A 46-year-old woman presents to the outpatient clinic for evaluation of a breast mass that was discovered by her primary care physician during a physical examination. The patient does not perform breast self-examination, and she has never noticed the mass prior to this time. Her past medical history is unremarkable. She has not had any prior history of breast complaints or trauma. The findings from the physical examination are unremarkable except for the breast examination. A hard, non-tender, 4-cm mass is noted in the upper outer quadrant of her left breast. The left axilla is without abnormalities. Examination of the right breast reveals no dominant mass or axillary adenopathy.

What is your next step?

What is the likely therapy for this patient if she is concerned about breast cosmetic appearance and preservation?
ANSWERS TO CASE 1: Breast Cancer

Summary: A 46-year-old female has a 4-cm palpable left breast mass. The findings from an examination of the left axilla and of her right breast are normal.

Next step: Obtain tissue for diagnosis, and if a malignancy is confirmed, proceed with cancer staging. Bilateral mammography may be helpful.

Likely therapy: If a biopsy confirms breast carcinoma, the disease is likely in clinical stage IIa (Table 1–1), which is generally best managed by (1) first surgery and then adjuvant therapy or (2) initially systemic therapy (chemotherapy) to shrink the tumor, followed by locoregional surgical therapy (neoadjuvant). Neoadjuvant therapy is probably the best choice in this case because the patient is concerned about cosmetic appearance and desires breast conservation.

Analysis

Objectives

1. Review the initial workup and staging process for a patient with newly diagnosed breast cancer.
2. Be familiar with the options for locoregional and systemic therapy of breast cancer and the basis for selecting neoadjuvant therapy for certain patients.

Considerations

The initial workup for this patient requires confirmation of breast cancer, including bilateral mammography and core needle or excisional biopsy. If carcinoma is confirmed, an additional metastatic workup should include a complete blood count (CBC), liver function tests, and chest radiography (CXR). If a biopsy confirms breast carcinoma, it is
likely to be stage IIa (Table 1–1), which is best managed by surgery and adjuvant therapy or by systemic therapy (neoadjuvant) prior to locoregional therapy. This patient is a candidate for mastectomy or breast conservation therapy because the extent of local surgery does not impact her overall survival. Because she desires breast conservation therapy, neoadjuvant therapy is probably the best choice. The breast/tumor size ratio is another reason for providing systemic therapy before surgery.

**Table 1–1**

**BREAST CANCER STAGING**

| Stage 0 | Tis | N0 | M0 | Tx: Cannot assess |
| Stage I | T1 | N0 | M0 | T0: No evidence of primary tumor |
|         | Tis | In situ |
| Stage IIA | T0–T1 | N1 | M0 | T1: ≤2 cm |
|           | T1a: ≤0.5 cm |
|           | T1b: >0.5 cm, ≤1 cm |
|           | T1c: >1 cm, ≤2 cm |
| Stage IIB | T2 | N0 | M0 | T2: >2 cm, ≤5 cm |
| Stage IIIA | T0–T2 | N2 | M0 | T3: >5 cm |
|           | T4: Extension to chest wall or skin |
|           | T4a: Extension to chest wall |
|           | T4b: Edema or ulceration of the skin |
|           | T4c: Both chest wall extension and skin involvement |
|           | T4d: Inflammatory carcinoma |
| Stage IIIB | T4 | N0–N2 | M0 | N1: Ipsilateral internal mammary nodal metastases |
|           | N2: Fixed ipsilateral axillary nodal metastases |
|           | Tany N3 | M0 |
| Stage IV | Tany | Nany | M1 | Mx: Cannot be assessed |
|           | M0: No distant metastases |
|           | M1: Distant metastases |
APPROACH TO BREAST CARCINOMA

Definitions

**Fine-needle aspiration (FNA):** A diagnostic procedure using a small-gauge needle and a syringe under vacuum for cytologic analysis, with or without image guidance. FNA can identify cancer but cannot differentiate invasive cancers from in situ cancers.

**Core needle biopsy:** Large-bore needle (usually 10- to 14-gauge) biopsy that provides a histologic diagnosis. This procedure can be done with image guidance via stereotactic techniques (Figure 1–1).

**Neoadjuvant chemotherapy:** Chemotherapy given *prior* to surgery to shrink the tumor and provide a better cosmetic result. Adjuvant therapy is chemotherapy or radiotherapy *following* surgery.

![Figure 1–1. Stereotactic core breast biopsy.](image-url) The patient is prone on a table undergoing a biopsy with image guidance.
Level 1, 2, and 3 axillary nodes: Level 1 nodes are lateral to the pectoral minor muscles; level 2 nodes are deep to the pectoral minor muscles; and level 3 nodes are medial to the pectoral minor muscles.

Clinical Approach

The steps in breast cancer management include diagnosis, locoregional therapy, and systemic therapy. The history, physical examination, imaging, and tissue biopsy are involved in the diagnosis in most cases. Breast imaging for most patients consists primarily of mammography, although in selective cases ultrasound or magnetic resonance imaging (MRI) can also be considered. A tissue diagnosis can be obtained with FNA, core needle biopsy, or excisional biopsy. Once the tissue diagnosis confirms cancer, the extent of disease and metastasis must be defined, including evaluation of the ipsilateral and contralateral breasts. Stage I and II tumors should be staged with a CBC, liver function tests, and a chest radiograph (CXR). Individuals with bone pain or abdominal symptoms should be evaluated with a bone scan or an abdominal computed tomography (CT) scan to image the liver. Stage III disease should be evaluated with a CBC, liver function tests, a CXR, a bone scan, an abdominal CT scan, and brain CT or MRI if the patient has headaches or neurologic complaints (Figure 1–2).

The surgical options are individualized. If the patient desires breast conservation therapy, feasibility is based on the likely cosmetic outcome, the ability to safely obtain negative margins without a total mastectomy, and the patient’s compliance with postoperative radiation therapy and follow-up breast cancer surveillance. Large lesions requiring partial mastectomy may cause significant cosmetic distortion; in such cases patients commonly undergo neoadjuvant chemotherapy to shrink the tumor to obtain better cosmetic results. Alternatively, with a more favorable tumor/breast size ratio, it is often possible to perform a partial mastectomy and obtain a good cosmetic result without the use of neoadjuvant chemotherapy.

Management

1. The first step is obtaining a tissue diagnosis and staging the breast cancer.
Figure 1–2. The evaluation of a palpable breast mass. MRI, magnetic resonance imaging; FNA; fine-needle aspiration.
2. **Locoregional therapy**: Breast conservation therapy and mastectomy offer equivalent survival benefits with proper patient selection and follow-up. In addition to resection of the primary tumor, assessment of the regional lymph node basin for local control, complete staging, and determination of the appropriate adjuvant therapy (such as chemotherapy and/or radiation therapy) are undertaken. **Options for nodal staging include levels 1 and 2 axillary dissection versus sentinel lymph node biopsy.** The rationale for sentinel node sampling is to identify the primary lymphatic drainage of the tumor and perform a biopsy on only these nodes. The primary nodal drainage is identified by injecting radiotracers and blue dye at the site of the primary tumor. A gamma probe is used to identify the location of the sentinel node. A small incision is then made over the targeted node, which is further identified with the gamma probe as well as being stained with the blue dye. A biopsy of the sentinel nodes allows for a smaller incision and less axillary morbidity compared to complete nodal basin dissection. However, if the sentinel node is positive for metastatic disease, a complete dissection of the nodes level 1 and 2 axillary should be performed. A sentinel node biopsy can also be used to assess the axillary basin following neoadjuvant chemotherapy.

3. **Systemic therapy**: Systemic therapy is given to patients who are at risk for or who have known distant metastases (stage IV). The options for treatment include surgery followed by chemotherapy, or preoperative (neoadjuvant) chemotherapy followed by surgery. **Patients with stage II breast cancer have a 33% to 44% risk of recurrence of the disease at 20 years with locoregional control only. For this reason, the majority of patients with stage II disease or greater are offered systemic chemotherapy in addition to locoregional control, with radiation therapy for breast-conserving surgery.** Chemotherapy options include doxorubicin, paclitaxel, and antiestrogen-based therapies. The most common chemotherapy regimens currently used in the United States include 5-fluorouracil/doxorubicin (Adriamycin)/cyclophosphamide (FAC) and cyclophosphamide/methotrexate/5-fluorouracil (CMF). CMF is often reserved for patients with comorbidities that preclude the use of
doxorubicin-based therapy. **Generally, antiestrogen therapy is given for 5 years to patients with estrogen and/or progesterone receptor-positive tumors.** This therapy is offered after adjuvant chemotherapy if adjuvant therapy is required based on the stage of the disease. Tamoxifen is the most commonly used antiestrogen therapy, but recent trials with aromatase inhibitors have shown equivalent efficacy in the treatment of postmenopausal breast cancer and a similar or slightly improved side effects profile.

Additionally, there must be consideration of neoadjuvant versus adjuvant chemotherapy. The advantages of neoadjuvant chemotherapy include in vivo determination of tumor sensitivity to therapy, an improved breast conservation rate, and therefore likely improved cosmetic results. The disadvantages of neoadjuvant therapy may be difficulty in assessing the actual pathologic stage after therapy and difficulty in accurately assessing the pretreatment stage without a tissue assessment of the axillary nodal basin or tumor size at the initial presentation. **Current evidence has not demonstrated a survival difference between patients treated with neoadjuvant versus adjuvant therapy.**

**Comprehension Questions**

[1.1] A 42-year-old woman with a 2-cm mobile lesion and a single palpable 2-cm mobile node in the axilla has what clinical stage of cancer?

A. Ia  
B. IIa  
C. IIb  
D. IIIc

[1.2] Which of the following most accurately describes a sentinel lymph node?

A. A lymph node containing cancer metastases  
B. The lymph node that is most likely to become infected postoperatively
C. The first lymph node in the lymph node basin draining a tumor
D. The surgical margins of an axillary dissection

[1.3] A 45-year-old woman undergoes breast-conserving surgery (a lumpectomy) for a 1.5-cm tumor. The axillary lymph nodes are negative. Which of the following is the best therapy?

A. Radiation therapy to the affected breast
B. No further therapy and observation
C. Combined chemotherapy such as the CMF regimen
D. A radical mastectomy

[1.4] A 62-year-old woman complains of painful enlargement of her right breast. She has no family history of breast cancer. The right breast reveals warmth, redness, and right axilla nontender adenopathy. Which of the following is the most likely diagnosis?

A. Mastitis
B. Cellulitis
C. Breast abscess
D. Breast cancer

Answers

[1.1] **B.** T1 N1 disease in this patient puts her disease at stage IIA.

[1.2] **C.** The sentinel node is the first lymph node in the lymph node basin draining a tumor.

[1.3] **A.** Radiation therapy is indicated for a patient with stage I disease treated with breast conservation therapy. The addition of radiation therapy reduces the local recurrence rate from approximately 30% to 9%, and it is an integral part of the treatment program.

[1.4] **D.** A postmenopausal or nonlactating woman who presents with red and/or tender breasts should be assumed to have breast cancer until it is proven otherwise. Inflammatory breast cancer is
characterized by edema, redness, and tenderness due to tumor occlusion of the dermal lymphatic channels.

**CLINICAL PEARLS**

- Tamoxifen therapy is associated with the development of uterine cancer.
- The initial workup for a dominant breast mass generally involves obtaining tissue to identify the breast mass and mammography to assess for other nonpalpable masses.
- A sentinel node biopsy can eliminate the need for axillary node dissection in selected patients.
- Systemic therapy (chemotherapy) is given when widespread metastasis is diagnosed or when the patient is at high risk for distant metastasis.

**REFERENCES**
