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:* eczematous 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

Disorders of the Breast

Figure 1

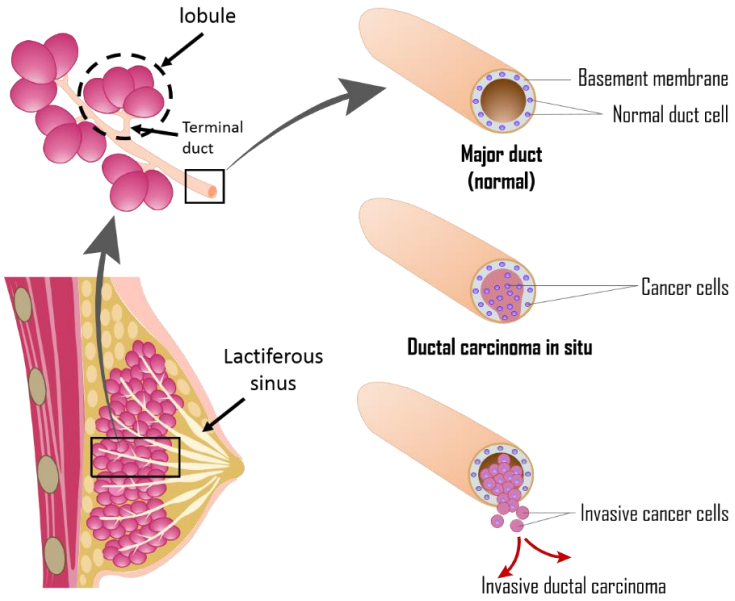
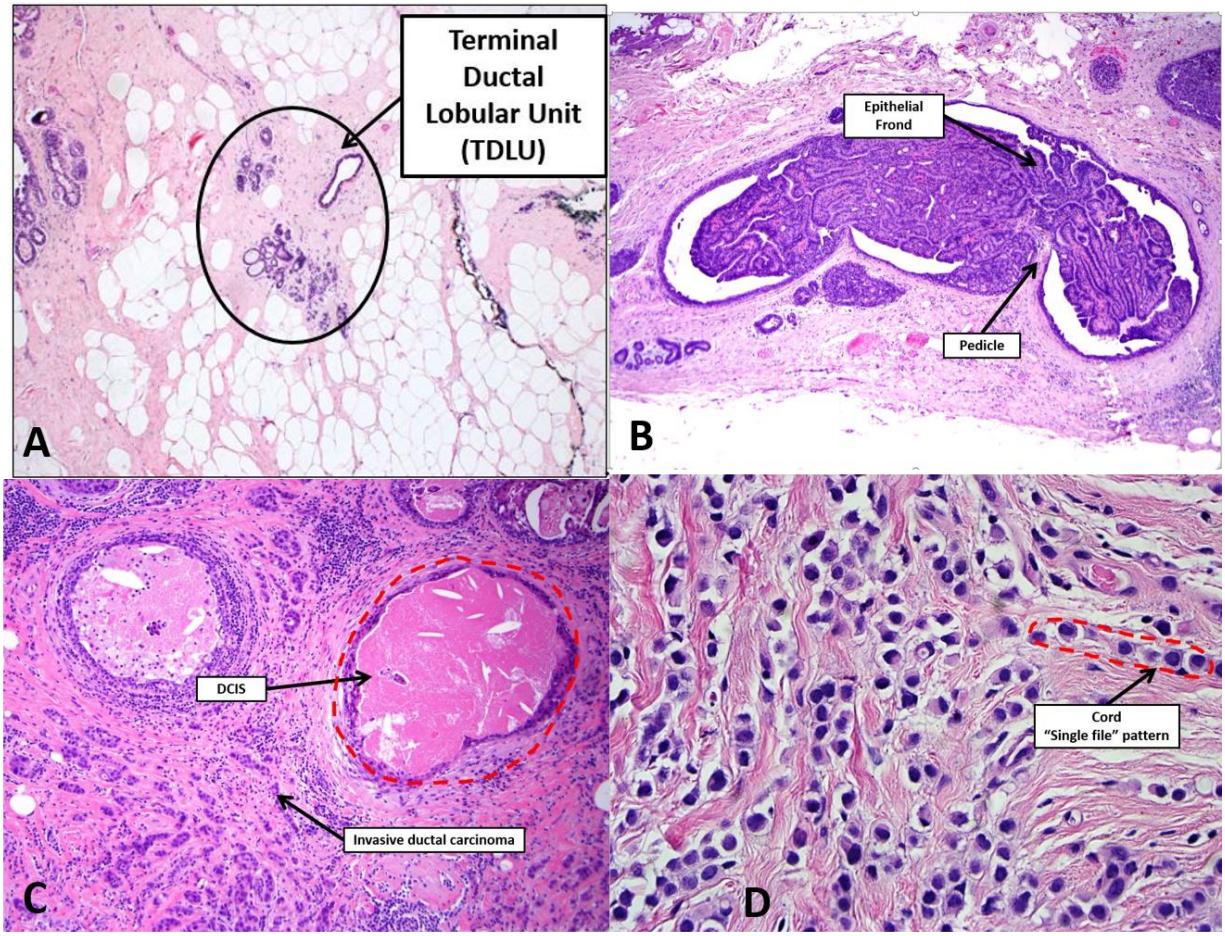


Figure 2: **Images courtesy of Andy Sciallis, MD**



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

References

-Hoffman, BL, Schorge, JO, Bradshaw KD, Halvorson LM, Schaffer JI, Corton MM. Chapter 12 Breast Disease. *Williams Gynecology, 3e* New York, NY: McGraw-Hill; 2016.
- Sabel, MS. Overview of benign breast disease. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (2017)
- Russo, J. Breast development and morphology. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (2017)
- Fuqua, SAW. Schiff, R. Mechanism of action of selective estrogen receptor modulators and down-regulators. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (2016)