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Scar and non-scar ductal cancer of the female breast

Observations on patient age, tumour size, and hormone receptors

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Summary. Ductal cancers of human female breasts were classified as scar or non-scar type. Of 274 cancers, 144 were scar and 130 non-scar type. Estrogen and progesterone receptors were determined in 191 cases; the cancer was classified as hormone receptor positive if either the estrogen or progesterone receptor level, or both, was over 10 fmol/mg of cytosol protein. The mean age of patients with scar cancer was higher than that of patients with non-scar cancer (59.8 ± 13.5 and 49.4 ± 12.0 years, respectively, $p < 0.001$). A higher number of hormone receptor positive cases was found among the scar than among the non-scar cancers (68 of 94 and 48 of 97 cases, respectively, $p < 0.01$). Within the two groups, the patient's age was not associated with hormone receptor status. Our results indicate that the generally observed tendency for postmenopausal breast cancer to be more often hormone receptor positive than premenopausal cancer may be associated with the histological type and not with the patient's age. Scar cancers were also smaller than 2 cm more frequently than non-scar cancers ($p < 0.001$) and as a group, ductal cancers were smaller in postmenopausal patients than in premenopausal patients ($p = 0.088$). Again, this tendency seemed to be linked with the type of cancer rather than with the patient's age.

Key words: Breast cancer – Scar type – Patient age – Tumour size – Hormone receptors

Introduction

Many female breast cancers grow as macroscopically visible stellate fibrotic scars. This type of breast cancer has been recognized for a long time and many of these lesions are classified as infiltrating ductal cancers (Foote and Stewart 1946; Azzopardi 1979). About half of breast cancers were found to be of scar type in the study of Linell et al. (1980, 1981) in another study the scar type was found in 38% of infiltrating breast cancers (Fisher et al. 1983). In addition to the typical growth pattern, scar cancers have been suggested to originate from small, unremarkable radial scars (Linell et al. 1980, 1981); thus it may be possible that they have a different histogenesis from that of the non-scar type. The latter often has prominent, widely distributed intraductal growth, lobular cancerization and little surrounding elastosis in the early stages (Foote and Stewart 1946; Azzopardi 1979; Linell et al. 1980; Fisher et al. 1983). Most scirrhous cancers are probably identical with the scar type and they have been suggested to arise in the terminal ductal lobular unit (Wellings 1980).

The mean age of patients with scar or non-scar cancers was found to be about the same in a study which included cancers detected in mammographic mass screening (Linell et al. 1980). The average size of scar cancers was reported to be 2–3 cm (Foote and Stewart 1946) they were statistically more often ≤ 2 cm than non-scar cancers (Fisher et al. 1983). Moreover scar and non-scar cancers differed with respect to many other histopathological features (Fisher et al. 1983).

The present study was undertaken further to evaluate the clinicopathological differences between the scar and non-scar type of ductal cancers of the female breast, namely the patient's age, tumour size, and the estrogen and progesterone receptor content.

Materials and methods

All the breast cancers of this study were found in patients examined for breast lumps or discomfort; no cases from mammo-

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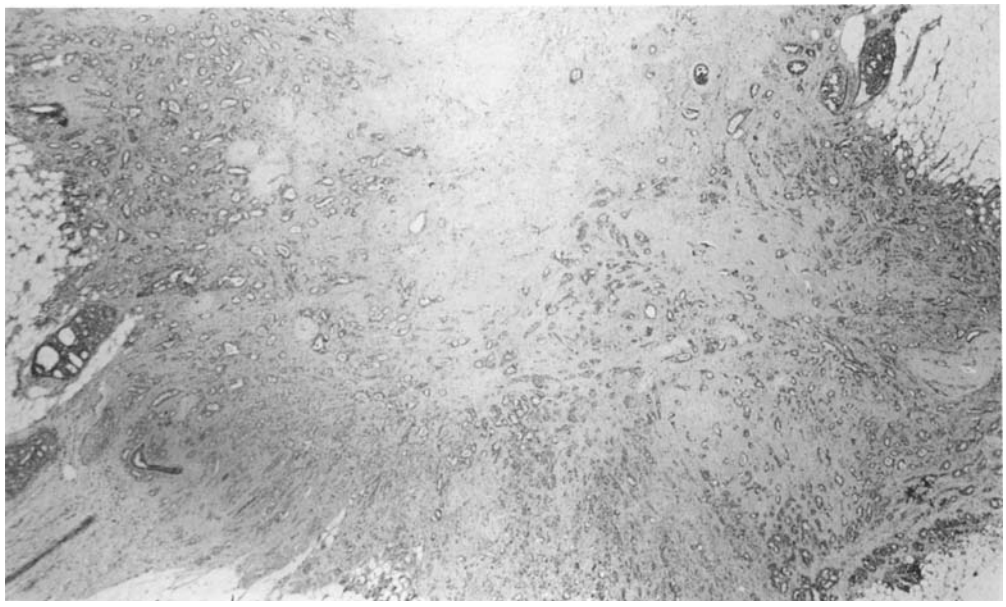

Fig. 1. Scar type of ductal breast cancer (× 25)

graphic mass screenings were included. A total number of 302 consecutive female breast cancers were diagnosed histologically or verified at the Department of Pathology, Jorvi Hospital, Espoo, Finland during 1979–1984. After exclusion of 27 typical cases that were not ductal (20 lobular, 4 mucinous, 1 medullary, 1 squamous and 1 carcinomatous lymphangitis) according to the criteria of Azzopardi (1979) the remaining 274 ductal cancers were re-examined. The series contained one patient with ductal cancer in one breast and lobular cancer in another breast. In one patient with bilateral ductal cancer, the larger tumour was included in the study. After reviewing the haematoxylin-eosin stained sections at low microscopic magnification (× 25), all ductal cancers were classified as either scar or non-scar type according to the pathological features described by Linell et al. (1980, 1981). The criteria for the scar type were 1) stellate shape of the tumour with radially distributed fibrous bands to the surrounding area, 2) radially infiltrating cancer cells in connective tissue, 3) a fibrosclerotic center with abundant elastoid material containing few or no cancer cells. Non-scar cancers lacked these features; they had prominent, widely distributed intraductal growth of cancer, and lobular cancerization was common. Tumour size was determined from macroscopical measurement of bisected specimen and/or from microscopic sections and was divided in two groups; <2 cm or ≥ 2 cm. In 191 cases cancerous tissue sample was analyzed for estrogen (ER) and progesterone (PgR) receptors (Medix Oy, Kauniainen, Finland). Values greater than 10 fmol/mg of cytosol protein were considered to be receptor positive (Wittliff 1984). The cancer was classified as hormone receptor positive if it was positive for either ER or PgR, or for both. Patients younger than 55 years were considered as premenopausal, those 55 years or older as postmenopausal (Wittliff 1984). The results were statistically tested with student's t-test and x^2 (2×2) test.

Results

A total number of 274 ductal cancers of female breasts were classified as either scar or non-scar type; 144 scar cancers (Fig. 1) and 130 non-scar cancers (Fig. 2) were found. ER and PgR receptors were determined in 191 cases. In 94 scar cancers 68 cases (72%) were hormone receptor positive; the following combinations were found: ER+ and PgR+, 42 cases (62%); ER+ and PgR−, 11 cases (16%); and ER− and PgR+, 15 cases (22%). In 97 non-scar cancers 48 cases (49%) were hormone

Table 1. Cancer type, patient's age and hormone receptor (HR) positivity of ductal cancer of human female breast. The cancer was considered HR positive if it contained either estrogen or progesterone receptors, or both over 10 fmol/mg of cytosol protein

Cancer type HR positivity	Cases (No)	Patient's mean age	SD	Age range	P[a]
Total series	274	54.9	13.8	25–93	
Scar	144	59.8	13.5	31–93	
Non-scar	130	49.4	12.0	25–79	0.001[a]
HR determined	191	53.4	12.9	25–86	
Scar	94	58.2	12.2	31–86	
Non-scar	97	48.8	11.8	25–79	0.001[a]
HR+ (scar and non-scar)	116	54.9	13.3	35–86	
HR− (scar and non-scar)	75	51.2	12.0	28–79	NS[b]
Scar, HR+	68	59.2	12.4	37–86	
Scar, HR−	26	55.7	11.6	31–79	NS[b]
Non-scar, HR+	48	48.8	12.1	25–73	
Non-scar, HR−	49	48.8	11.6	28–79	NS[b]

SD; standard deviation. [a] P; statistical significance. [b] NS; not significant

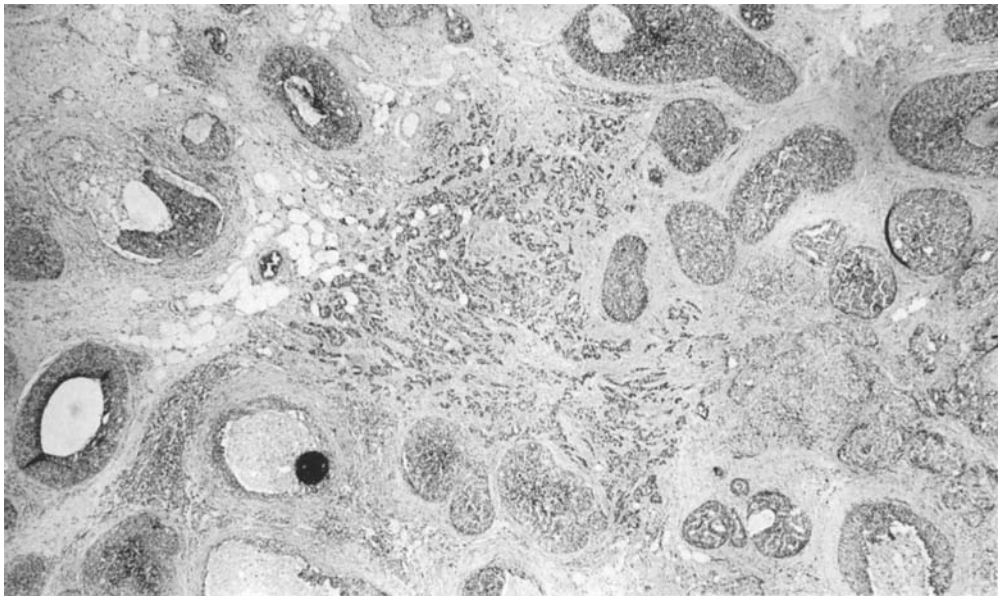

Fig. 2. Non-scar type of ductal breast cancer (×25)

Table 2. Cancer type, hormone receptor (HR) content (see Table 1) and menopausal status

Cancer type HR status	Cases (No)		P[a]
	<55 years	≥55 years	
Total series			
HR+	60	56	
HR−	48	27	NS[b] (0.0906)
Scar			
HR+	26	42	
HR−	12	14	NS[b] (0.4913)
Non-scar			
HR+	34	14	
HR−	36	13	NS[b] (0.7647)
Scar, HR+ and HR−	38	56	
Non-scar, HR+ and HR−	70	27	<0.0001[a]

[a] P; statistical significance. [b] NS; not significant

Table 3. Hormone receptor (HR) status (see Table 1) of cancer type and of non-scar cancers according to in situ and infiltrating type

HR status	Cases (No)		P[a]
	Scar	Non-scar	
HR+	68	48	
HR−	26	49	<0.01 (0.0016)[a]
HR+		In situ 1; infiltrating 32	
HR−		In situ 6; infiltrating 31	NS[b] (0.0629)

[a] P; statistical significance. [b] NS; not significant

receptor positive; the following combinations were found: ER+ and PgR+, 33 cases (69%); ER+ and PgR−, 6 cases (13%); and ER− and PgR+, 9 cases (19%).

In both the entire series and that in which hormone receptors were determined the mean age of patients with scar cancer was statistically significantly higher (just at the menopause), than that of patients with non-scar cancer (Tables 1, 2). The mean age of patients with hormone receptor positive tumours was higher than that of hormone receptor negative tumours, although the difference was not statistically significant (Tables 1, 2). In scar and non-scar cancers there was no statistically significant difference between the mean age of patients with hormone receptor positive or negative tumours (Tables 1, 2). In the non-scar cancer group, seven cancers were classified as in situ, and were rarely positive for hormone receptors. The difference was, however, not statistically significant when compared with infiltrating non-scar cancer (Table 3).

Classification of hormone receptor positive cancers according to scar and non-scar type revealed that the scar type cancer was statistically significantly more often hormone receptor positive than the non-scar type (Table 3).

Table 4. Size of ductal cancer distributed according to cancer type and menopausal status

Size (cm)	Cases (No)		P[a]	Cases (No)		P[a]
	<55 years	≥55 years		Non-scar	Scar	
Total series						
<2	65	71		47	89	
≥2	80	58	NS[b] (0.0875)	83	55	0.0001[a]
Non-scar						
<2	32	15				
≥2	58	25	NS[b] (0.8140)			
Scar						
<2	33	56				
≥2	22	33	NS[b] (0.7243)			

[a] P; statistical significance. [b] NS; not significant

The size of ductal cancers with respect to menopausal status and cancer type is given in Table 4. Scar cancers were smaller than 2 cm significantly more often than non-scar cancers. The menopausal status was not related to tumour size in the scar and non-scar groups. In the entire series there was a tendency for postmenopausal ductal cancers to be smaller than 2 cm more often than premenopausal ones. This tendency is well explained by different distribution of scar and non-scar cancers in respective age groups (Tables 1, 2).

Discussion

In the present study ductal cancers of human female breast were classified as scar and non-scar type according to the criteria presented by Linell et al. (1980, 1981). The scar type has been further divided into five subtypes by Fisher et al. (1983), but this division was not applied in the present study. Slightly over half of the ductal cancers were found to be of the scar type. Scar cancers were found significantly more often in older patients than non-scar cancers; no such difference was found in previous study (Linell et al. 1980). Scar cancers in the present study were smaller than non-scar cancers, a finding which agrees with previously reported results (Fisher et al. 1983), and this difference was observed both in premenopausal and postmenopausal patients. The difference is well explained by a prominent fibrosclerotic stromal response in scar cancers, which produces a hard and rather solitary tumour, which is more easily detected than non-scar cancers (Foote and Stewart 1946; Linell et al. 1980; Fisher et al. 1983). In the present study ductal cancers, when considered as a group, were smaller in postmenopausal patients than in premenopausal patients. This finding is explained by the distribution of scar and non-scar types in the respective age groups.

There are numerous studies in which the hormone receptors of breast cancers have been correlated with many histopathological features of cancers (see ref. Stanford et al. 1986). Little attention has, however, been paid to scar and non-scar type of breast cancer and their hormone receptors. One typical feature of scar cancer, the marked accumulation of elastoid material, is often visible even macroscopically but occurs rarely, and then only in small amounts, in non-scar cancer (Azzopardi 1979; Linell et al. 1980; Fisher et al. 1983). Marked elastosis of breast cancers has reported to correlate positively with the presence of hormone receptors, especially ER (Masters et al. 1976; Fisher et al. 1980; Millis 1980; Glaubitz et al. 1984; Lima-De-Almeida et al. 1985) these findings agree with the results of the present study, which demonstrated a higher frequency of hormone receptors in scar cancers than in non-scar cancers.

Breast cancers are more often hormone receptor positive in postmenopausal patients than in premenopausal patients (Jensen 1975; Knight et al. 1980; Vorherr 1980; Stanford et al. 1986); this tendency was also observed in the present study. Scar cancers were statistically significantly more often hormone receptor positive than non-scar cancers. It should be noted that there was no significant difference in hormone receptor positivity between premenopausal and postmenopausal patients in the scar and non-scar cancer groups. Thus it seems that hormone receptor positivity is linked with the type of ductal cancer but not with the patient's age. The higher number of hormone receptor positive ductal cancers at postmenopause is explained by the higher number of scar cancers than non-scar cancers and the higher number of hormone receptor positive tumours in scar cancers than in non-scar cancers.

In non-scar cancers in the present study, the in situ type contained hormone receptors less frequently than infiltrating cancer, but the difference was not statistically significant. Similar observations on hormone receptor positivity between in situ and infiltrating cancer have been reported previously (Lesser et al. 1981). It is possible that, in the beginning, non-scar cancers are hormone receptor negative and that later, when the growth reaches the infiltrating phase, some cancer cells become "differentiated" hormone receptor positive.

Both the smaller size and higher rate of hormone receptor positivity of scar cancers when compared with non-scar cancers may be due to their

different origin in mammary ducts. In the human breast a peculiar lesion known by several names, the most common of which is radial scar, is formed where ducts terminate in lobules. A typical radial scar contains a fibrosclerotic center with elastoid material, from which connective tissue and epithelial components branch out to surrounding breast parenchyma (Fenoglio and Lattes 1974; Hamperl 1975; Linell et al. 1980; Fisher et al. 1983). The true neoplastic nature of radial scar is controversial; it is considered to be both benign (Fenoglio and Lattes 1974; Azzopardi 1979; Andersen and Gram 1984) and premalignant, at least in some cases and cancers derived from radial scars are also of scar type (Hamperl 1975; Linell et al. 1980, 1981; Fisher et al. 1983). It seems that a radial scar is a singular type of lesion in the human breast the epithelial components of which are derived from terminal ductal-lobular epithelium (Hamperl 1975; Azzopardi 1979).

In women of fertile age, proliferative activity of the cells in terminal ducts is cyclic, being greater at the luteal than at the follicular phase of the menstrual cycle. It seems therefore that both estrogen and progesterone are associated with proliferation of the terminal ductal cells (Masters et al. 1977; Meyer 1977; Anderson et al. 1982). Experiments in mice indicate that the epithelial cells of larger mammary ducts do not respond to estrogen at estrus cycle, and DNA synthesis occurs only in terminal ducts (Bresciani 1971). It may be that the higher number of hormone receptor positive cases in scar cancers than in non-scar cancers depends on the origin of the former in epithelial cells of terminal ducts, which are sensitive to estrogen and progesterone, a feature which is apparently retained during carcinogenesis and in cancer cells. Cancer of non-scar type is probably derived from the epithelium of larger mammary ducts, whether independent or only weakly dependent on estrogen and progesterone.

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