clinicians.[1,2] Cytomorphologic and cytophotometric studies, and also studies of irradiation with test doses did not give an adequate answer.[3,4] Most of these studies were on patients with advanced cervical carcinoma who underwent radiotherapy.[5–7]

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Retrospective and also prospective studies of cervical carcinoma showed an increasing evidence questioning the efficacy of post-operative irradiation in patients with lower stages of cervical cancer; they are treated surgically. There are no objective factors to determine the responsiveness of cancer cells to irradiation.

Therefore, we analysed the survived malignant cells after preoperative brachytherapy in order to asses the radiosensibility of the tumor as a prognostic factor and in order to make a decision on further treatment.

Material and methods

From 1979 to 1991 a non-randomized group of 109 patients underwent radical surgery for the cervical carcinoma at the Institute of Oncology, Department of Gynaecology. Seventy-one of them were preoperatively intracavitary irradiated. Patients with stages IB, IIA, and IIB with initial parametrial infiltration, but primary cancer more than 5 cm in the greatest dimension with huge necrosis, haemorrhage, and superimposed infection were preoperatively irradiated. Brachytherapy with radium (226-Ra) or cesium (137-Cs) sources was performed. Tumor dose 40 Gy was delivered to point A.

Seventy-one patients with early cervical carcinoma (median age 44, range 23 to 70 years) underwent pretreatment evaluation. As it has several objectives, the most important of these is to establish the clinical extent of the disease, both in pelvis and elsewhere in the body if possible. Complicating disease, anaemia, infection, impaired function of kidney, and performance status of the patient have also been taken into consideration, although the size and the extent of tumor growth, its histopathological type, and necrosis, haemorrhage or infection of the tumor were taken in account.

All cases were histologically confirmed. Planocellular carcinomas were classified according to the WHO classification, but planocellullar carcinomas, undetermined, were added. This was a retrospective study; the patients were treated at our Institute and after initial diagnostic workup in other centres. That is why the histopathological differentation did not correspond to WHO classification in all cases or was less precisely. A group of patients with adenocarcinoma was added to the patients who underwent both preoperative brachytherapy and than radical surgery.

The time interval from brachytherapy to surgery varied and ranged from 5 to 43 days. There were no objectives for such a different time interval. To determine the optimal time for surgery, we analysed the survival of malignant cells of different histopathological types or the disappearance of cervical cancer after initial brachytherapy. As there are no objective tests to determine the radiosensibility of cancer cells, the local responsiveness could give an information of it.

As surgical treatment, radical hysterectomy and pelvic lymph nodes dissection were performed.

Results

Results of brachytherapy were divided into three groups: no residual disease (NRD) with positive or negative pelvic lymph nodes, residual disease (RD) with positive lymph nodes and residual disease with negative pelvic lymph nodes (Table 1).

Table 1. The outcome of preoperative intracavitary brachytherapy according to the histopathological types of cervical carcinoma.

Histopathological type	Pathological status of specimen		
	NRD/L–	RD/L–	RD/L+
Planocellular cornescens	2	5	4
Planocellular undifferen.	4	19	9
Macrocellular	3	7	4
Microcellular	3	1	2
Adenocarcinoma	1	5	1
	13 (+1 NRD/L+)	37	20

NRD no residual disease, RD residual disease, L+ positive lymph nodes, L– negative lymph nodes. In the group of no residual disease is only one patient with positive lymph nodes.

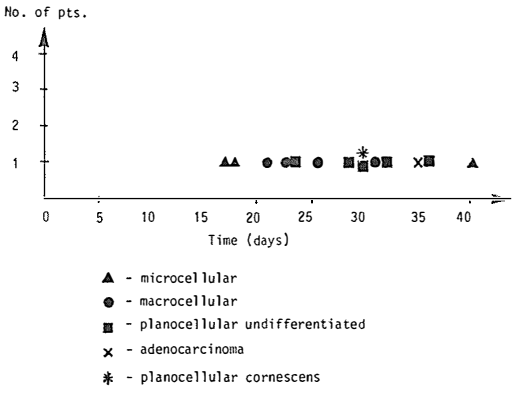

Figure 1. Disaperance of malignant cells after preoperative intracavitary brachytherapy.

As the time interval between brachytherapy and surgery was not determined, it was different. The first negative surgical specimen appeared after 17 days, most of them between 20 and 30 days after brachytherapy (Figure 1). Negative surgical specimen were in all histopathological types.

Comparing with stages, positive and negative surgical specimen were in all (Table 2).

There is a minimum follow-up of three years for all patients. Thirteen patients with NRD and negative lymph nodes survived three years and more, with no evidence of recurrent disease or distant metastases. Only one patient with NRD and positive lymph node was post-operatively irradiated, but no follow-up was possible, because she was from another country.

In the group of patients with RD and negative lymph nodes 7 (18,4 %) of 38 died, in the group of patients with RD and positive lymph nodes 9 (47,3 %) of 19 died within three years.

Table 2. Stages and residual disease after brachytherapy.

Stage of disease	Pathological status of specimen NRD/L–	RD/L–	RD/L +
Stage IB	7	27	8
Stage IIA	2	7	0
Stage IIB	4	4	11
	13 (+1 NRD/L +)	38	19

NRD no residual disease, RD residual disease, L + positive lymph nodes, L– negative lymph nodes.

Discussion

There is little data of the time interval after preoperative irradiation to surgery. As preoperative irradiation consists either of teletherapy or brachytherapy, we collected in our group only the patients intracavitary irradiated to get information about radiosensibility of the tumor. Several studies show that the therapeutic results obtained with radiation or surgery alone or with the combination of both in patients with stage IB and IIA carcinoma of the cervix are approximately the same.[8]

A prospective surgical-pathological study of disease free interval in patients with stage IB of planocellular carcinoma of the cervix published by Delgado identified independing prognostic factors. These factors were: clinical size of the primary tumor, capillary/lymphatic space (CLS) involvement, and depth of tumor invasion.[9]

Post-operatively in the surgical specimen CLS involvement and depth of invasion could not be measured in patients with preoperative radiation because of necrosis and partial disappearance of the primary tumor.

As the time interval was very different, althought not exactly determined, most of the patients underwent surgery between two and six weeks.[8,10] In the group of patients studied, no residual tumor was found between the 17th and the 40th day after brachytherapy.

In the same time-interval most of the tumor disappeared in other cases, although vital malignant cells were still present and huge necrosis of the tumour persisted (groups with residual diseases). One would expect that the combination of preoperative irradiation followed by hysterectomy to remove the residual tumor should improve pelvic control or survival. There are two groups with residual tumors: one with positive and another with negative pelvic lymph nodes. Our results are more or less the same as the ones discussed above, although the mini-

mum follow-up was three years. Three years survival for patients with residual desease and positive lymph nodes is 52,7%, and with residual disease and negative lymph nodes 81,6% and it is consistent with other reports in the literature.[11,12]

Only in the group of patients with no residual disease regardless the clinical stage and the histopathologic types of tumors, a better prognosis can be expected.

Preoperative brachytherapy as a mode of combined therapy for cervical carcinoma can only be accounted for on the basis that preoperative irradiation consistently sterilizes the tumor and reduces its extension into adjoining lymphatics. The only problem is what to do when residual disease is present and pelvic lymph nodes are positive. In our group, patients with positive lymph nodes were post-operatively irradiated, but the survival is at least as disappointing as by the patients who were not irradiated. All patients were irradiated only to the true pelvis, but extended-field irradiation gives better survival as reported.[13]

As most of primary tumor disappeared between the 20th and the 30th day after brachytherapy, delayed surgery is of no choice to get information about radiosensibility of the tumor. As the group with residual carcinoma and positive lymph nodes had a bad prognosis although they are irradiated post-operatively, another mode of treatment should be carried on.

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