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MALE BREAST CANCER

Report of a series of 50 cases

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Fifty consecutive cases of male breast cancer (MBC) treated in a single institution were studied. Presentation of the disease, histology, pattern of relapse, and major prognostic factors were similar to those known in female breast cancer (FBC). Five-year disease-free interval and survival were 59% and 75% respectively. Endocrine therapy for treatment of metastatic MBC was proven to be effective with a response rate of about 50% of patients, unselected with regard to oestrogen receptors. A group of patients receiving adjuvant treatment showed lower recurrence rate and a trend toward better outcome than similar stage patients without adjuvant treatment. The present study combined with the recent literature suggests that MBC and FBC are biologically comparable and that inference from experience in treatment of FBC may be justified.

Male breast cancer (MBC) is a rare disease accounting for about 0.7–1% of all breast cancers (1). Breast cancer makes up approximately 0.2–1% of malignancies developing in males (2). Since MBC is rare, the literature about it, especially with regard to prognostic factors, adjuvant therapy, and treatment of advanced disease, is scarce. We have therefore reviewed the experience with patients referred to our hospital for treatment of MBC.

Material and Methods

The records of all patients referred to the Hospital Sta. Creu i St. Pau with the diagnosis of MBC were reviewed. Information relating to patient characteristics, pathological data, treatment, and outcome was collected. The patients were staged according to UICC using the same criteria as applied for female breast cancer (FBC) (3). When oestrogen-receptor (ER) assays were performed, the dextran charcoal method (4) was used (positive if specific oestrogen binding > 10 fmol/mg of cytosol protein). Survival curves were calculated using the Kaplan-Meier method, and differences were assessed with the log-rank test. Patients lost to follow-up were removed from risk after the last evaluation by the physician

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Results

Patient characteristics. Fifty patients with histologically proved MBC were treated at our institution over a period of 26 years (1964 to 1990): 5 (10%) before 1970, 16 (32%) between 1970 and 1979, and 29 (58%) between 1980 and 1990. Their characteristics are summarized in Table 1. No patient had a history of gynaecomastia, clinical Klinefelter's syndrome (no plasma steroid levels and chromosomal analysis were performed), radiotherapy, or oestrogen therapy. Four patients (8%) had first-degree related females with breast cancer. Pathological staging was possible in 33 patients (66%) (30 axillary dissection, 2 pT4 and 1 pM1). Nine patients could not be fully staged due to imprecise information regarding T or N status. However, the available data were sufficient to ascertain that those patients were neither stage I nor stage IV.

Treatment and outcome. Most patients were referred for postoperative treatment: 48 were treated by either radical or simple mastectomy, one by lumpectomy, and one had a

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Table 1

Patient characteristics in male breast cancer

Characteristic	Number of cases
Number of patients	50
Median age (range)	60 years (38–82)
Presenting symptom	
breast mass[1]	49 (98%)
bone pain	1 (2%)
Location	
left	25 (50%)
right	25 (50%)
Median duration symptoms (range)	8 months (1–90)
Stage	
I	8 (16%)
II	21 (42%)
III	8 (16%)
IV	4 (8%)
Unknown[2]	9 (18%)
T status[3]	
T1	14 (28%)
T2	18 (36%)
T3	3 (6%)
T4	8 (16%)
TX	7 (14%)
N status[3]	
N0	13 (26%)
N1	20 (40%)
N2	2 (4%)
NX	15 (30%)
M status	
M0	46 (92%)
M1	4 (8%)
Histology	
infiltrating ductal	45 (90%)
in situ ductal	5 (10%)
Oestrogen receptor (n = 12)	
positive	11 (92%)
negative	1 (8%)

[1] The majority situated in the subareolar region. In 10 patients (20%) associated with nipple retraction and/or ulceration. Five patients had sanguineous nipple discharge.
[2] But neither stage I nor IV (see text).
[3] TX NX: T and N status unknown.

biopsy only. Thirty patients had axillary lymph node dissections performed; 11 (37%) had negative and 19 (63%) had positive lymph nodes. Postoperative radiotherapy was given to 37 patients (74%). Overall, 14/46 (30%) patients without metastatic disease at diagnosis had recurrent disease (bone in 9 patients (64%), lung in 8 (57%), locoregional in 5 (36%), and other sites in 5 (36%)). No patient had liver metastases at initial recurrence. None of the 8 stage I patients had relapse after surgery (median follow-up 60 months; range 9–171). Three patients with stage IV disease died of breast cancer and one was lost to follow-up with progressive disease (median survival was 16 months (range 1–50)). There were 38 non-stage I or non-stage IV patients in this series (21 stage II, 8 stage III, and 9 stage unknown but neither stage I nor IV) (Table 2).

Before 1979, no adjuvant treatment was given. Since 1980, most patients with stage II (N+) and stage III have received adjuvant endocrine therapy and/or chemotherapy. In total, 17 patients were treated in an adjuvant setting: 6 received tamoxifen (TMX), 4 CMF (cyclophosphamide, methotrexate, and 5-fluorouracil), 1 FAC (5-fluorouracil, doxorubicin and cyclophosphamide), 5 CMF plus TMX, and 1 FAC plus TMX. Of the 21 patients without adjuvant treatment (median follow-up 65 months), 11 (52%) developed recurrent disease, and of the 17 patients treated adjuvantly (median follow-up 32 months), only 3 (18%) did so (Table 2).

Ten patients had hormonal treatment for metastatic disease (4 initial stage IV and 6 at recurrence). Four underwent orchidectomy, 4 oestrogen therapy, and 2 TMX. Objective remission, including two complete responses (CR), was seen in 5 patients (50%; 2 ER-positive, 3 ER-unknown) for a period ranging from 3 to 60 months (median duration 34 months). Two patients had stable disease for 10 and 12 months respectively (1 ER-positive, 1 ER-unknown). Interestingly, one patient (ER-unknown) received oestrogen therapy for lung metastases achieving CR which lasted 60 months. He then developed bone progression and received TMX which resulted in CR for 39 months.

Table 2

Non-stage I/IV MBC patients with or without adjuvant treatment

Patient characteristics	No adjuvant treatment	Adjuvant treatment
Number	21	17
Median age (range)	63 (42 to 76)	60 (38 to 82)
Stage		
II	12 (57%)	9 (53%)
III	3 (14%)	5 (29%)
Unknown[1]	6 (29%)	3 (18%)
T status		
T1 or T2	14 (67%)	8 (47%)
T3 or T4	3 (14%)	6 (35%)
Unknown	4 (19%)	3 (18%)
Nodal status		
Negative	5 (24%)	0 (0%)
Positive	7 (33%)	13 (76%)
Unknown	9 (43%)	4 (24%)
Median follow-up in months (range)	65 (3 to 185)	32 (4 to 72)
Number with recurrent disease	11 (52%)	3 (18%)
Estimated 5-yr DFI	47%	72%

[1] But neither stage I nor stage IV. DFI: disease free interval.

Survival analysis. The actuarial 5-year survival and disease-free interval (DFI) were 75% and 59% respectively (Fig. 1). There was a significant worsening of DFI from stage I to III ($p = 0.005$) (Fig. 2) and of survival from stage I/II to stage III/IV patients ($p = 0.009$) (Fig. 3). The T status did significantly affect the survival ($p = 0.006$) (Fig. 4). There was a trend toward improved DFI and survival in both patients with negative nodes (compared to positive nodes) and non-stage I/IV patients who received adjuvant treatment (compared to no adjuvant treatment). There was no trend suggesting any prognostic impact of age at diagnosis.

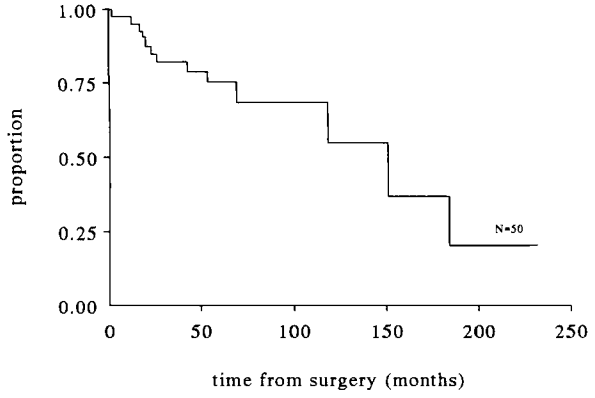

Fig. 1. Survival from surgery for the 50 patients included in this study. The actuarial 5-year survival rate was 75%.

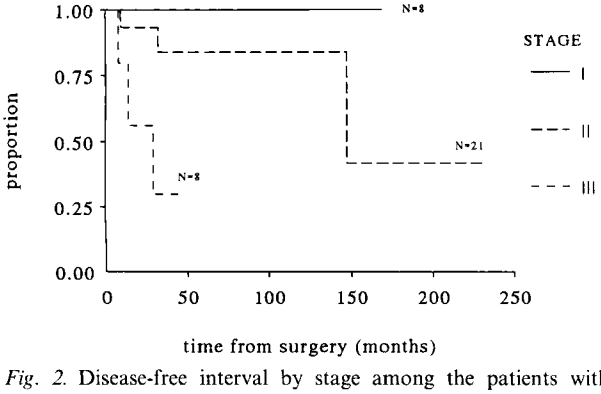

Fig. 2. Disease-free interval by stage among the patients with non-metastatic disease at presentation ($p = 0.005$). The 9 patients with unknown stage were excluded.

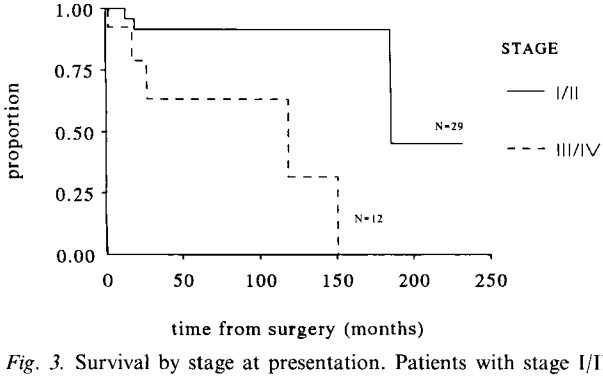

Fig. 3. Survival by stage at presentation. Patients with stage I/II did better than stage II/IV patients ($p = 0.009$). The 9 patients with unknown stage were excluded.

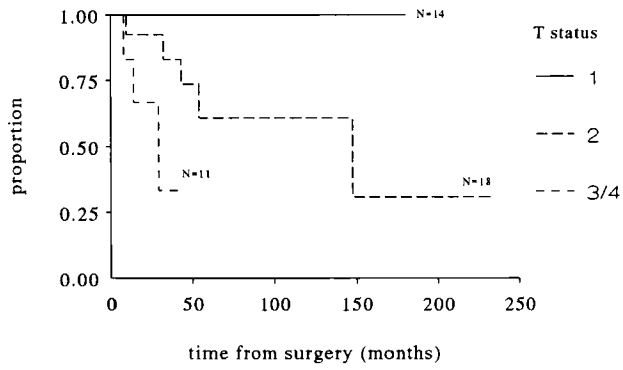

Fig. 4. Survival according to T status at presentation ($p = 0.006$). The 7 patients with unknown T status were excluded.

Discussion

We found 4 patients (8%) who had female relatives with first-degree breast cancer. As it is not sure whether full detailed family histories were taken, the real number could have been even greater. Pedigrees of MBC patients having first-degree relatives with breast cancer have been reported (5), and case–control studies have shown an increased risk of breast cancer in first-degree relatives of MBC patients (6). We would advise first-degree relatives of MBC patients to undergo periodic check-ups.

Some earlier reports describe a more aggressive biological behaviour of MBC than of FBC (7–9). In contrast, our study (with most patients treated after 1980), in agreement with more recent reports (10–12), suggests that its natural history parallels that of FBC (13). MBC and FBC appear to share several major clinical and biological features, some of which used to decide treatment. These features include presenting symptom (breast mass) (13), commonest histology (ductal carcinoma) (14, 15), stage at presentation (> 50% stage I/II) (10, 12, 13, 17, 18), sites of initial relapse (bone, lung) (13), and major prognostic factors (stage, T, and N status) (12, 13, 17, 20, 21). Some discrepancies between earlier and more recent reports may be due to earlier diagnosis in recent years (median duration of symptoms about 18 months in older studies (14, 15) and 3–12 months in recent studies (10, 12, 18). Absence of lobular carcinoma histology (8, 12, 14–17) and liver metastases at initial relapse (12) in MBC has been reported before, and the reasons for this remain unknown. The median age of 60 years in our series is comparable to the literature (10, 14, 15), and is about 10 years higher than in FBC (13). As in the present study, most authors report that age is not a prognostic factor in MBC (11, 14, 18); however, in one series age was reported to be an independent prognostic factor (21). Positive ER is found in 80–90% of MBC (10, 14, 17), which is almost double that in FBC (13).

Endocrine therapy has been proven effective in metastatic MBC with a response rate of about 50% in

Table 3

Studies of adjuvant treatment in male breast cancer

Reference	No. of patients	Stage	Adjuvant treatment	No. with recurrent disease	Estimated 5-yr DFI	Estimated 5-yr survival	Median follow-up in months
Bagley et al. (27)	24	II	CMF	4 (16%)	NS	>80%	46
Patel et al. (28)	11	II/III	FAC or CMF	4 (36%)	NS	>85%	52
Ribeiro et al. (29)	39	II/III	TMX	NS	56%	61%	49
Izquierdo et al.[1]	17	II/III	TMX/ CMF/ FAC[2]	3 (18%)	72%	80%	32

DFI: disease free interval; CMF: cyclophosphamide, methotrexate, 5-fluorouracil; FAC: 5-fluorouracil, doxorubicin, cyclophosphamide; TMX: tamoxifen; NS: not specified; [1] current study; [2] see text.

unselected patients, as regards ER (12, 14, 15, 18, 22–24). TMX seems to be a preferable first choice as it gives about the same response rate as orchidectomy and lacks significant side-effects (14, 18, 22–24). As illustrated by one of our patients who had CR to second-line treatment with TMX, progression after previously effective hormonal therapy should not exclude patients from subsequent hormonal maneuvers (12, 21, 24, 25). The ER status seems to be predictive of response (14, 25). A response rate of 71% has been reported in ER-positive patients (14), while in our review of the literature, no responses were found in 10 ER-negative patients (22–26). If this is confirmed in a large group, it may be responsible to use chemotherapy as first-line treatment for these patients, similar to FBC (13, 20).

Adjuvant chemotherapy or TMX affords a survival benefit in FBC (13, 20). To our knowledge, only three series using adjuvant treatment in MBC have been reported (Table 3) (27–29). All suggest a significant benefit of adjuvant treatment compared to historical controls. Our results are similar to those studies (Table 3), and compare favourably with earlier reports of similar stage patients (16, 18). In addition, we observed a trend toward better outcome in 17 patients receiving adjuvant treatment compared with 21 patients who did not receive it, despite the adjuvant treatment group including more patients with stage III, T3/T4 status, and positive nodes (Table 2). As all these studies involve some drawbacks like small sample size, comparison with historical data, and short follow-up period, the results must be viewed with caution. However, this may be the only plausible approach to deal with this rare disease. These encouraging data, and those extrapolated from FBC (13, 20), support the use of adjuvant systemic therapy for stage II (N+) and stage III MBC (12, 20, 27–29). As far as we know, there is no reported experience with adjuvant treatment in node-negative MBC. Similar strategy to that in node-negative FBC may be reasonable (10–13). Controlled therapeutic studies in FBC are not likely ever to become available. The present study combined with the recent literature suggests that MBC and FBC are biologically comparable, and supports a similar approach to systemic treatment in both cases.

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