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Abbreviation:

PEV = Pousse evolutive

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Inflammatory Breast Carcinoma: Mammographic, Ultrasonographic, Clinical, and Pathologic Findings in 142 Cases¹

PURPOSE: To determine and quantitate radiologic characteristics of inflammatory breast carcinoma and to report clinical and pathologic findings.

MATERIALS AND METHODS: A retrospective review of records of 2,733 women who received a diagnosis of breast carcinoma between January 1988 and May 2000 revealed 142 histologically proved inflammatory carcinomas. Analysis included history; findings at physical examination, mammography, and ultrasonography (US); and histologic type of inflammatory carcinoma.

RESULTS: At physical examination, skin changes ($n = 115$, 81%) were the most common findings. A palpable mass was noted in 62% ($n = 88$), with axillary lymph node involvement in 68% ($n = 96$) of the carcinomas. Mammography revealed findings in carcinomas: skin thickening, 84% ($n = 119$); diffusely increased density, 37% ($n = 53$); trabecular thickening, 81% ($n = 115$); mass, 16% ($n = 23$); asymmetric focal density, 61% ($n = 87$); microcalcifications, 56% ($n = 80$); nipple retraction, 43% ($n = 61$); and axillary lymphadenopathy, 24% ($n = 34$). US showed changes in carcinomas: skin thickening, 96% ($n = 136$); parenchymal echogenicity changes, 73% ($n = 104$); dilated lymphatic channels, 68% ($n = 96$); solid mass, 80% ($n = 114$); pectoral muscle invasion, 10% ($n = 14$); focal areas of parenchymal acoustic shadowing, 37% ($n = 52$); and axillary lymphadenopathy, 73% ($n = 104$).

CONCLUSION: Presence of isolated inflammatory signs is sufficient to suggest inflammatory breast carcinoma clinically. Inflammatory breast carcinoma has a mammographic pattern of inflammatory changes, such as skin thickening and stromal coarsening and/or diffusely increased breast density with or without an associated mass and/or malignant-type microcalcifications. US is helpful not only in depiction of masses masked by the edema pattern but also in demonstration of skin and pectoral muscle invasion and axillary involvement.

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Inflammatory carcinoma of the breast is an infrequent form of invasive breast carcinoma that manifests clinically with rapid onset of warmth, erythema, and edema of the breast (1). Haagensen (2) described the clinical features of this fulminant disease as increased volume and induration of the breast, increased temperature, tenderness or pain, peau d'orange or cutaneous edema, redness of the skin of at least one-third of the breast, and the presence of a palpable ridge at the margin of induration. Pathologically, any subtype of primary breast carcinoma may be present, but dermal lymphatic vessels must be involved (3,4).

The occurrence of inflammatory breast carcinoma, although uncommon when compared with that of other malignancies, remains a very aggressive malignancy, with a tendency to metastasize at an early stage. Therefore, information about this carcinoma is considered of value and interest to both radiologists and clinicians. Mammographic

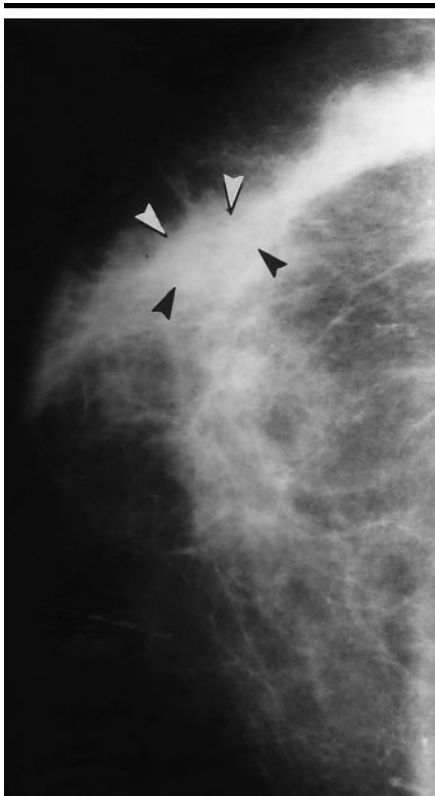


Figure 1. Craniocaudal mammogram obtained in a 58-year-old woman with a palpable mass in the right breast. The left breast was normal. A spiculated mass (arrowheads) is seen in the right breast. Neither radiologic findings nor a clinical pattern of inflammatory carcinoma was present. However, tumor emboli in the dermal lymphatics were detected at the histopathologic examination of the surgical specimen removed at mastectomy, and on the basis of these findings, a diagnosis of inflammatory breast carcinoma was determined. Histologic subtype and size: invasive ductal carcinoma, 3.4 cm in longest diameter.

findings in inflammatory carcinoma were reported by Berger (5) in a series of 12 cases, by Dershaw et al (4) in 22 patients, by Tardivon et al (6) in 92 patients, and by Kushwaha et al (1) in 26 patients. However, the ultrasonographic (US) findings have not been described extensively and, to our knowledge, have not been previously reported in a large series. The purpose of this study was to identify and quantitate mammographic and US findings in women with inflammatory carcinoma seen at the Radiology Department, Ege University, Bornova, Izmir, Turkey, and to report the clinical and pathologic findings.

MATERIALS AND METHODS

A retrospective review of the records of 2,733 women with 2,863 breast carcino-

TABLE 1
History and Clinical Findings in Patients with Inflammatory Breast Carcinoma

Clinical Data	No. of Cases*	CI (%)†
Risk factors determined (<i>n</i> = 139 cases)	31 (22)	15.68, 30.14
Breast cancer (personal or family history)	15 (11)	6.17, 17.17
Nulliparity	8 (6)	2.52, 11.03
Menarche before 12 y	3 (2)	0.45, 6.18
Menopause after 50 y	2 (1)	0.17, 5.10
First child born after 30 y	3 (2)	0.45, 6.18
Topography (<i>n</i> = 139 cases)		
Right breast only	79 (57)	48.17, 65.20
Left breast only	57 (41)	32.74, 49.66
Both breasts	3 (2)	0.45, 6.18
Physical examination (<i>n</i> = 142 breasts)		
Skin changes	115 (81)	73.56, 87.08
Erythema	108 (76)	68.18, 82.81
Skin thickening	115 (81)	73.56, 87.08
Nipple retraction	61 (43)	34.69, 51.53
Palpable mass	88 (62)	53.45, 69.98
Size (<i>n</i> = 88 breasts)		
<5 cm	37 (42)	31.60, 53.05
≥5 cm	51 (58)	46.95, 68.40
Mobility (<i>n</i> = 88 breasts)		
Mobile	2 (2)	0.28, 7.97
Nonmobile	86 (98)	92.03, 99.72
Location (<i>n</i> = 88 breasts)		
Upper outer quadrant	58 (66)	55.03, 75.68
Upper inner quadrant	5 (6)	1.87, 12.76
Lower outer quadrant	6 (7)	2.54, 14.25
Lower inner quadrant	3 (3)	0.71, 9.64
Subareolar	16 (18)	10.76, 27.84
Multifocal, multicentric	6 (4)	1.57, 8.97
Diffuse hardness	32 (22)	15.95, 30.30
Axillary adenopathy	96 (68)	59.25, 75.21

* Data in parentheses are percentages.

† Binomial CIs were calculated by using Clopper-Pearson intervals.

mas (130 with bilateral carcinoma) who received diagnoses at Ege University between January 1988 and May 2000 revealed 142 histologically proved inflammatory carcinomas (ie, tumors in dermal lymphatics at histologic examination) in 139 women (mean age, 48 years; age range, 22–81 years). In each patient, questionnaires, physical examination records, mammograms (at the time of diagnosis and of follow-up), US prints and records, and histopathologic results were recorded and archived in the mammography unit. The history, physical examination and initial imaging (mammographic and US) findings, and histopathologic analysis results were retrospectively analyzed. The Research Ethics Committee of the university did not require its approval or informed consent from each patient for this retrospective study.

The questionnaires and physical examination records of all patients were retrospectively reviewed (I.G.B.). Records of the patients were searched for age at time of diagnosis, risk factors such as personal or family history of breast cancer, nulliparity, menarche before the age of 12 years, menopause after the age of 50

years, and birth of the first child after the age of 30 years (7,8). The start and duration of complaints were noted if the information was available.

In all patients, the physical examination was performed by radiologists. Some of these patients were first seen by clinicians (surgeons), and some patients referred themselves for mammography. At physical examination, the presence of a mass (including its location, size, mobility, and multiplicity), skin changes (erythema or increased warmth of the breast, skin edema or peau d'orange, and wheals or ridging of the skin), nipple retraction, diffuse hardness, and axillary lymphadenopathy were noted.

Mammography in two standard planes of imaging (craniocaudal and mediolateral oblique) was performed with two machines (Senographe 600 T Senix HF, General Electric CGR, Issy-les-Moulineaux, France; Mammomat 3000, Siemens, Solna, Sweden). All mammograms were retrospectively reviewed by two radiologists (I.G.B., A.M.). During the mammogram review sessions, magnifying glasses and bright light were used to facilitate evaluation of the skin and the subcutaneous

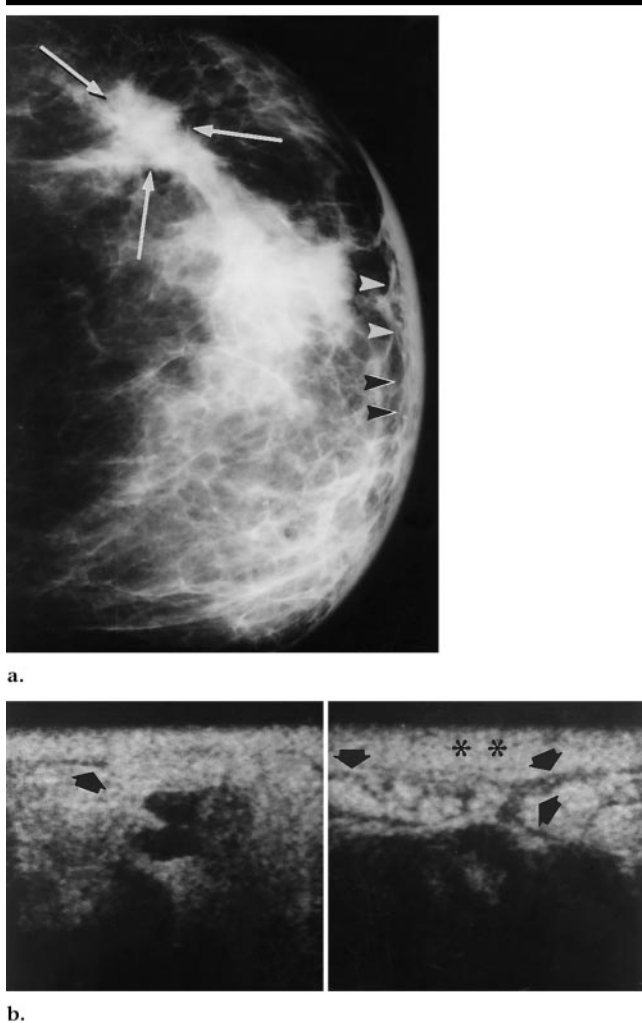


Figure 2. Images obtained in a 64-year-old woman with a mass 6 cm in longest diameter in the upper outer quadrant of the left breast, peau d'orange, and nipple retraction. (a) Craniocaudal mammogram of the left breast shows diffuse skin thickening (arrowheads), trabecular coarsening, and a spiculated mass (arrows) 5.5 cm in longest diameter in the outer quadrant. (b) Transverse US scans show marked skin thickening (*) and dilated lymphatic channels (arrows) that are typical of the breast edema pattern. Hypoechoic masses are also seen. Histologic subtype and size: invasive ductal carcinoma, 6 cm in longest diameter.

tissues. The evaluation was performed with consensus readings. Mammograms were evaluated with the radiologists blinded to information from the physical examination or the US records.

With comparative study of the mammograms of the two breasts, the following mammographic features were analyzed: inflammatory signs, such as skin thickening (skin of the involved breast thicker than that of the contralateral breast); trabecular coarsening and increased density of breast parenchyma; and other findings, such as nipple retraction, presence of a mass, asymmetric focal density (asymmetry of tissue density with a similar shape seen on

two views but completely lacking borders and the conspicuity of a true mass) (9), microcalcifications, and axillary lymphadenopathy. When a mass was present, size, location, and contours were noted; when an asymmetric focal density was present, location was noted. Mammographic evaluation criteria were based on the Breast Imaging Reporting and Data System, or BI-RADS (9). Axillary lymphadenopathy was identified on the basis of two or more of the following criteria: size larger than 2 cm, replacement of fatty hilum, round shape, and generalized increased density (10).

All patients underwent both axillary and breast US, which was performed

(I.G.B., E.E.U., A.M.) by using a 7.5-MHz transducer (SAL 70; Toshiba, Tokyo, Japan) ($n = 113$) or a broadband 5–11-MHz transducer (HDI 1000; ATL Ultrasound, Bothell, Wash) ($n = 29$). US was performed either to detect or to evaluate solid masses or axillary lymphadenopathy or for academic interest at the time of diagnosis, and findings were prospectively recorded. All of the US prints and records, which were archived with the questionnaires and mammograms, were retrospectively reevaluated (I.G.B.).

In addition to mammographic findings, other findings were noted. These findings included the following: skin thickening (skin thickness > 2 mm and/or skin of the involved breast was thicker than that of the contralateral breast), skin invasion (interruption of the deep echogenic line of the skin, the dermis, or the subcutaneous fat interface) (11), dilated lymphatic channels (branching anechoic tubular structures in the subcutaneous fatty tissues) (11), pectoral muscle invasion (the mass was in contact with the pectoral muscle, and the tissue planes between the two were obliterated), multifocality (the mass was within the same quadrant or within 5 cm of the primary lesion) (12), multicentricity (the mass was in different quadrants or beyond 5 cm from the primary lesion) (12), and axillary lymphadenopathy (a hypoechoic smoothly or irregularly outlined mass with a long-to-short axis ratio of less than 1.5 and absence of the echogenic hilum) (11,13). When a mass was present, the location, size, contour, and acoustic features were evaluated. In nine carcinomas, the sizes of the mass before and after neoadjuvant chemotherapy were compared.

In all patients, the diagnosis of inflammatory breast carcinoma was confirmed pathologically, either by means of skin biopsy (ie, punch biopsy that included skin and dermal lymphatics) ($n = 34$) or surgical biopsy ($n = 108$). One hundred eight patients underwent mastectomy and axillary lymph node dissection.

In statistical analysis, binomial CIs were calculated by using Clopper-Pearson intervals.

RESULTS

All patients were women who were 22–81 years old (mean age, 48 years) at the time of diagnosis. When patients were grouped according to age, four carcinomas were found in patients in the 3rd decade of life; 34 carcinomas, in the 4th decade of life; 41 carcinomas, in the 5th decade of life; 34 carcinomas, in the 6th dec-

ade of life; 18 carcinomas, in the 7th decade of life; and 11 carcinomas, in the 8th decade of life. Thirty-one (22%) patients had risk factors for carcinoma. The duration of clinical symptoms ranged from less than 1 month to as long as 8 months.

The most common finding at physical examination was a change in the skin, such as peau d'orange or erythema, which was seen in 115 (81%) of 142 breasts. Masses were detected in 88 (62%) breasts at palpation, and they were 1–12 cm in diameter (mean, 4.5 cm). The most common location was the upper outer quadrant. In 27 (19%) breasts with palpable masses, no clinical evidence of inflammatory carcinoma was present (Fig 1). The history and clinical findings are summarized in Table 1.

All initial mammograms were abnormal, and multiple findings were present in all women. The most common mammographic finding was skin thickening, which was present in 119 (84%) carcinomas (Fig 2a). Trabecular prominence compatible with edema was seen in 115 (81%) carcinomas. In three patients, the skin and trabecular thickening were bilateral. In four patients, edema or skin thickening was the only abnormal finding (ie, no mass or abnormal calcifications) on the mammogram. In another two patients, the contralateral breast had a spiculated mass without skin changes.

Microcalcifications were present in 80 (56%) of 142 carcinomas. In eight (10%) of 80 carcinomas with microcalcifications, the calcifications were diffuse, scattered, round, or punctate and were considered benign or probably benign. In 43 (54%) of 80 carcinomas, the microcalcifications were pleomorphic, which meant that they were suspected of being malignant, and in 29 (36%) carcinomas, the microcalcifications were linear and branching, which meant that they were highly suggestive of malignancy. Of those carcinomas with calcifications, 59 (74%) of 80 had an accompanying density (ie, a mass and/or an asymmetric focal density) (Fig 3a, 3b), and 21 (26%) of 80 did not have an accompanying density. A diffuse increase in density of the involved breast when compared with the contralateral breast was noted in 53 (37%) carcinomas, and an asymmetric focal density (Fig 4a) when compared with the contralateral breast (Fig 4b) was noted in 87 (61%) carcinomas. In 23 (16%) carcinomas, a total of 28 masses with irregular contour were demonstrated on mammograms (Fig 5a). The size of the masses varied from 1.0–6.5 cm in longest diameter.

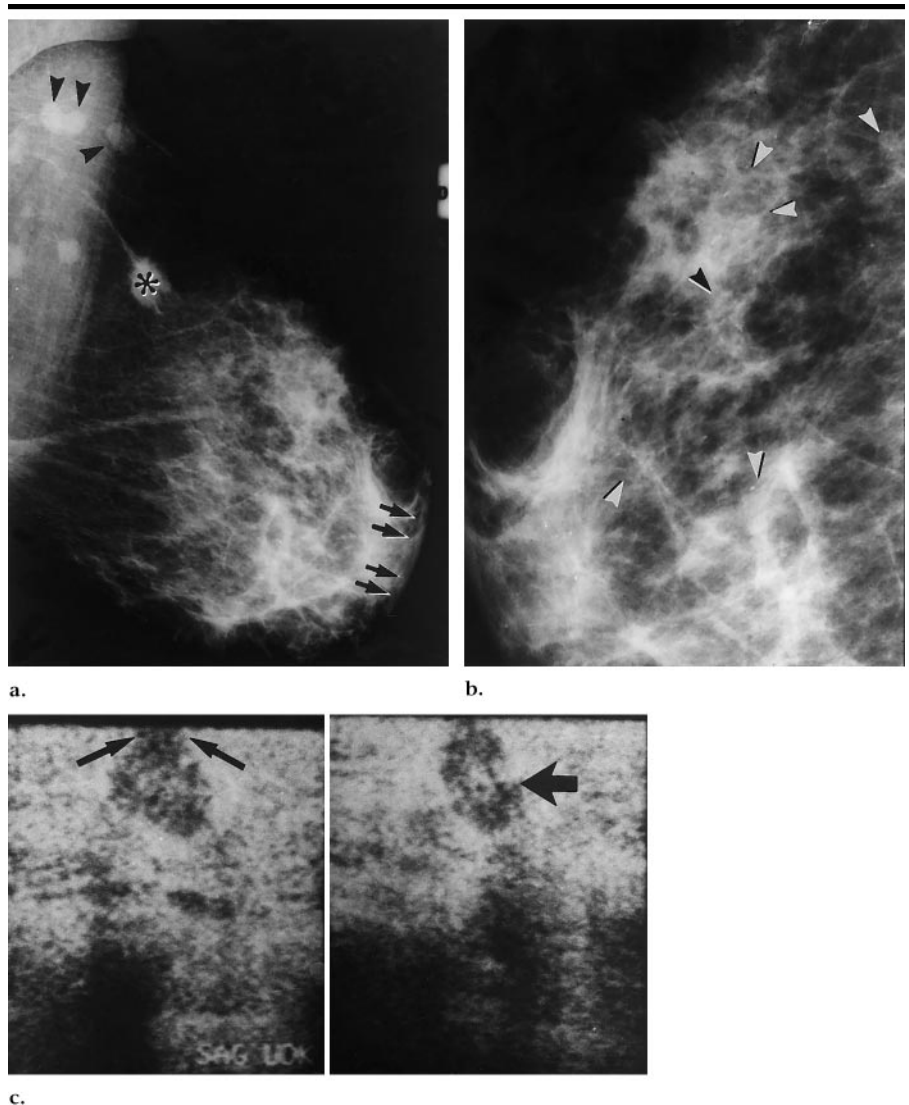


Figure 3. Images obtained in a 66-year-old woman with a palpable mass in the upper quadrant of the left breast and breast erythema. The right breast was normal. (a) Mediolateral oblique mammogram of the left breast shows trabecular thickening (arrows), a spiculated mass (*) 1.5 cm in longest diameter, and diffuse pleomorphic microcalcifications suggestive of malignancy. Round axillary nodes (arrowheads) with increased density and loss of lucent fatty hilum are consistent with axillary lymphadenopathy. (b) Pleomorphic microcalcifications (arrowheads) are better seen on the close-up image (photographic enlargement). (c) Transverse US scans show that the mass (thick arrow) with irregular contour has invaded the skin (thin arrows). Findings at histopathologic examination of the surgical specimen removed at mastectomy confirmed direct dermal invasion. Histologic subtype and size: invasive ductal carcinoma, 1.7 cm in longest diameter.

The mammographic findings are summarized in Table 2.

At US, skin thickening and parenchymal echogenicity changes owing to edema and thickening of Cooper ligaments were noted in 136 (96%) carcinomas. The skin thickening could be measured and compared with that of the contralateral breast more sensitively and confidently at US than at mammography. The lymphatic and vascular channels were dilated in 96 (68%) carcinomas (Fig 2b). A total of 135 solid masses in

114 (80%) of 142 carcinomas were depicted at US. In 12 carcinomas, the cancer was multifocal and multicentric (Fig 5b). The size of the masses varied from 0.7–9.5 cm in longest diameter. One hundred eleven (82%) of 135 masses were lobulated or had irregular contours with posterior acoustic shadowing, whereas 24 (18%) of 135 had smooth contours without posterior acoustic shadowing.

In 14 carcinomas, it was hard to demonstrate the mass because the breast was thick owing to parenchymal edema and

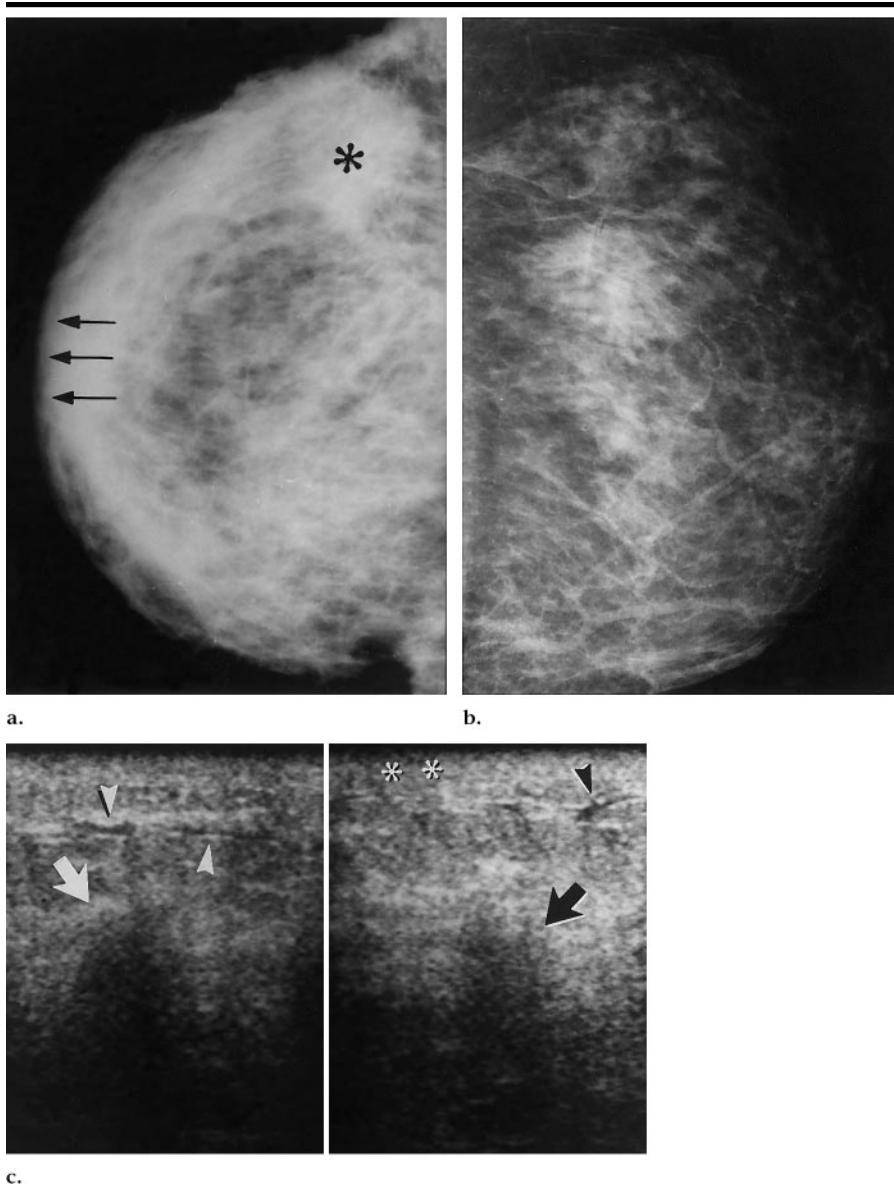


Figure 4. Images obtained in a 47-year-old woman with peau d'orange. (a) Craniocaudal mammogram of the right breast shows skin thickening (arrows), parenchymal edema, and focal asymmetric density (*) in the outer quadrant. At US, a solid mass 3 cm in longest diameter with irregular contour was seen in this location. (b) Craniocaudal mammogram of the left breast is normal. (c) Transverse US scans of the lower inner quadrant of the right breast show marked skin thickening (*), dilated lymphatic channels (arrowheads), and focal areas of parenchymal acoustic shadowing (arrows). Histologic subtype and size: invasive ductal carcinoma, 3.3 cm in longest diameter.

the mass was very deeply localized. Pectoral muscle invasion was seen in 14 (10%) carcinomas, and skin invasion was seen in three (2%) (Fig 3c). In 52 (37%) carcinomas, focal areas of parenchymal acoustic shadowing without a mass configuration were prominent (Fig 4c). US of the axillary fossa demonstrated metastatic lymph nodes that were enlarged and hypoechoic (without the echogenic hilum) in 104 (73%) carcinomas. The US findings are summarized in Table 3. Nine

patients were referred for the evaluation of response to neoadjuvant chemotherapy. Follow-up US was performed regularly every 3 months. The mean follow-up period for the nine patients was 12.6 months (range, 6–21 months). At follow-up in these patients, US demonstrated an increase in the size of the initial mass in one carcinoma, a decrease in three, complete disappearance in one (Fig 6), and no change in four carcinomas.

Contralateral breast cancer was present

synchronously in five cases, three of which were inflammatory and two of which were noninflammatory carcinoma (one case with invasive ductal carcinoma and one case with Paget disease).

In all patients, the clinical and radiologic diagnosis of inflammatory breast carcinoma was confirmed pathologically by means of either skin or surgical biopsy. Findings at histopathologic examination of the specimen removed at mastectomy in 108 patients revealed invasive ductal carcinoma in 92 (85%) patients, invasive lobular carcinoma in one (1%) patient, and both in six (6%) patients. Two (2%) patients had areas of microinvasive ductal carcinoma in situ and satellite nodules along the lymphatics. However, a macroscopic mass could not be demonstrated in these two patients. Mammograms in these two patients showed an edema pattern and diffuse calcifications, of which some were pleomorphic and others uniform.

US demonstrated marked skin thickening, parenchymal acoustic shadowing, and hypoechoic areas that did not demonstrate a mass configuration and were localized close to the skin. In seven (6%) of 108 patients, the diagnosis was undifferentiated carcinoma. In 12 (11%) of 108 patients, multifocal, multicentric carcinoma was present. The pathologic sizes of the masses were 0.8–10.0 cm (mean, 4.2 cm). Areolar invasion in 31 (29%) and pectoral muscle invasion in 18 (17%) of 108 patients were present. Four patients had accompanying Paget disease. Axillary lymph node metastasis was present in all 108 patients who underwent axillary lymph node dissection.

DISCUSSION

Inflammatory carcinoma of the breast accounts for 1%–4% of breast cancer (14,15). The average age range at onset is 45–54 years (4,14,16). The incidence (142 [5%] of 2,863) was higher in our practice than in any of the earlier reports. The reasons for this finding could be the following: (a) The series included a period of 12 years, going back to 1988 when patients with carcinoma in late stages would be referred to health care. (b) We practice in a large tumor institute where patients are frequently referred for treatment of late-stage breast cancer. The average age (48 years) at onset in our study is in agreement with that in the literature. The frequency of clinical findings was similar to that in previously published articles (4,17), but there was a

trend toward higher incidence in the right breast than in the left ($P = .07$, binomial test).

Bilateral breast cancer, which was present in five patients in this series, previously was reported to be a common finding in patients with inflammatory carcinoma. This finding was present in 30% of the patients in the study of Haagensen (2), in 9% of those in the study of Dershaw et al (4), and in 55% of those in the study of Taylor and Meltzer (18). In the series of Tardivon et al (6) with 92 patients, this percentage decreased to 0.9%. Among 139 patients in this study, five (4%) had bilateral breast carcinoma (three patients with inflammatory carcinoma, one with Paget disease, and one with invasive ductal carcinoma) synchronously.

Haagensen (2) described the clinical features of inflammatory carcinoma in his series of 89 patients. The diagnosis was not determined unless at least one-third of the breast was affected with redness or edema. In that study (2), tumor was present in 57% of the patients; erythema, in 57%; breast enlargement, in 48%; edema of the skin, in 13%; warmth of the skin, in 8%; nipple retraction, in 13%; and pain, in 29%. In the patients in this study, skin changes were seen in 81%, and a palpable mass was present in 62%. In the histologic examination of 27 (19%) carcinomas with palpable masses, in patients who did not have any clinical findings (eg, erythema or increased warmth of the breast, skin edema or peau d'orange, wheals or ridging of the skin) of inflammatory carcinoma, tumor emboli were detected in the dermal lymphatics.

Saltzstein (19) described four patients who had no clinical evidence of inflammatory carcinoma but had dermal lymphatic invasion histologically. These patients all died rapidly. He suggested the term "clinical occult inflammatory carcinoma" and concluded that inflammatory carcinoma was a histologic rather than a clinical diagnosis.

Although the diagnosis of inflammatory breast carcinoma can be determined on the basis of clinical symptoms or pathologic findings, coexistent mammographic findings of tumor mass and/or malignant microcalcifications and of inflammatory changes, such as extensive skin and trabecular thickening, and diffusely increased breast density are important clues that should lead the radiologist to suggest the diagnosis. All patients in this study had abnormal initial mammograms. The frequency of mammographic signs that indicated inflammation of

TABLE 2
Distribution of Initial Mammographic Findings

Mammographic Finding	No. of Carcinomas*	CI (%)†
Skin thickening	119 (84)	76.69, 89.45
Diffusely increased density	53 (37)	29.36, 45.83
Trabecular thickening	115 (81)	73.56, 87.08
Nipple retraction	61 (43)	34.69, 51.53
Mass	23 (16)	10.55, 23.31
Total no.	28	
Location		
Upper outer quadrant	18 (64)‡	44.07, 81.36
Upper inner quadrant	3 (11)‡	2.27, 28.23
Lower outer quadrant	4 (14)‡	4.03, 32.67
Lower inner quadrant	3 (11)‡	2.37, 28.23
Size		
≤5 cm	21 (75)‡	55.13, 89.31
>5 cm	7 (25)‡	10.69, 44.87
Contour, irregular	28 (100)‡	87.66, 100
Multifocal, multicentric	5 (4)	1.15, 8.03
Asymmetric focal density	87 (61)	52.74, 69.32
Located in upper outer quadrant	52 (60)§	48.71, 70.15
Located in upper inner quadrant	5 (6)§	1.89, 12.90
Located in lower outer quadrant	4 (4)§	1.27, 11.36
Located in lower inner quadrant	2 (2)§	0.28, 8.06
Located in subareolar area	24 (28)§	18.54, 38.21
Microcalcifications	80 (56)	47.77, 64.64
Benign	8 (10)¶	4.42, 18.76
Malignant	72 (90)¶	81.24, 95.58
With asymmetric density and/or mass	59 (74)¶	62.71, 82.96
Without asymmetric density and/or mass	21 (26)¶	17.04, 37.29
Axillary adenopathy	34 (24)	17.19, 31.82
Contralateral breast cancer (synchrony)	5 (4)	1.15, 8.03

* Data in parentheses are percentages. Unless otherwise indicated, percentages were calculated on the basis of a total of 142 carcinomas.

† Binomial CIs were calculated by using Clopper-Pearson intervals.

‡ Percentages were calculated on the basis of 28 masses.

§ Percentages were calculated on the basis of 87 carcinomas.

¶ Percentages were calculated on the basis of 80 microcalcifications.

breast tissue was in agreement with the findings in previously published literature (1,6), but diffusely increased breast density (37%) was less frequently noted in this study, which was in agreement with the data (41%) in the study of Dershaw et al (4).

At mammographic evaluation, the most common finding was skin thickening (84%). Although skin thickness varies between individuals, it is usually thicker in small breasts (20). Wilson et al (21) reported that skin thickness should not exceed 2.5–3 mm. On mammograms, skin thickening becomes obvious first in the inferior areolar region, and from there it spreads quickly to the whole breast, and this finding helps in the differentiation of inflammatory carcinoma from other inflammatory processes and from scirrhous carcinoma, which show local or segmental skin thickening (20). Skin thickening, increased breast density, and stromal coarsening on mammograms are caused by tumor invasion, obstruction of lymphatic vessels, subepidermal capillaries, and venules (22).

Inflammatory breast carcinoma is a T4 tumor according to the standard TNM staging classification of the Union Internationale Contre le Cancer, or UICC, and the American Joint Committee on Cancer, or AJCC (23,24). The definition of inflammatory carcinoma of the breast differs among studies and often includes locally advanced breast carcinoma with secondary inflammatory changes, which usually manifests as a large mass with localized skin changes adjacent to the underlying mass (1,4,6). Findings in other reports about the mammographic appearance of inflammatory carcinoma of the breast are conflicting. These discrepancies may result from differences in the clinical definition of inflammatory carcinoma of the breast (1). In their report published in 1995, Buzdar et al (25) suggested that primary inflammatory carcinoma of the breast and locally advanced carcinoma with secondary inflammatory changes are two distinct clinical entities with differing incidence trends and survival curves.

It is also important to evaluate tumor

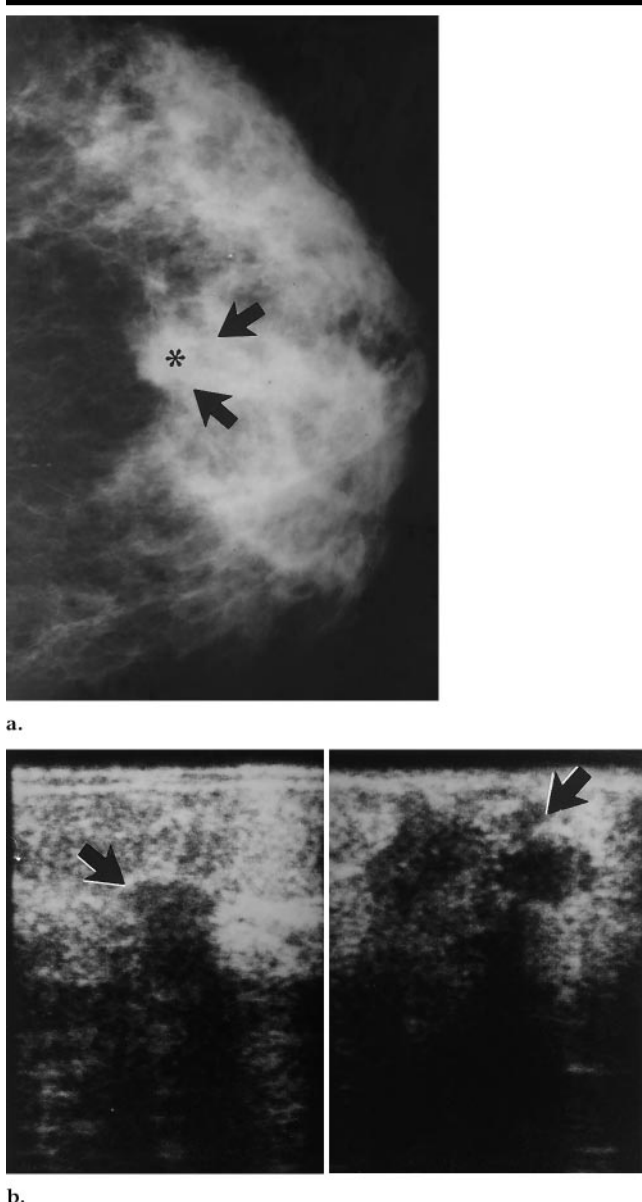


Figure 5. Images obtained in a 50-year-old woman with a subareolar mass 4 cm in longest diameter. The right breast was normal. **(a)** Craniocaudal mammogram of the left breast shows skin thickening that was seen with bright light (not seen on the image) and a mass (*). The anterior contour of the mass (arrows) is obscured by the fibroglandular tissue opacities; the posterior contour shows irregularity. **(b)** Transverse US scans show two solid masses (arrows) with irregular contours in the subareolar region, which is consistent with multifocal carcinoma. Histologic subtypes and sizes: invasive ductal carcinoma and multifocal carcinoma, 4.5 and 0.7 cm in longest diameter, respectively.

growth over time, according to Pousse evolutive (PEV) criteria, to differentiate inflammatory breast carcinoma from secondary inflammatory breast cancers (1,6). PEV is a classification of breast cancer that was created by investigators at the Institut Gustave-Roussy, Villejuif, France. This classification, which differs

from the TNM staging system, is descriptive and takes recent tumor growth and inflammatory signs into consideration. The PEV categories are defined as follows: PEV 0, a tumor without recent increase in volume and without inflammatory signs; PEV 1, a tumor showing marked increase in volume during the past 2 months but

without inflammatory signs; PEV 2, a tumor with overlying breast tissue, skin in particular, that is affected by subacute inflammation and edema involving less than one-half of the breast surface; and PEV 3, a tumor with acute or subacute inflammation and edema involving more than one-half of the breast surface (14).

PEV 2 corresponds to a palpable mass with inflammatory signs localized beneath the lesion with evolution that exceeds 4 months, whereas PEV 3 corresponds to a palpable mass with inflammatory signs with evolution of less than 4 months (6,26). In their study of 26 primary inflammatory carcinomas of the breast, Kushwaha et al (1) reported that a history of rapid onset of clinical signs within 3 months of presentation is required to distinguish primary inflammatory carcinoma of the breast from locally advanced carcinoma with secondary lymphatic invasion. This study is a retrospective analysis of patient records and mammograms from 1988, and we do not have complete information on the duration of symptoms. As a result, we cannot classify the inflammatory breast carcinoma cases in this study as primary or secondary.

The most important prognostic factor in breast cancer is the presence and extent of axillary nodal involvement with carcinoma; nodal disease is indicative of systemic microscopic metastatic disease. An overwhelming majority of patients with inflammatory breast cancer have nodal involvement that is not only microscopic but also clinical (14). In metastatic lymph nodes, the internal texture is usually homogeneous, but it can be heterogeneous in large nodes; microcalcification is not as frequent as it is in the primary lesions. US is particularly useful for examination of level II and III lymph nodes, which lie too high in the axilla to be palpated. These lymph nodes have the same appearances as level I metastatic nodes but are behind the pectoral muscles (11).

US is reported (27,28) to be more sensitive in the detection of metastatic axillary lymph nodes than palpation or mammography. In this study, detection of axillary lymph node involvement was underestimated with mammography. Only 34 (24%) carcinomas had lymph nodes that appeared to be involved (metastatic) on standard views. However, clinically, 96 (68%) carcinomas had palpable lymph nodes, and US demonstrated lymph nodes that appeared to be involved (metastatic) in 104 (73%) carcinomas. Although US is more successful than physical examination and mammography in the detection

of axillary lymphadenopathy, axillary dissection or sentinel lymph node imaging (not performed in the patients in this study) should be mandatory in these cases.

To our knowledge, this is the first study of a large series of US findings in inflammatory carcinoma. In this study, US evaluation was helpful not only in depiction of axillary involvement but also in depiction of skin and pectoral muscle invasion. In posterior lesions, especially those close to the chest wall musculature, accurate assessment of tumor size and extension may not be possible with mammography prior to surgery (29). If tumor extends to and superficially invades the greater pectoral muscle, a portion of the muscle will be removed to obtain a negative posterior margin. Thus, it is critical to map the extent of disease so that the appropriate treatment is planned (29,30). Among the 18 patients with histopathologically proved pectoral muscle invasion, US demonstrated the invasion in 14 cases. Mammographically, such an observation was not possible in any of the patients.

Although US failed to demonstrate pectoral muscle invasion in four of 18 patients, it was superior to mammography. Other modalities, such as computed tomography (CT) and magnetic resonance (MR) imaging, have been useful in assessing the presence of chest wall invasion by tumor (29,31). MR imaging is superior to CT with respect to in-plane resolution, anatomic detail, and detection of subtle enhancement within the muscles (29). Morris et al (29), in their study in 19 patients with posterior breast masses, could identify muscle invasion (muscle enhancement on MR images) with 100% accuracy. We did not perform MR imaging in our patients, so we could not make true comparisons. US results in this study, when compared with the MR imaging results in the literature, might have a high false-negative rate compared with rates with MR imaging. However, our results show that US was superior to mammography.

US, when compared with mammography, more commonly demonstrated skin thickening, which is an important finding in the diagnosis of inflammatory carcinoma. Comparison with the contralateral breast was useful, especially when slight thickening was suspected. In 17 carcinomas, unilateral skin thickening was shown by using comparative (right versus left breast of the individual) measurements on US prints, whereas on mammograms obtained in the same patients it

TABLE 3
Distribution of Initial US Findings

US Finding	No. of Carcinomas*	CI (%)†
Skin thickening	136 (96)	91.03, 98.43
Diffuse increase in parenchymal echogenicity	104 (73)	65.17, 80.32
Dilated lymphatic channels	96 (68)	59.25, 75.21
Solid mass	114 (80)	72.78, 86.48
Total no.	135	
Location		
Upper outer quadrant	80 (59)‡	50.47, 67.63
Upper inner quadrant	10 (7)‡	3.61, 13.20
Lower outer quadrant	12 (9)‡	4.68, 15.01
Lower inner quadrant	6 (4)‡	1.65, 9.42
Subareolar area	27 (20)‡	13.61, 27.75
Size		
<2 cm	28 (21)‡	14.25, 28.56
2-5 cm	61 (45)‡	36.61, 53.98
>5 cm	46 (34)‡	26.14, 42.72
Contour		
Lobulated or irregular	111 (82)‡	74.71, 88.27
Smooth	24 (18)‡	11.74, 25.29
Acoustic features		
With posterior acoustic shadowing	111 (82)‡	74.71, 88.27
Without posterior acoustic shadowing	24 (18)‡	11.74, 25.29
Multifocal, multicentric	12 (8)	4.44, 14.30
Pectoral muscle invasion	14 (10)	5.50, 15.99
Focal parenchymal acoustic shadowing	52 (37)	28.70, 45.11
Axillary adenopathy	104 (73)	65.17, 80.32

* Data in parentheses are percentages. Unless otherwise indicated, percentages were calculated on the basis of 142 carcinomas.

† Binomial CIs were calculated by using Clopper-Pearson intervals.

‡ Percentages were calculated on the basis of 135 solid masses.

was not obvious even when bright light was used to facilitate evaluation. On US prints, as the skin thickened, the two echogenic lines that are normally demonstrable became less distinct. With progressive edema, the echogenicity of the skin decreased, and it became isoechoic with the subcutaneous tissue.

Other than the common finding of diffuse increase in the parenchymal echogenicity caused by edema, the finding of focal areas of acoustic shadowing without a mass configuration was an additional US finding seen in 52 (37%) carcinomas. At mammographic correlation, all 52 carcinomas had marked breast edema (skin and trabecular thickening and/or diffusely increased density), whereas only 24 carcinomas had microcalcifications and none had macrocalcifications. Thus, we believe that this finding is caused by a prominent pattern of edema (increased water content that changes parenchymal sound transmission of different tissue interfaces) rather than by microcalcifications because microcalcifications of the breast, which may appear as bright punctate echoes on US scans, do not cause acoustic shadowing with current transducers.

There is no consistent histologic type of breast carcinoma associated with in-

flammatory breast disease. The histologic characteristics range from infiltrating ductal to medullary carcinoma. The series of Haagensen (32) in 40 patients included 19 (47%) with the large cell undifferentiated type (14). The distinct pathologic feature, however, is the dermal lymphatic invasion. That is, pathologically, for diagnosis of inflammatory carcinoma, the dermal lymphatic vessels must be involved (3,4). In the series in this study, the most common subtype was invasive ductal carcinoma.

Unlike other types of breast cancer in which surgery is the first modality of treatment, chemotherapy before surgery or radiation therapy is the current standard treatment of inflammatory breast carcinoma (33,34). The accurate assessment of tumor response to induction chemotherapy in locally advanced breast carcinoma, including inoperable stage IIIB and IV inflammatory carcinoma, is important, since the response influences subsequent patient treatment and the selection of postoperative chemotherapy regimens and is an indicator of prognosis (35,36). For assessment of final tumor size, US is reported to be better than mammography, and US is the most practical and accurate method for monitoring response (37,38).

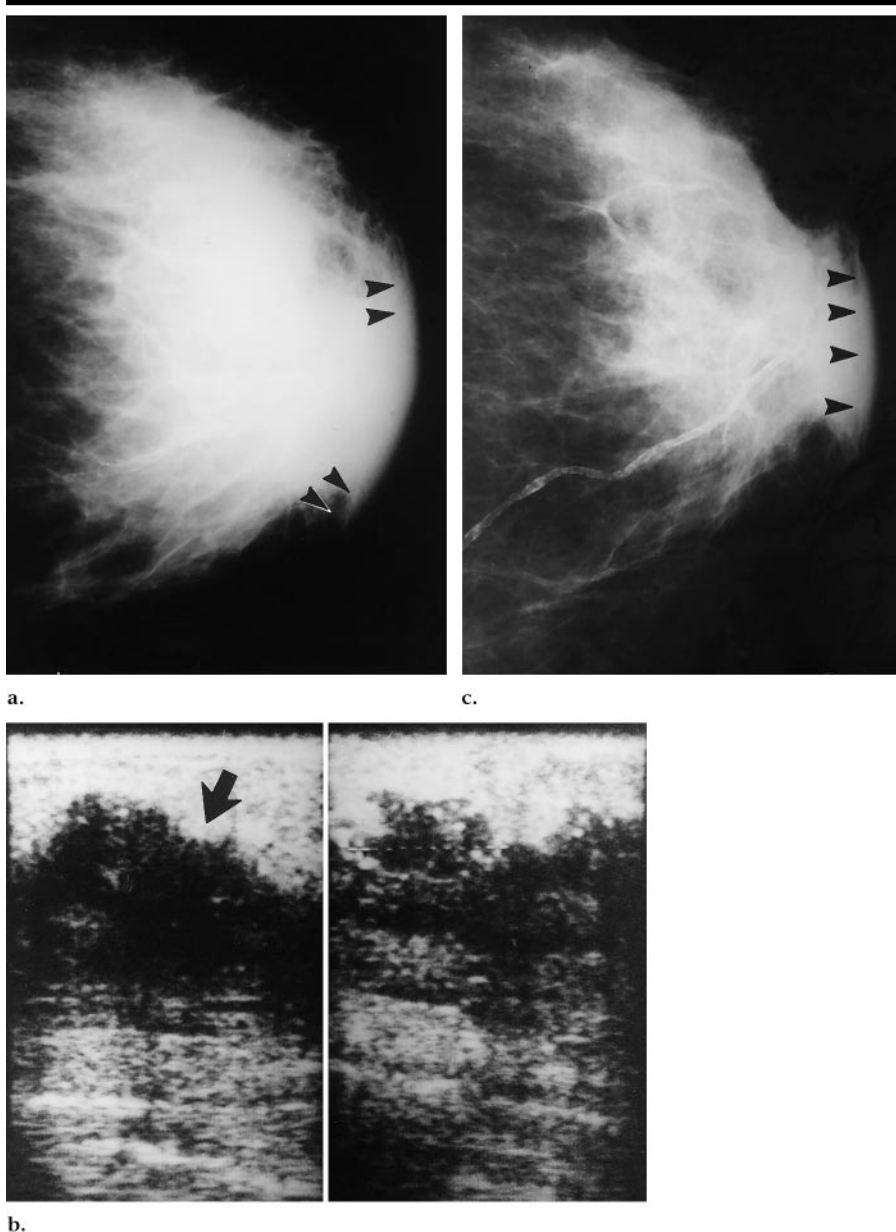


Figure 6. Images in a 60-year-old woman with peau d'orange and a subareolar mass 3 cm in longest diameter. (a) Initial craniocaudal mammogram of the left breast shows skin thickening (arrowheads) and diffuse increased density. Biopsy of the skin disclosed inflammatory carcinoma. (b) Transverse US scans, obtained at the same time, depict a mass (arrow) 4 cm in longest diameter with irregular contour in the subareolar region. (c) Craniocaudal mammogram of the same breast 1 year after neoadjuvant chemotherapy shows that the pattern of edema regressed substantially, although there is still some skin thickening (arrowheads). No mass was depicted at US. Findings at histopathologic examination of the specimen removed at mastectomy showed that the invasive component of the tumor had totally resolved and had left behind only fibrosis and in situ foci.

As experience with MR imaging of the breast has increased, the potential for it to assist in the evaluation of response has developed. MR imaging can be used to differentiate postchemotherapy residual tumor from postchemotherapy fibrosis and glandular tissue (39,40). Gilles et al (41) demonstrated that timing and inten-

sity of contrast enhancement on dynamic MR images correspond with the amount of residual carcinoma in treated breasts. In nine of the patients in this study who were referred for the evaluation of response to neoadjuvant chemotherapy, the diffuse density on the initial mammograms precluded determination

of the accurate size of the lesion. US provided information complementary to physical examination and mammographic findings and was essential in the accurate assessment of the response to chemotherapy. However, MR imaging was not performed in our patients, which precludes the determination of comparisons.

Mammographic signs of inflammation of breast tissue are encountered after surgery, after radiation therapy, and in different benign breast disorders, such as trauma, infection, and dermatoses (6,16,42,43). Superior vena cava or subclavian vein thrombosis, congestive heart failure, and lymphoma are also reported as extramammary causes of breast edema (44). In the differential diagnosis, clinical history is very important. In patients with inflammatory signs, which continue despite treatment with antibiotics, biopsy is indicated to eliminate inflammatory breast carcinoma definitively (6).

The presence of isolated inflammatory signs is sufficient to suspect inflammatory breast carcinoma clinically. Radiologically, this carcinoma has a mammographic pattern of inflammatory changes, such as skin thickening and stromal coarsening and/or diffusely increased breast density. Associated mass and/or malignant-type microcalcifications are usually evident but may be absent. The assessment of the mass may not be made precisely because of the diffusely increased density on mammograms. US evaluation is helpful not only in depiction of masses but also in depiction of skin and pectoral muscle invasion and axillary involvement in inflammatory carcinoma, and it is useful in documentation of the size of masses if neoadjuvant chemotherapy is contemplated.

References

1. Kushwaha AC, Whitman GJ, Stelling CB, Cristofanilli MC, Buzdar AU. Primary inflammatory carcinoma of the breast: retrospective review of mammographic findings. *AJR Am J Roentgenol* 2000; 174:535-538.
2. Haagensen CD. *Diseases of the breast*. 2nd ed. Philadelphia, Pa: Saunders, 1971; 576-584.
3. Ellis DL, Teitelbaum SL. Inflammatory carcinoma of the breast: a pathologic definition. *Cancer* 1974; 33:1045-1047.
4. Dershaw DD, Moore MP, Liberman L, Deutch BM. Inflammatory breast carcinoma: mammographic findings. *Radiology* 1994; 190:831-834.
5. Berger SM. Inflammatory carcinoma of the breast. *AJR Am J Roentgenol* 1962; 88:1109-1116.
6. Tardivon AA, Viala J, Rudelli AC, Guinebretiere JM, Vanel D. Mammographic patterns of inflammatory breast carcinoma.

- oma: a retrospective study of 92 cases. *Eur J Radiol* 1997; 24:124-130.
7. Maass H. Mammakarzinom: epidemiologie. *Gynakologe* 1994; 27:3-6.
 8. Stoll BA. Defining breast cancer prevention. In: Stoll BA, ed. *Approaches to breast cancer prevention*. London, England: Kluwer, 1991; 4-78.
 9. American College of Radiology (ACR). *Illustrated breast imaging reporting and data system (BI-RADS)*. 3rd ed. Reston, Va: American College of Radiology, 1998; 121-139.
 10. Murray ME, Given-Wilson RM. The clinical importance of axillary lymphadenopathy detected on screening mammography. *Clin Radiol* 1997; 52:458-461.
 11. Tohno E, Cosgrove DO, Sloane JP, eds. *Ultrasound diagnosis of breast diseases*. New York, NY: Churchill Livingstone, 1994; 49-73, 157-180.
 12. Berg WA, Gilbreath PL. Multicentric and multifocal cancer: whole breast US in preoperative evaluation. *Radiology* 2000; 214:59-66.
 13. Feu J, Tresserra F, Fabregas R, et al. Metastatic breast carcinoma in axillary lymph nodes: in vitro US detection. *Radiology* 1997; 205:831-835.
 14. Swain SM, Lippman M. Locally advanced breast cancer. In: Bland KI, Copeland EM, eds. *The breast: comprehensive management of benign and malignant diseases*. Philadelphia, Pa: Saunders, 1991; 851-862.
 15. Chang S, Parker SL, Pham T, Buzdar AU, Hursting SD. Inflammatory breast carcinoma incidence and survival: the surveillance, epidemiology and end results program of the National Cancer Institute, 1975-1992. *Cancer* 1998; 82:2366-2372.
 16. Parker LM, Boyages J, Eberlein TJ. Inflammatory carcinoma of the breast. In: Harris JR, Hellman S, Henderson IC, Kinne DW, eds. *Breast diseases*. 2nd ed. Philadelphia, Pa: Lippincott, 1991; 775-782.
 17. Bozzetti F, Saccozzi R, Delena M, Salvatori B. Inflammatory cancer of the breast: analysis of 114 cases. *J Surg Oncol* 1981; 18:355-361.
 18. Taylor GW, Meltzer A. "Inflammatory carcinoma" of the breast. *Am J Cancer* 1938; 33:33-49.
 19. Saltzstein SI. Clinically occult inflammatory carcinoma of the breast. *Cancer* 1974; 34:382-388.
 20. Heywang-Kobrunner SH, Schreer I, Dershaw DD. *Diagnostic breast imaging*. Stuttgart, Germany: Thieme, 1997; 11-23.
 21. Wilson SA, Adam EJ, Tucker AK. Patterns of breast skin thickness in normal mammograms. *Clin Radiol* 1982; 33:691-693.
 22. Droullias CA, Sewell CW, McSweeney MB, Powell RW. Inflammatory carcinoma of the breast: a correlation of clinical, radiological and pathological findings. *Ann Surg* 1976; 184:217-222.
 23. Behrs OH, Myers MH, eds. *Manual for staging of cancer*. 2nd ed. Philadelphia, Pa: Lippincott, 1983; 127-135.
 24. Hermanek P, Sobin LH, eds. *TNM classification of malignant tumors: UICC International Union Against Cancer*. 4th ed. Berlin, Germany: Springer-Verlag, 1987; 93-99.
 25. Buzdar AU, Singletary SE, Booser DJ, Frye DK, Wasaff B, Hortobagyi GN. Combined modality treatment of stage III and inflammatory breast cancer: M.D. Anderson Cancer Center experience. *Surg Oncol Clin N Am* 1995; 4:715-733.
 26. Attia-Sobol I, Ferriere IP, Cur GH, et al. Treatment results, survival and prognostic factors in 109 inflammatory breast cancers: univariate and multivariate analysis. *Eur J Cancer* 1993; 29A:1081-1088.
 27. Bruneton JN, Caramella E, Hery M. Axillary lymph node metastasis in breast cancer: preoperative detection with US. *Radiology* 1986; 158:325-326.
 28. Pamilo M, Soiva M, Lavast E. Real-time ultrasound, axillary mammography, and clinical examination in the detection of axillary lymph node metastasis in breast cancer patients. *J Ultrasound Med* 1989; 8:115-120.
 29. Morris EA, Schwartz LH, Drotman MB, et al. Evaluation of pectoralis major muscle in patients with posterior breast tumors on breast MR images: early experience. *Radiology* 2000; 214:67-72.
 30. Harris JR, Lippman ME, Veronesi U, et al. Breast cancer. *N Engl J Med* 1992; 327:390-398.
 31. Stomper PC, Tsangaris TN. CT of pectoralis muscle invasion by breast carcinoma. *J Comput Assist Tomogr* 1993; 17:829-831.
 32. Haagensen CD. *Diseases of the breast*. 3rd ed. Philadelphia, Pa: Saunders, 1986; 808-814.
 33. Perez CA, Fields JN, Fracasso PM. Management of locally advanced carcinoma of the breast. II. Inflammatory carcinoma. *Cancer* 1994; 74:466-476.
 34. Jaiyesimi IA, Buzdar AU, Hortobagyi G. Inflammatory breast cancer: a review. *J Clin Oncol* 1992; 10:1014-1024.
 35. Vinnicombe SJ, MacVicar DA, Guy RL, et al. Primary breast cancer: mammographic changes after neoadjuvant chemotherapy with pathologic correlation. *Radiology* 1996; 198:333-340.
 36. Segel MC, Paulus DD, Hortobagyi GN. Advanced breast cancer: assessment at mammography of response to induction chemotherapy. *Radiology* 1988; 169:49-54.
 37. Gawne-Cain ML, Smith E, Darby M, Given-Wilson R. The use of ultrasound for monitoring breast tumor response to preadjuvant therapy. *Clin Radiol* 1995; 50:681-686.
 38. Forouhi P, Walsh JS, Anderson TJ, Chetty U. Ultrasonography as a method of measuring breast tumor size and monitoring response to primary systemic treatment. *Br J Surg* 1994; 81:223-225.
 39. Davis PL, McCarty SK. Technologic considerations for breast tumor size assessment. *Magn Reson Imaging Clin N Am* 1994; 2:623-631.
 40. Abraham DC, Jones RC, Jones SE, et al. Evaluation of neoadjuvant chemotherapeutic response of locally advanced breast cancer by magnetic resonance imaging. *Cancer* 1996; 78:91-100.
 41. Gilles R, Guinebretiere J, Toussaint C, et al. Locally advanced breast cancer: contrast-enhanced subtraction MR imaging of response to preoperative chemotherapy. *Radiology* 1994; 191:633-638.
 42. Mendelson EB. Evaluation of the postoperative breast. *Radiol Clin North Am* 1992; 30:107-138.
 43. Dershaw DD, Shank B, Reisinger S. Mammographic findings following breast cancer treatment by local excision and definitive irradiation. *Radiology* 1987; 164:455-461.
 44. Gold RH, Montgomery CK, Minagi H. The significance of mammary skin thickening in disorders other than primary carcinoma: a roentgenologic pathologic correlation. *AJR Am J Roentgenol* 1971; 112:613-621.