Disorders of the Breast

Clinical case applicability: Breast mass/discharge, screening mammography, breast cancer

Learning Objectives:
1. Understand normal breast anatomy and histology
2. Identify common breast disorders & breast cancer
3. Understand the mechanism of action for hormonal therapies for breast cancer

Describe the normal anatomy of the breast (figure 1 & 2): Stromal: majority of breast volume, adipose & fibrous connective tissue & Epithelial: Ductal system 12-20 lobes; each lobe consists of: Lobules (consist of milk-producing alveoli or acini; surrounded by myoepithelial cells to allow for milk ejection) → drain into terminal duct → major duct → lactiferous sinus → 6-8 openings to the nipple

Blood supply – internal thoracic artery (previously the internal mammary A.), 1/3 (mainly the upper outer quadrant) lateral thoracic arteries

Lymphatic drainage – majority drains to the axillary chain (most frequently involved with metastases), internal mammary (more likely in inner breast lesions) & supraclavicular lymph nodes

What are common benign breast disorders?
Non-proliferative: generally not associated with increased risk of breast cancer
- Breast cysts: Most common age 35-50 years, fluid-filled, round/ovoid
- Fibrocystic change: Very common in reproductive aged women, cause cyclic mastalgia, palpably nodular tissue; encompasses wide variety of change - dilation of acini & ducts with dense stroma

Proliferative without atypia: 1.5-2 x increased risk of developing breast cancer
- Intraductal papilloma: serous or bloody nipple discharge, most commonly found < 2 cm from the nipple; Polyps w/in the ducts; papillary cells w/ central fibrovascular stalk; tx: generally surgical excision (fig 2)
- Fibroadenoma: most common in age 15-35; well-defined mobile mass; benign solid tumors containing glandular & fibrous tissue; +hormonal relationship (↑ in size during pregnancy or with estrogen); generally does not ↑ risk of cancer; tx: repeat imaging/observation vs surgical excision
- Usual ductal hyperplasia: ↑ number of cells in the ductal space, retain cytological features of benign cells, no additional treatment indicated

Atypical hyperplasia: ↑ in risk of breast cancer, ↑ risk of both ipsi- & contralateral cancer
- Atypical ductal hyperplasia (ADH): proliferation of monomorphic cells filling part, but not the entire involved duct; rates of upgrade to DCIS >20%, surgical excision generally recommended (RR 3.7-5.3)
- Atypical lobular hyperplasia (ALH): proliferation of monomorphic cells filling part, but not all acini in an involved lobule; rate of upgrade of pathology low (<5%), tx: observation (RR 3.7-5.3)
- Lobular carcinoma in situ (LCIS) –marker of ↑ risk rather than anatomic precursor; greater extent of disease than ALH w/ ↑ acini distention; tx: observation (RR higher 7-10)

Describe the types of malignant breast tumors. 2/3 of cases are ER & PR (+); prognosis & treatment: hormone receptor status, nuclear grade & Her-2/neu expression
- Ductal carcinoma in situ (DCIS): stage 0 breast cancer, cancer cells fill portions of the ductal system without invading beyond the duct’s basement membrane (figure 2)
- Invasive ductal: 80% of all breast cancers; perimenopausal/menopausal women; solitary, firm mass, poorly defined margins; 75% ER(+) (figure 2)
- Invasive lobular: 15% of all breast cancers; small cells with rounded nuclei, scant cytoplasm – arranged in a “single file”; >90% ER(+) 
- Inflammatory: rapidly progressive; dermal lymphatic invasion by breast carcinoma; hormone receptor (-)
- Paget’s: eczematosus patches on nipple; associated w/ underlying DCIS or invasive breast cancer

What is the mechanism of action for SERMs and aromatase inhibitors?
Selective estrogen-receptor modulators – competitive inhibitors of estrogen binding to estrogen receptors, with mixed agonist & antagonist activity, depending on the target tissue
- Tamoxifen: antagonist effect on breast, agonist effect on bone, cholesterol (↓ LDL) endometrium (↑ risk hyperplasia, polyps, cancer)

Aromatase inhibitors – used in postmenopause; ↓ conversion of androgens to estradiol in the periphery
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Figure 1

Figure 2: Images courtesy of Andy Sciallis, MD

A. Benign TDLU  B. Intraductal papilloma  C. Ductal carcinoma/DCIS  D. Lobular carcinoma

References

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