Breast

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Nipple Discharge

Concept

Nipple discharge can be from benign or malignant causes. Benign discharge typically is nonspontaneous, bilateral, clear or milky, and from multiple ducts. Bloody discharge typically is caused by an intraductal papilloma (45%), duct ectasia (35%), or infection (~5%), but it may be cancer (~5%; this is a common curveball).

Way Question May Be Asked?

“A 45-year-old woman presents to your office with the complaint of unilateral bloody nipple discharge for the past one month.”

When given just the complaint of nipple discharge, you should work through type, spontaneity, laterality, and recent medications that have been started. The question may also be concerning nipple discharge in a young woman.

How to Answer?

Full history
- Whether discharge occurs when stimulated or spontaneous
  (spontaneous is worrisome)
- Risk factors for malignancy
- Trauma
- Fluid characteristics (clear, milky, serous, bloody)
- Bilateral or unilateral

Discharge from one duct or multiple ducts
- Trauma
- Thyroid disorder
- Recent new medications
- Any other symptoms such as pain, swelling, or masses

Full physical examination
- Examination of both breasts in upright and supine positions
- Examination of lymph node basins
- Try to determine a responsible quadrant/responsible ducts
- The color and nature of the fluid
- The number of ducts producing fluid (multiple is usually benign, whereas single has higher risk of cancer)

Diagnostic tests
- Mammogram (mandatory)
- Ultrasound (subareolar area images poorly on mammogram)
- Hemoccult test
- Cytology (rarely helpful, and negative result does not exclude malignancy)
- Ductogram (painful and rarely helpful)
- Magnetic resonance imaging (MRI; rarely helpful for papilloma, but may detect other lesions)

For bloody discharge, you are in one of several situations:
1. Negative mammogram, negative physical examination for mass, and negative responsible quadrant:
   - Have patient follow-up in several weeks and check for responsible quadrant on breast self-examination. Then, on follow-up, consider the following situations:
   - (a) Negative mammogram, positive physical examination for mass, and negative responsible quadrant:
     - Total subareolar ductal system resection
   - (b) Negative mammogram, positive physical examination for mass, and positive responsible quadrant:
     - Subareolar wedge resection of ductal system for that quadrant
   - (c) Positive mammogram, positive physical examination for mass, and positive responsible quadrant:
     - Excisional biopsy of mass and subareolar wedge resection

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2. Negative mammogram, positive physical examination, for mass, and positive responsible quadrant:
   Subareolar wedge resection of the ductal system draining that quadrant
3. Positive mammogram, positive physical examination for mass, and positive responsible quadrant:
   Excisional biopsy or core-needle biopsy of mass on mammogram and subareolar wedge resection

Surgical Procedure

Circumareolar incision (some surgeons make the incision at the nipple/areola border)
Elevate areola
Dissect ducts leading to areola
Identify abnormal duct by dilatation, stent, dye, or mass (if you can identify single duct, otherwise subareolar wedge resection of the ductal system draining that quadrant)
Tie off distal duct or it will still drain out of nipple postoperatively (your seroma!)

Common Curveballs

The pathology is not a benign intraductal papilloma but rather a type of breast cancer, which may range from lobular carcinoma in situ and ductal carcinoma in situ (DCIS) to invasive cancer. Do not forget about checking lymph nodes and adjuvant therapy!
The nipple discharge persists after a subareolar wedge resection. Early recurrence may be drainage of a seroma; the other possibility is that not all of the duct was excised.
There is not a responsible quadrant.
There is a mass in the same breast, different quadrant, or in the opposite breast. Always treat the cancer first.
Discharge is not bloody but there are persistent atypical cells on slide cytology. (Now what do you do?)
Patient is pregnant (can have bloody nipple discharge during third trimester).
Patient is a teenager.

Clean Kills

Performing surgery for nonspontaneous, bilateral, clear/milky discharge
Failing to check the same breast for palpable masses or examine the other breast
Failing to establish risk factors for malignancy
Failing to check nodal status if pathology returns malignancy
Failing to order a mammogram/ultrasound
Discussing ductoscopy
Performing mastectomy for bloody nipple discharge

Not being able to shift into discussion of malignancy if pathology does not reveal expected papilloma but rather an invasive carcinoma
Trustling slide cytology/hemoccult tests and not performing surgery on patient with suspicious nipple discharge
Wasting time working up a prolactinoma

Summary

When evaluating a any patient with a breast complaint, a thorough history is key. The most important factors are the type of drainage and whether or not the discharge is spontaneous. Mammogram, ultrasound, cytology, and ductography may be helpful but the definitive diagnosis is made via excision of the involved duct. It is very important to rule out a concurrent malignancy.

Ductal Carcinoma In Situ

Concept

DCIS is a pre-malignant lesion with various subtypes. A patient has about a 33% chance of developing invasive ductal carcinoma in their lifetime. Several key features from a pathologic standpoint include size of tumor, unifocal or multifocal, nuclear grade, necrosis, and level of differentiation.

Way Question May Be Asked?

“A 51-year-old woman presents to your office with an abnormal mammogram. A cluster of five microcalcifications were present in the upper outer quadrant of the left breast. She underwent a core-needle biopsy that revealed DCIS. What would you do?”

You may be given DCIS in a number of different ways, such as by a mammogram showing asymmetric density, nodule, and speculated lesion, but most commonly from clustered or branching heterogenous microcalcifications.

How to Answer?

For history, establish risk factors for breast cancer (menarche, breast-feeding, family history of breast/ovarian/prostate cancer, number of children, previous breast cancer, menopause, history of birth control pills or hormone replacement therapy, history of radiation, age at first pregnancy)
For physical examination, be sure to check both breasts.
Assess symmetry, dimpling, and erythema.
Try to palpate for any masses.
Examine for cervical/axillary supraclavicular adenopathy.
Consider the need to order bilateral mammograms and compare to previous.
Ultrasound is useful for palpable masses to determine if they are cystic or solid.
MRI is not used for screening purposes.
Any suspicious microcalcifications (clustered, branching, heterogeneous) need to be biopsied (stereotactic core needle or needle localization/excisional biopsy).
After biopsy has identified the lesion as DCIS, the patient still needs that area to be excised with adequate (>2–5 mm) free margins. If you do not get this after your needle localization, you will need to re-excite until you begin to distort the breast or you get free margins.
If DCIS is diffuse—multifocal (scattered in one quadrant) or other quadrants (multicentric)—the patient will need total mastectomy.
If the tumor is high grade, has comedo necrosis, or is large/multifocal, a total mastectomy is appropriate (no axillary lymph node dissection [ALND] is necessary here unless the final path reveals invasive carcinoma). Be sure to offer immediate reconstruction as an option.
The patient will need postoperative radiotherapy (unless she had mastectomy or has a low-grade, small tumor with >1 cm margin) to the breast and should be placed on 5 years of tamoxifen (unless contraindicated, such as in endometrial cancer or history of deep venous thrombosis).

Common Curveballs

There is a palpable mass (separate from mammographic finding).
There is more than one mammographically detected lesion.
There is a lesion in the opposite breast.
The patient has a recurrence after mastectomy to chest wall or incision site (scenario switch).
The patient has invasive carcinoma (scenario switch).
On pathology, the resection margin is positive or less than 1 mm.
The patient is pregnant.
Stereotactic core cannot be performed (too superficial, too deep, or the patient cannot lay prone on stereotactic table).
Lobular carcinoma in situ is shown on final pathology (maybe even at margins).

Clean Kills

Forgetting to examine both breasts
Forgetting to order bilateral mammograms
Forgetting postoperative chemotherapy/radiotherapy treatment when appropriate

Forgetting ALND if invasive cancer is identified
Not knowing indications for mastectomy in a patient with DCIS
Performing ALND for DCIS
Talking about sentinel lymph node biopsy for comedo DCIS (only in research protocols currently)
Talking about use of chemotherapy or the new medication you read about in a journal last week in an experimental trial for your patient with DCIS

Summary

A full history to establish the patient’s risk factors for breast cancer and a complete examination of both breasts and the lymph node basins are very important. For DCIS, bilateral mammogram and other imaging techniques will be key. Suspicious lesions on mammogram need to be biopsied and subsequently excised with greater than 2–5 mm margins. Patients are then treated with radiation and hormone therapy.

Inflammatory Breast Cancer

Concept

Inflammatory breast cancer has poor prognosis regardless of the type of therapy offered. You do want to try to provide local control. You need to look for tumor cells in subdermal lymphatics (lymphovascular invasion) and treat aggressively. Differential diagnosis includes mastitis, abscess, and Mondor’s disease.

Way Question May Be Asked?

“A 58-year-old woman presents to your office complaining of a breast infection. Examination reveals an erythematous, edematous right breast. What do you want to do?” The question may also include a failed course of antibiotics, a history of trauma, or recent breastfeeding/nursing to try to lead you astray.

How to Answer?

History
Risk factors
Menarche
Breast-feeding
Family history of breast cancer
Number of children
Previous breast cancer
Menopause
History of birth control pills or hormone replacement therapy
History of radiation
Age at first pregnancy
Important questions include the following:
History of trauma
Nursing
Time course
Breast self-examinations (palpable masses before inflammation?)
Physical examination
Examine both breasts (peau d’orange)
Examine lymph node basins (cervical/axillary)
Palpable cord (Mondor’s disease)
Diagnostic tests (as in all breast questions!)
Mammogram (bilateral)
Ultrasound (if mass)
MRI (usually for palpable lesion not seen on mammogram or ultrasound)
Differential diagnosis
Mastitis
Breast abscess
Superficial thrombophlebitis (palpable cord)
Inflammatory breast cancer

Surgical Treatment

1. It is acceptable to try a short course of antibiotics (1 week)
2. If symptoms fail to resolve or there is a strong suspicion for cancer, get an incisional biopsy (including skin) through the reddened area and include adjacent normal skin. Some clinicians recommend fine needle aspiration (FNA) because clinical grounds confirm the stage of disease and you just want a diagnosis of cancer to start chemotherapy. However, you will get more information from a core needle or incisional biopsy, including ER/PR receptor status.
3. If pathology confirms inflammatory breast cancer (tumor in subdermal lymphatics), proceed with metastatic workup as follows:
   (a) Chest x-ray
   (b) Computed tomography scan of the head, abdomen, and pelvis (look for metastases)
   (c) Bone scan
   (d) With or without positron emission tomography (PET) scan
4. Three cycles of chemotherapy (usually multi-agent)
5. Algorithm
   (a) If the patient has a complete response, perform a modified radical mastectomy to augment local control, followed by eight cycles of chemotherapy, chest wall radiation, and tamoxifen if ER/PR positive.
   (b) If the patient has no response, then perform chest wall radiation and modified radical mastectomy.
6. If the tumor is already eroding through skin, you can give upfront radiotherapy to shrink tumor (also works if grossly eroding through skin and infected).

Common Curveballs

Erosion through skin during treatment
Patient does not have response to chemotherapy
Patient is pregnant
Patient somewhat responds during antibiotic treatment
Patient has mass or abnormal mammogram for opposite breast
Patient develops deep vein thrombosis during chemotherapy (scenario switch)
Patient pushes to save her breast or have immediate reconstruction (no!)
FNA is positive but you cannot get any receptor information (need to do core or incisional biopsy)

Clean Kills

Performing FNA instead of incisional biopsy (need receptor status)
Not recognizing inflammatory breast cancer as a T4 lesion
Not performing biopsy but proceeding straight to chemotherapy
Not performing mastectomy at end of neoadjuvant therapy (even if complete clinical resolution)
Not treating first with chemotherapy but proceeding straight with mastectomy
Talking about MRI (PET scan is only appropriate here for complete staging purposes)
Trying breast conservation/breast reconstruction

Summary

Unlike ductal and lobular carcinoma of the breast, inflammatory breast cancer has a poor prognosis and is diagnosed via lymphovascular invasion on biopsy. A thorough history should be obtained. On examination, the breast is usually erythematous and edematous with possible peau d’orange. Standard imaging with bilateral mammogram should be obtained, followed by biopsy. If the biopsy is positive, a metastatic workup should be completed. Again, although the prognosis is poor, the treatment is normally a combination of mastectomy, chemotherapy, radiation, and hormone therapy, depending on receptor status.
Invasive Ductal Carcinoma

Concept

Invasive ductal carcinoma is a malignancy that needs complete staging workup and then adjuvant treatment. Most women are candidates for breast conservation therapy (BCT), but you need to know the contraindications to BCT.

Way Question May Be Asked?

“A 45-year-old woman presents to your office with a palpable mass in the upper outer quadrant of the right breast. What would you do?”

You will likely be presented with a patient who has either a palpable abnormality, a locally advanced lesion, or a suspicious mammographic abnormality. Just be systematic and do what you would normally do in your practice.

How to Answer?

History

Risk factors for breast cancer
Menarche
Breast-feeding
Family history of breast cancer
Number of children
Previous breast cancer
Menopause
History of birth control pills or hormone replacement therapy
History of radiation
Age at first pregnancy
Symptoms: bone pain, weight loss
Change in breast appearance
For the physical examination, assess symmetry, dimpling, erythema, and edema.
Try to palpate any mass (hard/soft, well circumscribed, mobile/fixed, tender).
Be sure to check both breasts!
Examine for cervical/axillary adenopathy.
Examine liver.

How to Answer

You need to order bilateral mammograms and compare to any previous mammograms.
Ultrasound is useful for palpable masses to determine if cystic or solid (especially in premenopausal breasts and may show characteristics of malignancy).
The role of MRI is still controversial: 13–15 % of patients with one tumor are found to have another mass on MRI.
FNA can be done in the office setting for any palpable lesion.

Core-needle biopsy can be done in the office or under stereotactic/ultrasound guidance. It is better than FNA because it provides information on invasion, hormone receptor status, tumor grade, and sometimes lymphovascular invasion.
Excisional biopsy should be performed on the following:
Solid mass
Cyst with bloody content
Cyst that recurs more than twice
If FNA reveals malignancy, then you can plan full cancer staging in one trip to the operating room.

Contraindications for breast conservation therapy

- Tumor ≥5 cm
- Large tumor-to-breast ratio (cosmetic outcome)
- Two or more primary tumors in separate quadrants (multifocal)
- Previous breast irradiation
- Collagen vascular disease (scleroderma or lupus cannot get radiotherapy)
- Diffuse suspicious or indeterminate calcifications
- Subareolar tumor
- First and second trimester of pregnancy

Surgical Options

1. Lumpectomy (with clear margins), ALND, and postoperative radiotherapy
2. Modified radical mastectomy (combines total mastectomy and ALND)

ALND includes level 1 and 2 (lateral to and behind the pectoralis minor muscle) and should be done in all patients. Sentinel lymph node biopsy is now an accepted technique. However, if frozen section or final pathology is positive, you would proceed to complete ALND.

Adjuvant chemotherapy treatment (combination of docetaxel/doxycycline/cyclophosphamide) is appropriate for the following patients:
1. All premenopausal women with invasive breast cancer > 1 cm in size
2. All postmenopausal women with positive lymph nodes
3. Postmenopausal women with T2 or greater lesions (>2 cm in size)

Adjuvant hormonal treatment is appropriate for the following patients:
1. All premenopausal women with invasive breast cancer >1 cm in size
2. All postmenopausal women (unless contraindicated)

Adjuvant radiotherapy decreases local recurrence but offers no difference in overall survival.
1. Use 5,000 rad in divided doses to the chest wall in all patients who underwent BCT. You cannot
administer during pregnancy, but you can usually delay until after pregnancy.

2. When more than four lymph nodes are involved with the tumor, radiotherapy to the axilla reduces local recurrence.

For pathology results, you need to know tumor characteristics: nuclear grade, vascular invasion, tumor size, ER/PR receptors, S-phase fraction, Her-2 Ne.

Staging

T1: less than or equal to 2 cm
T2: greater than 2 cm but less than or equal to 5 cm
T3: greater than 5 cm
T4: any size extending to the chest wall or skin
N1: movable same side axillary lymph nodes
N2: fixed same side axillary lymph nodes
N3: same side infraclavicular or inferior mammary and axillary same side or same side supraclavicular lymph nodes
M0: no distant metastasis
M1: distant metastasis

Galen Model for Chemotherapy

Low risk: node negative, grade 1 tumor, <2 cm, no lympho-vascular invasion, ER+ and/or PR+, Her2Neu negative, for which endocrine therapy is indicated
Intermediate: node negative, does not fit in low risk, ER+ and/or PR+, Her2Neu negative, for which endocrine therapy is the primary treatment but you can consider chemotherapy
High risk: node positive, for which the patient should receive chemotherapy and endocrine therapy; Her2Neu-positive patients should get trastuzumab

Common Curveballs

There is a separate mammographic finding.
There is a palpable lesion not seen on mammogram.
There is a lesion in the opposite breast.
The patient has a recurrence after your surgical treatment.
Margins are positive for cancer or DCIS (or less than 1 mm)
Sentinel node biopsy does not work or is the only positive lymph node
Patient is pregnant (no radiotherapy, sentinel lymph node biopsy, or antimetabolite-based chemotherapy); can give AC (adriamycin cytoxan) after late first trimester (only antimetabolite methotrexate unsafe during pregnancy); no radiotherapy until the patient delivers (needs 24 weeks chemotherapy so OK unless <14 weeks pregnant); no Tamoxifen or bone scan
Patient has contraindication to BCT
Patient has contraindication to adriamycin (poor ejection fraction)

Clean Kills

Forgetting to examine both breasts
Forgetting to order bilateral mammograms
Not asking about receptors on pathology
Forgetting postoperative chemo/radiotherapy treatment when appropriate
Forgetting ALND if invasive cancer is identified
Going into lengthy discussion about sentinel lymph node biopsy when you do not do these routinely in your practice
Performing therapeutic abortion for breast cancer in the pregnant patient
Not knowing contraindications to BCT
Not knowing who gets adjuvant treatment and with what chemotherapy/hormonal agents
Not recognizing stage IIIIB breast cancer; sign include chest wall invasion, inflammatory breast cancer and skin ulceration.

Summary

The treatment of breast cancer requires a complete history; physical examination that includes bilateral breasts, lymph node basins, and liver; bilateral mammogram; and biopsy of the lesion. Core needle biopsy yields more information than FNA. In the appropriate patients, studies have shown that breast conservation therapy and mastectomy have equal survival. There are several contraindications to breast conservation therapy. The definitive combination of surgical and oncological treatment ultimately depends on the size and location of the mass/masses as well as the lymph node status.
**Paget’s Disease**

**Concept**

These malignant cells have migrated from underlying DCIS or invasive cancer. Paget’s cells are identified in the epidermis. They may regress with topical steroids, so do not prescribe them! Bilateral eczematous changes to the nipple areolar complex (NAC) are likely benign. Approximately 50% of patients with Paget’s disease will have an associated invasive cancer or DCIS. Only 10% of patients will have disease confined to the nipple.

**Way Question May Be Asked?**

“A 43-year-old woman presents to your office with a 4-week history of itching to her left nipple. Examination reveals a reddened eczematous left nipple-areola complex (NAC) and a 1.5 cm mass in the upper outer quadrant approximately 4 cm from the NAC margin. What would you do?” There may or may not be an associated mass, but you should always perform a physical examination and mammogram/ultrasound.

**How to Answer?**

**History**
- Risk factors for breast cancer
  - Menarche
  - Breast-feeding
  - Family history of breast cancer
  - Number children
  - Previous breast cancer
  - Menopause
  - History of birth control pills or hormone replacement therapy
  - History of radiation
  - Age at first pregnancy

**Physical examination**
- Try to palpate a mass
- Check both breasts!
- Examine for cervical/axillary adenopathy

**How to Answer**
- You need to order bilateral mammograms.
- A couple of situations are possible:
  1. No palpable mass and no lesions on mammography: Perform a wedge resection of NAC and check pathology. If Paget’s cells are identified, you should proceed to simple mastectomy. If there is cancer in the mastectomy specimen, do not forget the ALND.
  2. Palpable mass or lesion on mammogram: Perform a wedge resection of NAC and excisional biopsy of mass. If Paget’s cells are identified and mass is invasive cancer, then perform a modified radical mastectomy.
  3. Palpable mass or lesion on mammogram: Perform a wedge resection of NAC and excisional biopsy of mass. If Paget’s cells are identified and mass is DCIS, then perform a simple mastectomy.

Do not forget radiation/chemotherapy/hormonal therapy when appropriate for DCIS or underlying invasive cancer.

**Common Curveballs**

- There is a palpable mass.
- There is a mammographically detected lesion.
- There is a lesion in the opposite breast.
- The patient has a recurrence after mastectomy to chest wall or incision site (scenario switch).

**Clean Kills**

- Forgetting to order mammograms
- Forgetting postoperative chemotherapy/radiotherapy treatment when appropriate
- Forgetting ALND if invasive cancer is identified
- Forgetting to obtain usual history/physical examination (establish risk factors, check masses in both breasts)
- Forgetting to examine both breasts/axillae
- Treating nipple with steroids (Paget’s can remit on steroids)

**Summary**

Paget's disease presents as an eczematous lesion of the nipple areolar complex. Although it may appear to be focal, Paget’s often extends past the NAC and is frequently associated with DCIS or invasive cancer. The same routine should be followed as with all other breast cancers, including a thorough history, physical examination, and mammogram. If Paget’s cells are identified on the wedge resection of the NAC, the definitive treatment is simple mastectomy.
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