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Correspondence and Short Communications

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COMBINED CHEMOTHERAPY, RADIOTHERAPY AND SURGERY IN INFLAMMATORY BREAST CARCINOMA

Inflammatory breast cancer (IBC) is an aggressive type of cancer which constitutes 1–4% of all breast carcinomas. Due to its rapid growth and early metastasizing capability it is generally considered as disseminated already at the time of the initial diagnosis. It is also generally accepted that its primary treatment requires both systematic and local modalities.

We now briefly present a prospective study which, from August 1976 to March 1990, included 35 previously untreated patients with clinical IBC, in whom comprehensive pretreatment evaluation did not show signs of distant metastatic disease. Six of the patients had no clinical evidence of involved lymph nodes, 7 had axillary lymphadenopathy, 18 fixed axillary lymphadenopathy and 4 both axillary and supraclavicular lymphadenopathy. Microscopic diagnosis was obtained by aspiration biopsy and cytology in 23 cases and by incisional biopsy and histology in 12. The mean age was 50 years (range 36–70), and 12 patients were premenopausal, 19 postmenopausal and 4 perimenopausal. Chemotherapy (CT) was administered as a combination of doxorubicin, 50 mg/m^2 i.v. on day 1, and cyclophosphamide, 500 mg/m^2 i.v. on day 1 every 21 days up to 3 cycles. Radiotherapy (RT) was given with start at the first CT cycle by a ^{60}Co-machine up to a total dose of 60 Gy, 2 Gy/day, 5 days a week. Two tangential fields for breast and axilla and one anterior field for supraclavicular fossa were usually employed. Response to treatment was evaluated according to UICC criteria. A modified mastectomy was performed in all patients who had achieved any clinical response. Three or four weeks after surgery, CT was again started in the fashion described previously and up to 3–4 additional cycles were given. Postmenopausal and estrogen-receptor positive premenopausal patients were given tamoxifen 20 mg/day for two years after finishing chemotherapy. Estradiol receptors in breast tissue were determined in 12 patients with diagnoses based upon biopsy and of those 7 were post-, 4 pre- and 1 perimenopausal. The estradiol receptors were positive in 7 of these patients (5 post- and 2 premenopausal) with a range of 15–62 fmol cytosol protein. Three out of these 7 patients are alive and free of disease; 2 are dead and one is alive with disease. Three out of the five estradiol receptor negative patients are dead, one is alive with disease and one alive free of disease. No conclusions can of course be drawn from these data.

Survival and disease-free survival were calculated by the Kaplan–Meier method from time of diagnosis until last control or time of death and/or time of relapse. Mean follow-up time was 40 months (range 12–158 months).

Results. The protocol was fully respected in 33 patients (94%). Two patients were not operated after the induction treatment; one because of progression and the other for medical reasons. All 35 patients were eligible for toxicity and response studies. Toxicity—mainly haematologic and gastrointestinal—was mild and easily managed by medical treatment. Only one patient presented grade 3 haematologic toxicity. There were no treatment-related deaths.

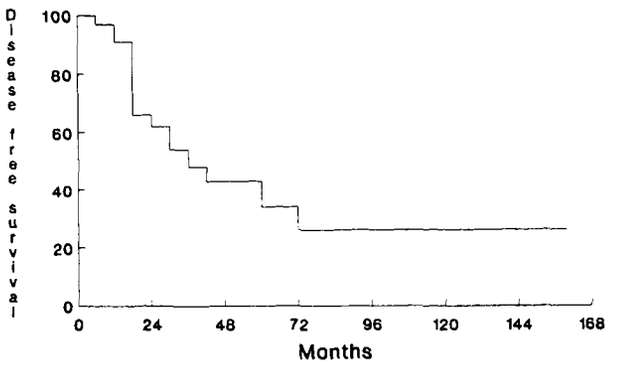

Fig. 1. Disease-free survival in 35 patients with inflammatory breast cancer.

All but one of the patients achieved clinical response after CT + RT with complete response in 19 (54%) and partial response in 15 patients (42%). Ten out of 19 clinical responders achieved a complete pathological response. The local control rate was 88% and 86% at 5 and 10 years respectively. Median survival time was 51 months (SE ± 14 months) for the group as a whole. Disease-free survival and survival were 48%, 34%, 26% and 58%, 43%, 32% at 3, 5, 10 years respectively (Figs. 1 and 2).

Discussion. In historical series with only loco-regional therapeutic procedures the 2-year survival was reported to be less than 10% (1) and it seems very likely that the introduction of chemotherapy has improved the prognosis of IBC. However, several features, such as suitable CT agents, treatment time and best way to combine CT with loco-regional therapy remain under discussion. Reported response rates to CT ranges from 14% to 98% (2–4). Although doxorubicin has been used in the majority of these studies, a good comparison between different CT schemes cannot be done due to differences in drugs, doses and response evaluation. IBC is a locally aggressive tumour which means that also local therapeutic approaches are of great importance. DeLena et al. (2), and Pouillart et al. (5) reported 100% local control rates after irradiation with 60–70 Gy. Bruckman et al. (6) reported a 65% actuarial local control rate at 5 years in 18 IBC patients treated with RT; local control was achieved in 11 out of 13 patients who received doses >60 Gy and only in one out of 5 who received doses <60 Gy. Similar observations have been reported by other authors (7). The role of surgery is still discussed. According to Perez et al. (8), a 30% relapse rate is obtained if only one local therapy modality is used; this drops to 5–10% when both surgery and radiotherapy are applied.

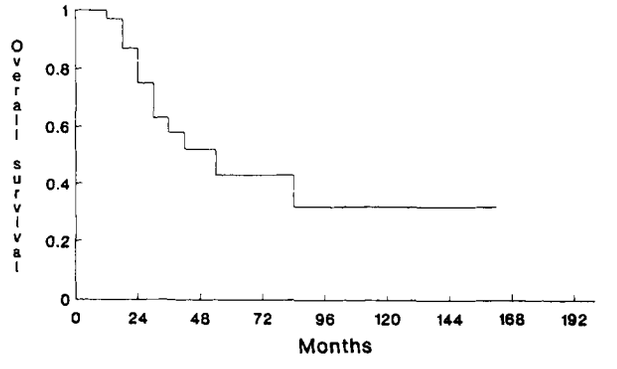

Fig. 2. Survival in 35 patients with inflammatory breast cancer.

Radiotherapy either alone or in combination with surgery was used in 107 IBC patients followed by Fields et al. (9). Relapse appeared in 45% of the patients. Only 19% of the patients relapsed in the combined surgery–radiotherapy group; whereas 70% relapsed in the non-surgery group. CT was included in both treatment groups. Also other authors have suggested that the local control is improved when surgery is included (10, 11). Shafer et al. (10) in a study of 21 patients, concluded that both mastectomy and loco-regional radiotherapy are required to obtain optimal local control. In their series, all patients underwent mastectomy but 7 of them did not receive radiotherapy; all the latter patients relapsed whereas among the 14 patients with combined RT and surgery only one patient who had received 33.5% relapsed (the other patient had received 50–65 Gy). Like Fields et al. (9) we are of the opinion that mastectomy allows an histologic immediate evaluation of the response to treatment and also that in some cases it gives a valuable reduction of the tumour burden. We therefore advocate the use of surgery also in chemotherapy–radiotherapy responsive patients. However, the best local management remains to be defined. The reported relapse-free 5-year survival after multimodal treatment usually ranges between 27 and 54% (13–15), whereas 5-year survival between 30 and 50% has been reported (3, 16). Our results are thus similar to those reported in the literature. However, it remains evident that about two-thirds of the patients with IBC will die from metastases even after multimodal treatment. Multicentric and randomized studies are needed to determine the best therapeutic approach for IBC. There is also a need for new ideas concerning prognostic and predictive factors. Intensive chemotherapy, made possible by growth factors and autologous bone marrow transplantation, may also be of special interest in IBC.

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OVARIAN CANCER—NOT EVERY ABDOMINAL MASS IS A RECURRENCE

Despite high response rates for chemotherapy, many ovarian cancer patients eventually will have progressive disease requiring additional therapy. In case of a clinical deterioration in a known ovarian cancer patient, the chance of having a recurrence is far higher than the possibility of a non-malignant pathology, but the latter is not completely excluded. In case of doubt, histological proof of the lesion is mandatory. For most of these patients a second-look operation is indicated not only for the confirmation of malignancy but also for reduction of the tumor mass before chemotherapy. This debulking surgery may result in enhanced survival and optimize patients for further treatment. We recently saw a patient with a large intrapelvic mass clinically believed to represent recurrence of an ovarian cancer. The question was asked whether to give chemotherapy to decrease the tumor burden and possibly render a second look operation easier. After discussion, however, we preferred a primary surgical exploration. This turned out to be a complete surprise.

Case report. A 72-year-old white female was admitted in February 1993 to the department of gynecology with a deterioration of the general status, vague low abdominal pain and a gastrointestinal subobstruction of two weeks duration. Almost two years earlier (March 1991) she had underwent abdominal hysterectomy with bilateral salpingo-oophorectomy and omentectomy for a right-sided ovarian cancer. During the operation a large cyst