

BREAST

Objectives

1. Identify and describe the clinical presentations of breast cancer.
2. List common risk factors for breast cancers.
3. List diagnostic modalities and their sequence in the work-up of a patient with a breast mass.
4. List and discuss the types of preinvasive and invasive breast cancer.
5. List and discuss the surgical treatment options of breast cancer.
6. Describe the rationale for adjuvant chemotherapy, radiation, and hormonal therapy in the treatment of breast cancer.

BREAST-Continued

A 46-year-old Caucasian woman, mother of two, actively menstruating, whose premenopausal sister has been treated for breast cancer, has never been screened for breast cancer. She now presents with a finger tip-sized, rock-hard mass in her right breast. The patient is a highly intelligent Ph.D., biochemist who comes to the first office visit in a very anxious state with her engineer husband.

1. What are the current American Cancer Society guidelines for screening of adult women in the United States for breast cancer?
2. What data show that screening for breast cancer is effective and improves survival in screened populations?
3. What are the risk factors associated with breast cancers?
4. Name presenting symptoms of breast cancer and their likelihood for malignancy.
5. Describe different biopsy options for this and other patients.
6. Describe current surgical options for invasive breast cancer.
7. What is the metastatic preoperative work-up for this patient? What is relevant review of system questions to determine this work-up?
8. What are eligibility criteria's for breast conservations surgery? Any contraindications.
9. Describe the risks of breast surgery, including risk for axillary dissection.
10. What are prognostic factors for this patient) on surgical specimen) and describe whether they contribute favorably or unfavorably to long-term survival.
11. If the patient has a contraindication to breast conservation surgery, what are her options for immediate reconstruction? Is local recurrence rather different for immediate versus delayed reconstruction?

BREAST-Continued

Case Study: DCIS

60-year-old female presents with new right breast microcalcifications on mammography. NO palpable breast masses, no nipple discharge, no abnormal retraction.

PMH: Diverticulosis and tubular adenoma

PSH: Colonoscopy and polypectomy

Risk factor assessment: Menarche age 11, Menopause age 49-50, G2P2 (age of first birth 25 yrs), no hx of breast-feeding.

FH: Mother diagnosed with breast cancer age 59, sister diagnosed age 45, maternal grandmother some type of cancer (?), father with colon cancer.

ROS: essentially negative

PE: Breast: right with core biopsy healing site at 9 o'clock, no masses, no nipple discharge, no abnormal retraction, no axillary or supraclavicular adenopathy.

Mammogram results

Questions:

1. What is your assessment of this patient's risk for breast cancer?
2. Discuss the Birads classification system for reading mammograms and the clinical significance of this system. How can the patient be incorporated into this decision-making?
3. What do you recommend for this patient?
4. Pathology report attached-what should be done next? (see report number one)
5. What adjuvant therapy recommendations should be made? What is the literature to support your decision making with this patient?
6. What is the long-term follow-up plan for this patient?

BREAST-Continued

Breast Conference Notes

Presenting Symptom	Likelihood malignancy	Risk of missed diagnosis
Palpable mass		
Abnormal mammogram		
Vague thickening/nodularity		
Nipple discharge		
Breast pain		
Breast infection		

Risk Factors

Age

Race

Hormonally related

- Age menarche <12
- Age menopause
- Nulliparity
- Age 1st pregnancy >29
- Absent history lactation
- Post-menopausal estrogens
- Use of other hormones (fertility regimens)
- ?Prolonged use BCP (before 1st pregnancy)

Family History

- Multiple affected relatives
- Early onset
- Bilaerality
- Ovarian CA

Pathological Findings

- Atypical hyperplasia
- Lobular carcinoma in situ
- Proliferative fibrocystic disease

Other

- Diet
- Exercise
- Environmental factors
- Previous breast CA
- Previous breast problems
- Previous breast operations
- Previous exposure to radiation

BREAST-Continued

Family History

Shattuck-Eidens et al: BRCA1 Sequence Analysis. JAMA 278:1242, October 1997.

- Lifetime risk breast CA 10% by age 70%
- One of eight women will develop breast CA
- 180,000 new cases invasive breast CA diagnosed per year
- 43,000 women succumb to disease each year
- 5-10% breast CA due to inheritance of an altered or mutated copy of 1 of 2 genes know as BRCA1 and BRCA2
- Inherit mutated copy of either gene increased lifetime risk up to 87% by 70yrs
- BRCA1 associated with ovarian CA (more so than (BRCA2)
- N=798 persons thought to be at elevated risk of BRCA1 because of risk factors
- Characteristics increased probability of carrying a BRCA! Mutation: early age of diagnosis, Ashkenazi Jewish ethnicity, family history of CA

Diet and Exercise

Thune et al: Physical Activity and the Risk of Breast CA: NEJM 336: 1269, May 1997.

- Norway health survey study
- 25624 women age 20-54 years
- Def. Exercise (Leisure time) grade 1=leisure time sitting, grade 2=four hours a week physical activity, grade 3=4 hours a week physical activity plus some recreations athletics, grade 4=regular vigorous training or competitive sports several times a week. (Work time) grade 1=sedentary, grade 2=walking, grade 3=walking plus lifting, grade 4=heavy manual labor.
- Reduced risk of breast CA (37%) in women who exercised regularly compared with sedentary women (greater risk reduction for pre-menopausal versus post menopausal women)
- Greater reduction in lean women, women <45 years, women who exercised over a three-five year period.
- Study prospective, large number of enrollees, adjusted for confounding factors such as age, body mass, dietary factors and parity.
- Mechanism: physical activity may influence the production, metabolism, and excretion of endogenous sex hormones. Exact details unknown.
- Exercise also reduces: CAD, diabetes, stroke osteoporosis, obesity, and disability. Lessens impact of chronic ailments such as arthritis and cognitive decline.
- Conclusion: physical activity during leisure time and work is associated with a reduced risk of breast CA

Huang et al: Weight gain and Breast CA. JAMA 278: 1407, Nov. 1997.

- Nurses Health Study 95,256 age 30-55 years (f/u 16yr.)
- Harvard School of Public Health
- 2517 with invasive breast CA

BREAST-Continued

- Pre-menopausal: obesity reduces the incidence of Breast CA but not death
- Post-menopausal: weight gain (>20kg) increases the risk of breast CA and death
- Stronger association between weight gain and breast CA in post-menopausal women who never used hormones.
- Conclusion avoiding adult weight gain may contribute importantly to the prevention of breast CA after menopause, particularly among women who do not use post-menopausal hormones.

Mammogram controversy

Wrong focus for mammogram debate? AMA New May 5, 1997.

- 80% breast CA in over 50 population, 20%<50 (4-5% less than 40)
- Mammos miss 10-15% palpable lesions (dense breasts and lobular carcinoma are contributing factors)
- NIH consensus panel Jan. 1997 did not support universal screening of women less than 50 because lack of convincing data (if women ages 50-69 had regular screening mammos, the death rate for that group would be reduced by one-third)
- National Cancer Advisory Board and NCI voted in Mar. 1997 to support advising women with average risk to undergo mammos every one to two years in their 40s.
- American Cancer Society Mar. 1997 opposed NIH recommendation and recommended that women should have mammos every year in their 40s.
- AMA suggests baselines 35-40 yrs., every two years from 40-49 and every one year from age 50.
- Medicare controversy: only pays 80% for one screening every two years (age 65 or greater)- has been changed to annual coverage (1998)

Breast conservation surgery data

Fisher B et al: Re-analysis of a trial comparing total mastectomy with lumpectomy. NEJM 333: 1456, Nov. 1995.

- Pts enrolled 1976-1984, average 12 year follow-up, B-06 protocol (pre-randomization procedure implemented Jan. 1978)
- Inclusion: tumors 4cm or less, + or – axillary nodes
- Three Rx arms: Total mastectomy, lumpectomy followed by breast irradiation or lumpectomy without irradiation
- This study analyzed three cohorts: 2105 randomized and analyzed according to the intention to treat, 1851 with know nodal status who agreed to be followed and accepted assigned therapy, 1529 (1851 minus the controversial St. Luc Hospital data).

BREAST-Continued

- Results: For all three cohorts, no significant differences in overall survival, disease-free survival (first recurrences of disease, second cancers, and death without recurrence of CA), or survival free of disease at distant sites, (distant mets as first recurrence, distant mets after locale or regional recurrence, second CA including tumor in contralateral breast) between all three Rx arms. Local recurrence in lumpectomy groups: 10% and 35% respectively. In those with node positive CA, local recurrence was lower, only 5%.
- Conclusion: lumpectomy followed by breast irradiation is appropriate Rx for women with either negative or positive axillary nodes and breast tumors 4 cm or less in diameter.

DCIS

Silverstein MJ et al: DCIS Prognostic Index. *Cancer* 77:2267, Jun. 1996.

- DCIS incorporates wide spectrum of disease, completely treated by mastectomy (argument of pts—"wait until my tumor becomes invasive then I can have breast conservation therapy"—role of limited surgery for DCIS is quite relevant)
- Rx controversy: local recurrence and need for breast irradiation.
- NSABP B1: local recurrence=10% for tumor excision and irradiation; 21% for tumor excision along but no subject analysis.
- Two centers total of 333 pts (195 by excision along, 138 by excision plus radiotherapy), no randomization.
- Scoring 3-9 based on size (<16mm, 16-40 mm, >40), margin width (<9mm, 1-9 mm, >9mm) and pathologic classification (non-high grade without necrosis, non-high grade with necrosis, high grade with or without necrosis) comedo=necrosis. (non-high grade defined as s1 and 2, 3=high grade)
- Conclusion: VNPI scores 3 or 4 excisions only, scores 5 or 6 or 7 = 17% decrease in local recurrence rates with radiation therapy, scores 8 or 9 extremely high local recurrence consider for mastectomy.

Adjuvant radiotherapy pre-menopausal women

Overgaard M et al: Postoperative radiotherapy in high-risk pre-menopausal women with breast CA, *NEJM* 337: 949, Oct. 1997. (Denmark study)

- 1708 with pathological stage II or III randomized CMF plus irradiation to chest wall and LNs (axilla, supraclav, internal mammary) of CMF along
- Def. High risk (one or more of the following): involvement of axillary LNs, a tumor size of more than 5 cm, invasion of the cancer to skin or pectoral fascia.
- Results: locoregional recurrence or distant mets 9% with radiotherapy vs 32% without radiotherapy. Survival free of disease 48% vs 34% and overall survival 54% vs. 45%.
- Conclusion: Addition of postoperative irradiation to mastectomy and adjuvant chemo reduces locoregional recurrences and prolongs survival in high risk-pre-meno women.

BREAST-Continued

Ragaz J et al: Adjuvant radiotherapy in node-positive pre-menopausal women with breast CA. NEJM 337: 956, Oct. 1997. (Vancouver study)

- 318 women with node-positive breast CA randomized to two groups (CMF with rays or CMF without rays).
- Inclusion: Stage I or II breast CA after mastectomy with any positive nodes
- Radiotherapy: axilla, supraclav, and internal mammary nodes treated
- Results after 15 yrs: 33% reduction in recurrence, 29% reduced mortality.
- Conclusion: Radiotherapy with chemo after MRM decreases rate of locoregional, systemic relapse and reduces mortality from breast CA.

Mammography Interpretation: The BI-RADS Method (American College of Radiology: Breast imaging reporting and data system 2nd edition. ACR, 1995)

- Negative: nothing suspicious
- Benign: clearly no malignant features, reporting of benign lesion.
- Probably Benign (Short interval follow-up): Characteristics suggest benign, slight chance of malignancy therefore follow-up at interval less than one year. (less than 2% chance malignant)
- Suspicious Abnormality-Biopsy suggested: most non-palpable lesions.
- Highly suggestive malignancy: Controversy to go straight to OR or perform biopsy. (If known ahead of time can be aggressive with margins)

CHAPTER 1 BREAST CANCER

Sheryl A Grabram, M.D.

Patient is a 67-year-old white female with a 3 month history of a left breast mass. She noticed the mass in the upper outer quadrant of her left breast while showering. The mass is non-tender and seems to be slowly enlarging. The patient has no family history of breast cancer and denies any history of trauma to the breast, pain, or nipple discharge.

The physical examination is remarkable for a 1.5 cm hard irregular mass in the upper out quadrant of the left breast. There is no dimpling of the skin, edema, or nipple retraction. The mass is mobile and not fixed to the chest wall. There is no obvious axillary, infraclavicular, or supraclavicular adenopathy.

Q: How common is breast cancer? Who gets breast cancer?

A: Breast cancer is the most common form of cancer in women. Women are Certainly at an increased risk compared to men with male breast cancer accounting for only 1% of all breast cancers. Age is also an important factor. Cancer in women under 20 is very rare, but increases with age, rising slowly after the age of 50. There is also a strong familial correlation to developing breast cancer; women whose mother's had breast cancer have 3 times the risk of the general population. Overall, 1 in 10 women will have breast cancer sometime in their life.

Q: How would you proceed with evaluation of the breast mass in this patient?

A: The obvious concern is whether the patient has carcinoma of the breast. A tissue diagnosis is required prior to definitive treatment. Options for obtaining a tissue diagnosis are fine needle aspiration biopsy, core needle biopsy, and open surgical biopsy (either incisional or excisional).

Q: What other test might influence the treatment of this patient? Should these tests be obtained prior to needle aspiration or biopsy.

A: Mammography would be useful because it may show other areas within the same breast that are suggestive of another carcinoma and it can be used to evaluate the contralateral breast. While positive mammographic findings in the same or opposite breast may influence the treatment plan, it is important to realize that a negative mammogram does not rule out malignancy. Any suspicious palpable lesion warrants biopsy whether seen on mammogram or not.

Additionally, the timing of the mammogram depends on the situation and the type of biopsy to be undertaken. A fine needle aspiration can be performed easily in the clinic, prior to a mammogram, without altering the

BREAST CANCER (cont'd)

mammography findings. However, mammography should always be formed prior to any open surgical biopsy. This prevents obscuring subtle findings in the area of question and prevents an unnecessary trip back to the operating room to biopsy a second, nonpalable lesion.

A mammography was obtained. It showed a stellate 1.5-cm lesion of the upper quadrant of the left breast with architectural disruption of the surrounding breast tissue and microcalcifications. All mammographic findings are suggestive of malignancy. There were no other abnormalities in the remainder of the left breast or in the right breast.

- A. What is the next step in the workup?
- Q. Fine needle aspiration (FNA) of the lesion is an excellent option because a diagnosis of carcinoma could be obtained prior to any surgical procedure. However, interpretation of tissue obtained from a fine needle aspiration requires a skillful cytopathologist for accurate diagnosis. A definitively positive FNA diagnosis of carcinoma would allow a final plan for surgical treatment to be made without a surgical biopsy. An equivocal FNA result may require a confirmation by surgical biopsy before either the surgeon or the patient undertakes more extensive treatment. Also, it is important to realize that a negative FNA biopsy does not rule out a malignancy. Similar to mammography, there is a well-defined false negative rate for FNA biopsies. Any suspicious lesion with a negative FNA still warrants an excisional biopsy.

If an excisional biopsy is undertaken when the lesion is suspected to be cancerous, a wide excision with an attempt to obtain pathologically free margins is appropriate. The biopsy of a small lesion, as seen in this patient, may serve as a lumpectomy if all margins are clear.

A fine needle aspiration was performed and was “highly suspicious” for carcinoma.

- Q. What are the treatment options?
- A. The term “highly suspicious” implies some level of doubt on the part of the pathologist. If there is any doubt, an open biopsy should be performed prior to operative treatment. If the diagnosis is definitive, surgical treatment may follow.

Several well-designed studies have shown that segmental mastectomy (lumpectomy) coupled with axillary node dissection and radiation therapy, is equivalent to modified radical mastectomy (removal of all breast tissue and axillary lymph nodes). The former procedure gives a superior cosmetic result.

BREAST CANCER (cont'd)

- Q. Why is it necessary to remove axillary nodes?
- A. There are several reasons. Removal of the axillary nodes allows for precise pathologic staging, which may be important in determining the need for subsequent chemotherapy. Also, removal of tumor-bearing lymph nodes limits the need for radiation of the axilla.
- Q. What are the reasons for not performing “breast conserving surgery” on all patients? That is, are there contraindications to segmental mastectomy and axillary dissection with subsequent radiation therapy?
- A. Although many women want breast-conserving surgery, some may prefer modified radical mastectomy when they have a clear understanding that equivalent results are obtained with both procedures. In addition, a large lesion in a small breast will cause significant unreconstructable deformity when appropriately excised. This situation is, therefore, a contraindication to breast conserving surgery.

Also, breast conserving surgery is contraindicated in patients with evidence of multiple cancers within the same breast (multiple palpable lesions or multiple “suspicious” areas in different quadrants, as evidenced by mammography). Central lesions and positive margins from a previous excisional biopsy can make segmental resections difficult and some series have also listed multifocal intraductal disease, pregnancy, and unfavorable histology (poorly differentiated or anaplastic lesions) as relative contraindications to breast conserving procedures.³

Patient elected to undergo a modified radical mastectomy.

- Q. What is the arterial blood supply to the breast?
- A. Perforating branches of the internal mammary artery, the pectoral branches of the thoracoacromial artery, and the lateral thoracic artery provide the majority of the blood supply to the breast. Branches of the subscapular artery and lateral intercostal perforators make a minor contribution to the blood supply.⁴
- Q. What nerves are encountered in an axillary dissection and what are the consequences of injury to these nerves?
- A. The long thoracic nerve innervates the serratus anterior. Injury to this nerve produces “winged scapula”, a considerable disability.

BREAST CANCER (cont'd)

The thoracodorsal nerve never innervates the latissimus dorsi. The latissimus dorsi is used to stabilize the shoulder and to adduct, and internally rotate the arm. The intercostal brachial nerve provides cutaneous sensation in the posterior axilla. Removal of this nerve causes paresthesia and dysesthesia, but does not cause motor dysfunction. This nerve can be sacrificed, if absolutely necessary, to allow for a proper axillary dissection, but some surgeons advocate its preservation if no gross disease is found in the axilla.⁴

- Q. What are the anatomic landmarks for describing axillary lymph nodes?
- A. The axillary nodes are defined in terms of the anatomic relationship to the pectoralis minor muscle. Level I axillary nodes are lateral to the pectoralis minor, level II nodes are posterior to the pectoralis minor, and level III nodes are medial to the pectoralis minor, and level III nodes are medial to the pectoralis minor.⁵

For adequate sampling and staging all of the patient's level I and II axillary nodes are removed.

- Q. What is the difference between a modified radical mastectomy and the radical mastectomy advocated by Drs. Halstead and Meyer at the turn of the century?
- A. Most surgeons today remove the breast, pectoral fascia, and axillary nodes as part of a modified radical mastectomy. The radical mastectomy involves removing the breast, pectoral fascia, axillary nodes and the pectoralis major. At the turn of the century the radical mastectomy proved to be an excellent technique for local cancer control in patients with large breast cancers. Because most of the patients treated by Dr. Halstead had large tumors with axillary nodal metastases and, therefore, occult systemic metastases to bone, lung, and brain, the radical mastectomy rarely "cured" a patient with breast cancer. This procedure prevented the pain and suffering associated with the continued growth of a large fungating, painful, necrotic, infected breast tumor.

Patient's specimen underwent pathologic evaluation.

- Q. Are there any special studies needed for breast cancer?
- A. Estrogen and progesterone receptor studies are mandatory. These provide useful information regarding prognosis and can influence treatment options. If a previous open biopsy has been performed, receptor studies should have been done on the specimen because it is common to have no residual tumor in the subsequent mastectomy specimen. Surgical margins are also a critical aspect of the pathologic evaluation. They are especially

BREAST CANCER (cont'd)

important in segmental mastectomy specimen because a missed positive margin on frozen section may require a follow-up mastectomy. More recently, additional studies of tumor nuclear ploidy, flow cytometry, DNA abnormalities, and percent of cells in S-Phase have become prevalent and are helpful in identifying aggressive histologies that may benefit from adjuvant radiation and chemotherapy.

Two large closed suction drains were placed in the wound, one in the axilla and one on the chest wall.

- Q. Why are drains necessary after a modified radical mastectomy?
- A. Drains are necessary for several reasons: First, the “suction” allows for apposition of the tissue and diminishes the amount of dead space. Second, because the lymphatic drainage of the arm has been removed there is a continued drainage of lymph from the arm, as well as serous exudates from the dissection surface. Without drains, this fluid would collect and form a seroma.
- Q. When should the drains be removed?
- A. A safe guideline is to remove the drain when the output is less than 30 ml for 24 hours.⁶ Even with this meticulous attention to drain management, seroma is the most common complication following modified radical mastectomy.
- Q. What are other complications of this operation?
- A. Other complications include (1) necrosis of the wound edges and poor wound healing (secondary to excessive tension on a wound closure or thin skin flaps with compromised blood supply); (2) hemorrhage; (3) atelectasis; (4) infection; (5) limitation of arm and shoulder motion; and (6) lymphedema.⁷
- Q. Should this patient be offered reconstructive surgery?
- A. Yes. If the treatment of breast cancer requires mastectomy, the option of breast reconstruction should be presented to the patient. If the patient is interested in reconstructive surgery, a plastic surgeon should be consulted prior to mastectomy. In some cases, the breast can be reconstructed at the time of the mastectomy, or a delayed operation can be performed.

The option of breast reconstruction was discussed with the patient prior to surgery and she did not desire breast reconstruction. The surgeon should not assume that because of the age of the patient reconstruction is not indicated.

BREAST CANCER (cont'd)

Patient remained in the hospital for 5 days. One of the drains was removed prior to discharge and the patient was sent home being taught how to monitor and record output of the remaining drain. The patient was seen in the office of postoperative day 7 and the second drain was removed. A review of the pathology report showed a moderately well differentiated infiltrating ductal carcinoma with 5 of 30 nodules positive for metastasis. The tumor was found to be estrogen and progesterone receptor positive.

Q. What is the most common histologic type of breast cancer?

A. The most common histologic type of breast cancer is infiltrating ductal carcinoma. Infiltrating lobular carcinoma, medullary carcinoma, and Paget's disease of the nipple are other invasive carcinomas arising from breast tissue. Ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS) are also common histologic types. However, neither is an invasive carcinoma, but rather both represent lesions indicative of women at a much higher risk of subsequently developing invasive carcinoma. The treatment of these noninvasive lesions is very controversial and is the focus of ongoing nationwide trials.

Q. Does this patient require further therapy?

A. Yes. This patient should be placed on tamoxifen with possible consideration of chemotherapy.

Q. What is tamoxifen?

A. Tamoxifen is an antiestrogen drug that is taken orally with few side effects. Because this patient's tumor was estrogen and progesterone receptor positive, tamoxifen is indicated and should prolong the disease-free survival and survival of this patient.

Q. Is this patient a candidate for chemotherapy?

A. Traditionally, it was believed that postmenopausal women do not benefit from adjuvant chemotherapy. Controversy has arisen recently, however, with studies showing some benefit from chemotherapy in postmenopausal women with positive nodes. Many physicians would still not recommend chemotherapy for this patient. However, this may change and the option of chemotherapy should at least be discussed with the patient. Optimally, the patient could enter a randomized trial to delineate the effects adjuvant chemotherapy in postmenopausal women.

BREAST CANCER (cont'd)

- Q. What is meant by adjuvant chemotherapy?
- A. Because this patient's lymph nodes were positive for cancer, the chance that she has occult distant metastases is 60 to 70%, although she has no clinical evidence of residual disease. "Adjuvant therapy" is used to treat patients at risk of having occult systemic disease but who have no obvious disease at the time of therapy.

The adjuvant treatment of breast cancer continues to evolve, as the result of ongoing studies are known. The treatment options remain complex, however, based on the menopausal state of the patient and the stage of disease. Also, because of ongoing therapies, the indications for treatment continue to evolve rapidly. The following recommendations have been widely accepted:⁷

1. Premenopausal women, node positive – Adjuvant chemotherapy.
2. Premenopausal women, node negative – no further therapy.
3. Premenopausal women, node negative – no further therapy.
4. Premenopausal women, node positive estrogen receptor positive – adjuvant tamoxifen.

BREAST CANCER (cont'd)

More recently, premenopausal node negative women have been extensively studied and many physicians now feel that adjuvant chemotherapy has demonstrated a significant increase in survival for these women. Also, postmenopausal node negative women that are estrogen receptor positive are frequently places on tamoxifen and postmenopausal node positive women that are estrogen receptor negative are considered for chemotherapy. The approaches, and others, are being evaluated in ongoing clinical trials.^{8,9} The study of possible prognostic factors such as nuclear grad, DNA content (ploidy), and percentage of cells in S-phase may add in the treatment of node negative patients. Optimally, all patients with breast cancer should be offered the opportunity to participate in one of the ongoing clinical trials.

Chemotherapeutic agents commonly used in adjuvant therapy of breast cancers, as well as metastatic disease, include cyclophosphamide, adriamycin, fluorouracil, methotrexate, etoposide, and cisplatin. These drugs are usually given as combination chemotherapy using two or more drugs.

Because treatment options and prognosis are based on the stage of the disease at diagnosis, accurate staging of breast cancer is important. The tumor, node, and metastasis (TNM) staging system should be defined for all patients.

TNM STAGING

Primary Tumor (T)

T _x	Primary tumor cannot be assessed
T ₀	No evidence of primary tumor
T _{is}	Carcinoma <i>in situ</i> . Intraductal carcinoma, lobular carcinoma <i>in situ</i> , or Paget's disease of the nipple with no tumor
T ₁	Tumor 2 cm or less in greatest dimension
T _{1a}	0.5 cm or less in greatest dimension
T _{1b}	More than 0.5 cm but not more than 1 cm in greatest dimension
T _{1c}	More than 1 cm but not more than 2 cm in greatest dimension
T ₂	Tumor more than 2 cm but not more than 5 cm in greatest dimension
T ₃	Tumor more than 5 cm in greatest dimension
T ₄	Tumor of any size with direct extension to chest wall or skin
T _{4a}	Extension to chest wall
T _{4b}	Edema (including peau d'orange) or ulceration of the skin of breast or satellite nodules confined to same breast
T _{4c}	Both T _{4a} and T _{4b}
T _{4d}	Inflammatory carcinoma

Lymph Node (N)

N _x	Regional lymph nodes cannot be assessed
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BREAST CANCER (cont'd)

- N₀ No regional lymph node metastasis
- N₁ Metastasis to moveable ipsilateral axillary lymph node(s)
- N₂ Metastasis to ipsilateral axillary lymph node(s) fixed to one another or to other structures
- N₃ Metastasis to ipsilateral mammary lymph node(s)

Distant Metastasis (M)

- M_x Presence of distant metastasis cannot be assessed
- M₀ No distant metastasis
- M₁ Distant metastasis (includes metastasis to ipsilateral supraclavicular lymph nodes)

Q. What factors determine the clinical-pathologic staging system for breast cancer?

- A. Stage I: Tumor size less than 2 cm, node negative
- Stage II: Tumor size greater than 2 cm but less than 5 cm, node positive
- Stage III: Tumor size greater than 5 cm, tumor fixation to chest wall, edema or ulceration of the skin, satellite skin nodules, ipsilateral axillary nodes fixed to one another or involving skin or chest wall.
- Stage IV: Distant metastases (including metastasis to ipsilateral supraclavicular lymph nodes).

Q. Breast complaints related to an underlying benign process are very common. A 17-year-old woman present with a 3 x 4 cm firm, mobile, well circumscribed, non-tender breast mass. What is the most like diagnosis?

- A. This is a classic presentation of fibroadenoma.

Q. How would you work up this lesion?

- A. This mass may possibly be a cyst, although this is unlikely based on the physical findings. One could obtain an ultrasound to determine if the lesion is cyst or solid. However, a more practical approach would be to aspirate the lesion with a fine needle. If no fluid is obtained, the lesion is solid.

Q. Does this patient require mammography?

- A. No. Breast tissue in young women (less than 35) is radiographically very dense and little useful information is obtained by mammography in this age group.

BREAST CANCER (cont'd)

Q. Does this mass require biopsy?

A. Yes. Because of the size of this lesion, a biopsy is indicated. A fibroadenoma is a benign tumor that is cured by an excisional biopsy, but it may be difficult to differentiate from cystocarcinoma phyllodes or even breast cancer. Invasive cancer may be seen in the late teens and early twenty's, albeit rarely.

Q. What is fibrocystic disease?

A. Fibrocystic disease (which is better referred to as "fibrocystic change" is a term describing changes in the breast that relate to varying degrees of glandular and stromal proliferation, secretion, and inflammation. Other names, frequently used are chronic cystic mastitis, mastopathy, mammary dysplasia, adenofibromatosis, nodular hyperplasia, fibroadenosis, and mastoplasia.⁵

Q. What complaints are commonly associated with fibrocystic disease?

A. Patients with fibrocystic disease often complain of tenderness, pain, swelling, and nodularity of the breast, occurring most frequently during menstruation.

Q. Is fibrocystic disease most common in young women?

A. No. The incidence of histologic lesions that clinically correlate with fibrocystic disease increase in frequency with age.

Q. Is fibrocystic disease a premalignant lesion?

A. No. However, a subgroup of patients with severe hyperplasia or atypia do have an increased incidence of breast cancer. The major significance of fibrocystic changes is that they may mimic or obscure a breast carcinoma.

Q. What are the treatment options for fibrocystic disease?

A. Analgesia using aspirin or other nonsteroidal anti-inflammatory agents is helpful. Restrictions of caffeine (and other xanthines) and the use of vitamin E has been suggested by some researchers as effective in reducing symptoms. The true effectiveness of these maneuvers has been doubted by other physicians. Finally, Danazol, an androgenic hormone, is effective, but its side effects make it rarely useful.

Summary

Breast cancer is the most common form of cancer in women, affecting 1 in 10 women. Women with a close family history of breast cancer are at an increased risk. Tissue for diagnosis may be obtained from either excisional biopsy or needle biopsy. Fine needle aspiration and cytologic examination is an effective diagnostic modality in the hands of an experienced cytopathologist. When cancer is diagnosed, the patient may choose between breast conserving surgery and modified radical mastectomy both have similar recurrence rates and mortality. In both procedures, axillary node dissection is important for tumor staging. Estrogen and progesterone receptor status of the specimen are important for the consideration of adjuvant tumoral therapy.

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