King Saud University
College of Medicine
Second year – Reproductive Block

Pathology of Benign Breast Diseases

Lecture 6

430 Pathology Team

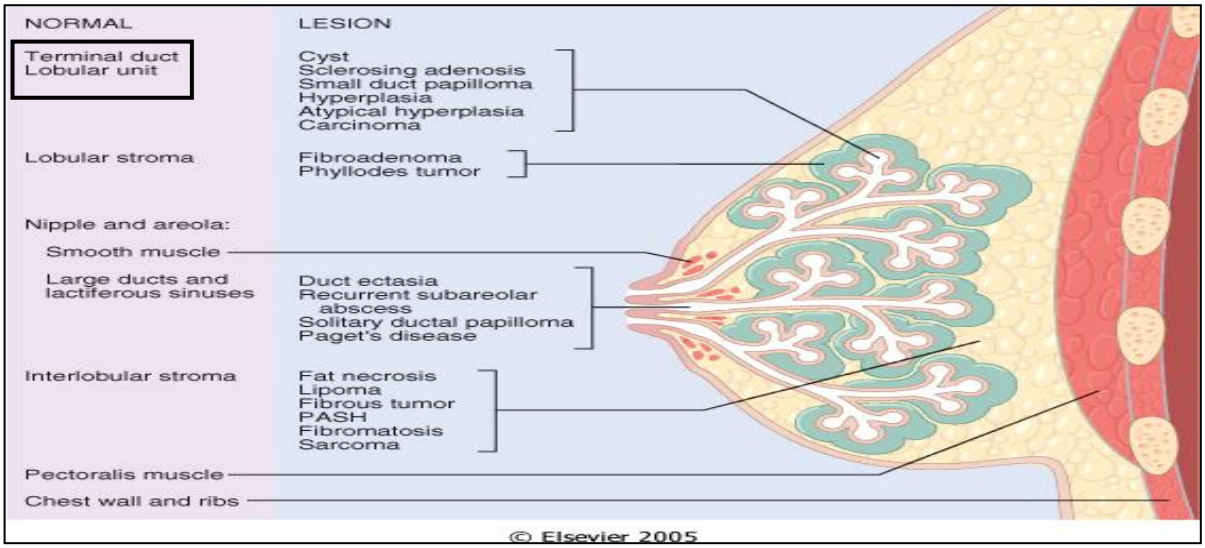
Seham AlArfaj

Ghadah AlSaleh

Red: Doctors' and important notes.
Green: Team notes.

Anatomy of Normal Breast:

- Specialized epithelium and stroma that gives rise to both benign and malignant lesions
- Six to ten major ductal systems originate at the nipple.
- Branching of the large ducts leads to the terminal duct lobular units. (majority of breast diseases arise from here)
- The TDU (terminal ductal units) branches into grapelike clusters of small acini to form the lobule.



Clinical Presentation:

1. **Pain (mastalgia):** is the most common breast symptom and may be cyclical with menses or noncyclical. Diffuse cyclical pain has no pathologic significance. Noncyclical pain is usually associated with a focal lesion in the breast. Causes include ruptured cysts or areas of prior injury or infections, or sometime no specific cause.
   Although the great majority of painful masses are benign, about 10% of breast cancers present with pain, and all masses need to be investigated.
2. **Palpable mass:** this is what brings the patient to the clinic.
3. **Nipple discharge:** milky discharge has not been associated with malignancy. Bloody or serous discharges are most commonly associated with benign lesions but, rarely, can be due to a malignancy.

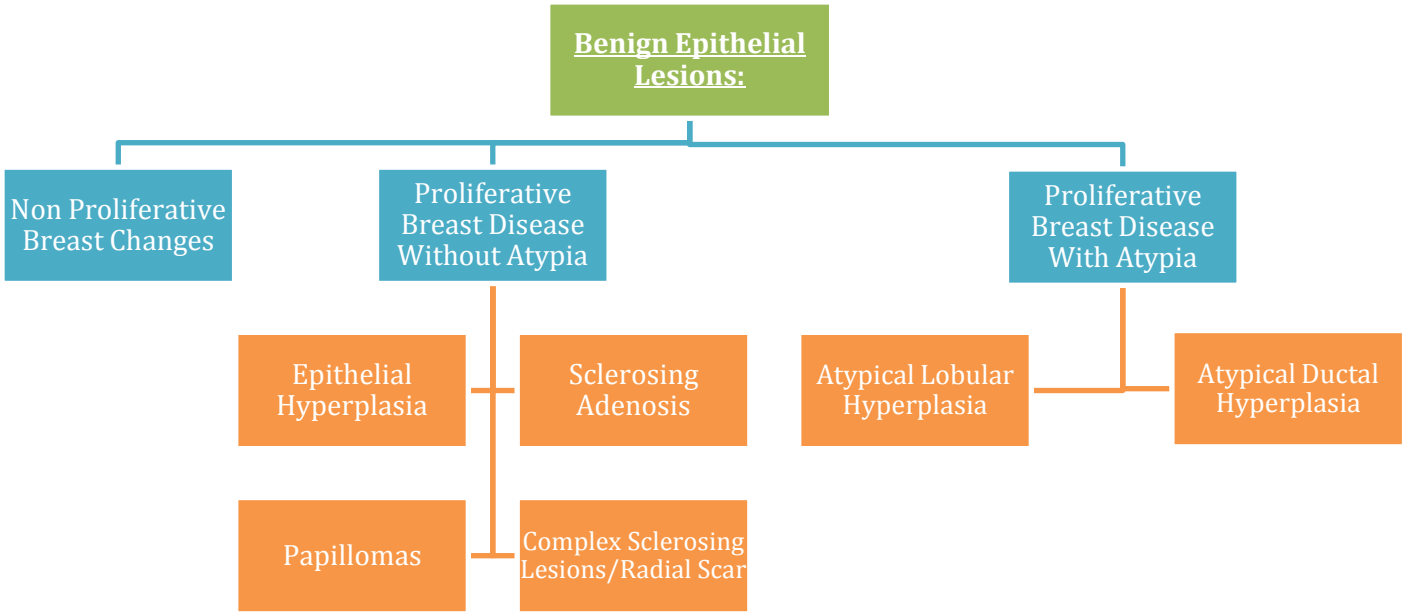
N.B: granulamatous inflammation of the breast gives similar findings to breast tumors during clinical examination.

Characteristics of Breast Carcinomas by Clinical Presentation:

1. Palpable mass
2. Mammographic density
3. Mammographic calcifications (important sign of malignancies)

Mammographic screening was introduced in the 1980s as a means to detect small, non-palpable breast carcinomas not associated with breast symptoms. Screening is generally recommended to start at age 40. Younger women usually undergo mammography only if they are at high risk for developing carcinoma. *The principal mammographic signs of breast carcinoma are densities and calcifications.*

Lesions of the breast can be benign or malignant.



N.B: each lesion has its own percentage in the risk of developing to cancers.

1. Non proliferative Breast Changes (Fibrocystic Changes):

- No increased risk for cancer
- Could produce palpable breast mass, mammographic densities, calcifications, or nipple discharge.
- Cysts are the most common cause of a palpable mass and they are alarming when they are solitary, firm.

Fibrocystic change:

- Often produce palpable lumps
- Characterized by various combinations of cysts, fibrous overgrowth, and epithelial proliferation.
- The cause of fibrocystic change is not known.
- It is also known as fibrocystic mastopathy.
- It is the single most common disorder of the breast.
- The condition is diagnosed frequently between the ages of 20 and 55 and decreases progressively after the menopause.
- Fibrocystic change presents with asymptomatic masses in the breast (results in heaviness of the breasts), which are discovered by palpation. The masses vary from diffuse small irregularities (lumpy bumpy breast) to a discrete mass or masses filled with fluid and is treated by fluid aspiration.
- It may also present with pain, which may be cyclical with midcycle or premenstrual discomfort.
- Pain may be focal or diffuse and may or may not be associated with the lumps.

Three patterns of morphologic changes:

A. Cyst formation: small to big in size, lined by benign epithelium with apocrine metaplasia = (cells will be large in size, pink eosinophilic cytoplasm, nuclei is large with prominent nucleoli, and most of the times it is a benign lesions). Semi-translucent or turbid fluid inside.
B. Fibrosis: contribute to the palpable firmness of the breast
C. Adenosis: Increase in the number of acini per lobule (epithelial proliferation), can be seen normally in pregnancy.

Histologically: cysts may be lined by flattened epithelium, columnar epithelium with features of apocrine cells or may completely lack an epithelial lining.

2. Proliferative Disease Without Atypia:

- Rarely form palpable masses
- If a lesion is mobile it's more likely to be benign.
- Usually occur in between the age 20-25 because it is related to hormonal changes.
- Detected as mammographic densities.
- Incidental finding
- e.g. Large duct papilloma (intraductal proliferation) present in 80% as nipple discharge.
- Risk for cancer is 1.5 – 2 times normal

Microscopically: proliferation of ductal epithelium and/or stroma without cellular abnormalities that are suggestive of cancer.

Many entities included here:

A. Epithelial hyperplasia
B. Sclerosing adenosis
C. complex sclerosing lesions/radial scar
D. Papillomas

A. Epithelial Hyperplasia.

- In the normal breast, only myoepithelial cells and a single layer of luminal cells. Epithelial or ductal hyperplasia is a proliferative condition in which there is an increase in the cellularity of the epithelium of the TDLU (Terminal duct lobular unit).
- Epithelial hyperplasia is defined by the presence of more than two cell layers. Hyperplasia ranges from mild, moderate to florid and from typical (i.e. without atypia) to atypical short of malignancy.
- The proliferating epithelium distends the ducts and ductules. It shows two distinct cell populations, epithelial and myoepithelial cells.
- It is a microscopic finding, which cannot be predicted clinically or by mammographic examination.
- The lesion may coexist with other features of fibrocystic change, but in some cases may form the predominant pattern.

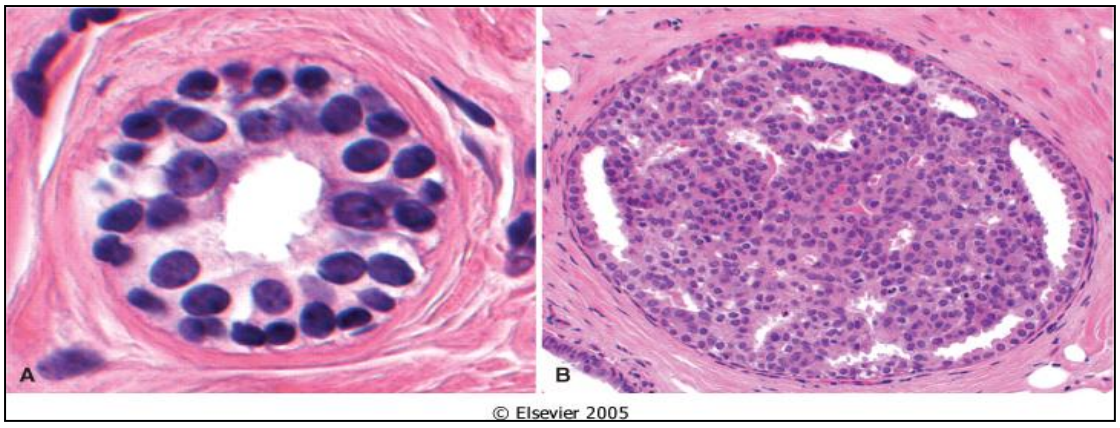


Figure 23-8 A, Normal. A normal duct or acinus has a single basally located myoepithelial cell layer (cells with dark, compact nuclei and scant cytoplasm) and a single luminal cell layer (cells with larger open nuclei, small nucleoli, and more abundant cytoplasm). B, Epithelial hyperplasia. The lumen is filled with a heterogeneous population of cells of different morphologies, often including both luminal and myoepithelial cell types. Irregular slitlike fenestrations are prominent at the periphary.

B. Sclerosing Adenosis:

- This condition most often occurs as an incidental microscopic finding but may manifest as a palpable mass that may be mistaken clinically for cancer duo to stromal and glandular

proliferation. However, the difference between this and the cancer is that the sclerosing adenosis has a well demarcated wall not infiltrating the nearby tissue.

- It is almost always associated with other forms of fibrocystic change.
- Diffuse micro-calcifications are commonly seen in the lesion, which may mimic carcinoma on mammography.

Microscopically: sclerosing adenosis consists of proliferation of ductular structures and stroma with distortion of the TDLU (Terminal duct lobular unit).

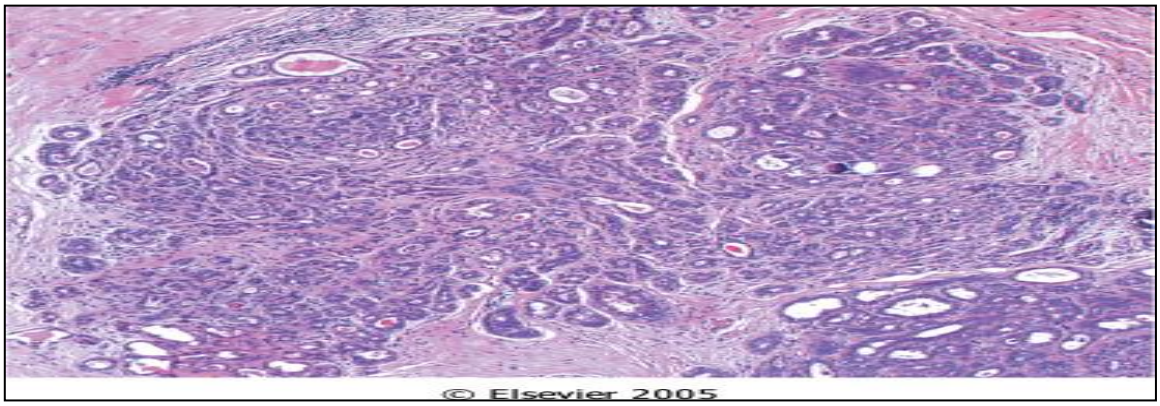
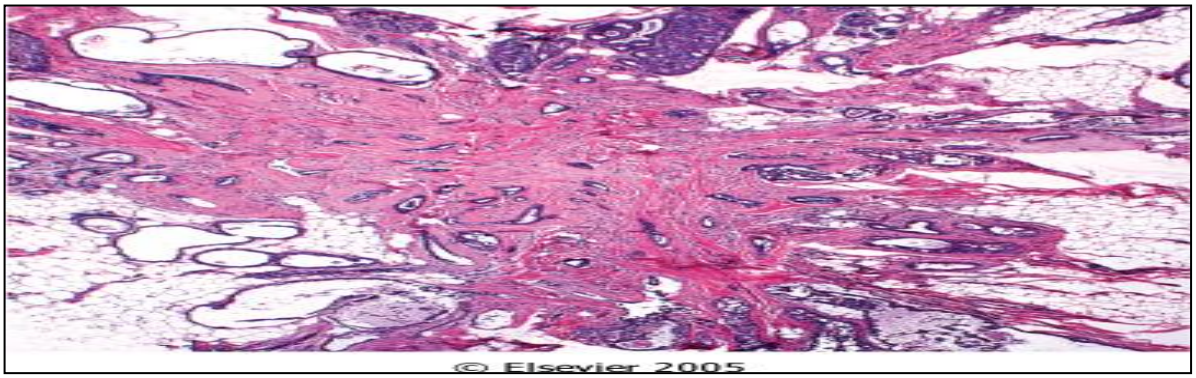


Figure 23-9 Sclerosing adenosis. The involved terminal duct lobular unit is enlarged, and the acini are compressed and distorted by the surrounding dense stroma. Calcifications are often present within the lumens. Although this lesion is frequently mistaken for an invasive carcinoma, unlike carcinomas, the acini are arranged in a swirling pattern, and the outer border is usually well circumscribed.

C. Complex Sclerosing Lesion (Radial Scar).

- Radial scars are stellate lesions characterized by a central nidus (origin) of entrapped glands in a hyalinized stroma
- Can resemble irregular invasive carcinomas mammographically or on gross examination and in order to differentiate between it and the carcinoma we look for the myoepithelial cells which will be present unlike in a malignant case.
- It resembles the tubular carcinoma and to differentiate between them we look at the glands shape if it is stellate then it is complex sclerosing while if it is angular then it is tubular.
- *Complex Sclerosing Lesion (Radial Scar).* "scar" refers to the morphologic appearance, as these lesions are not associated with prior trauma or surgery.



Complex sclerosing lesion (radial scar). There is a central nidus consisting of small tubules entrapped in a densely fibrotic stroma surrounded by radiating arms of epithelium with varying degrees of cyst formation and hyperplasia. These lesions typically present as an irregular mammographic density and closely mimic an invasive carcinoma.

D. Papillomas

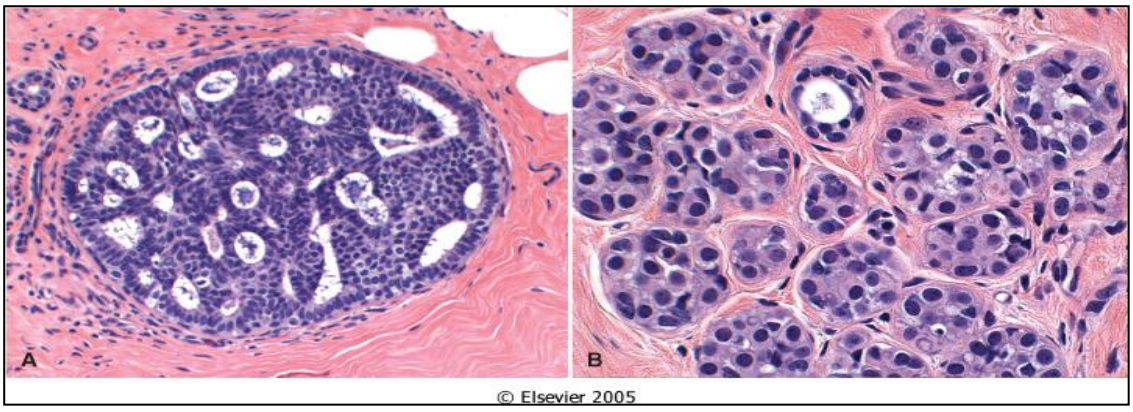
- This is a papillary tumor that arises from the duct epithelium including large ducts.
- It arises more often in the central part of the breast from the lactiferous ducts (75%) but can occur in any quadrant.

- It is more commonly solitary, consisting of a single tumor in one duct, but multiple discrete tumors, usually in contiguous branches of the ductal system may occur.
- Large duct papillomas are usually solitary and situated in the lactiferous sinuses of the nipple.
- Small duct papillomas are commonly multiple and located deeper within the ductal system.
- Small duct papillomas have been shown to increase the risk of subsequent carcinoma.
- Nipple discharge, which may be bloody, is the most common presentation for central papillomas and less commonly of peripheral tumors.
- A subareolar mass may be palpable and it is seen in cases of large ducts involvement.
- Age range is from 30 to 50 years.

Intraductal papilloma. A central fibrovascular core extends from the wall of a duct. The papillae arborize within the lumen and are lined by myoepithelial and luminal cells.

3. Proliferative Breast Disease with Atypia:

- Risk for cancer is 4-5 times normal
- Atypical hyperplasia is a cellular proliferation resembling ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) but lacking sufficient qualitative or quantitative features for a diagnosis of carcinoma in situ.
- Include two entities
  A. Atypical ductal hyperplasia
  B. Atypical lobular hyperplasia
- Atypical hyperplasia has some of the architectural and cytological features of carcinoma in situ but lacks the complete criteria for that diagnosis and is categorized as ductal or lobular in type.



A, Atypical ductal hyperplasia. A duct is filled with a mixed population of cells consisting of oriented columnar cells at the periphery and more rounded cells within the central portion. Although some of the spaces are round and regular, the peripheral spaces are irregular and slitlike. These features are highly atypical but fall short of a diagnosis of DCIS. B, Atypical lobular hyperplasia. A population of monomorphic small, rounded, loosely cohesive cells partially fill a lobule. Some intracellular lumina can be seen. Although the cells are morphologically identical to the cells of LCIS, the extent of involvement is not sufficient for this diagnosis.

Summary:

- **Fibrocystic Changes**: No increased risks for cancer, cysts are the most common cause of a palpable mass. It is the single most common disorder of the breast. The condition is diagnosed frequently between the ages of 20 and 55 and decreases progressively after the menopause. It may also present with pain, which may be cyclical with midcycle or premenstrual discomfort. Three patterns of morphologic changes: cyst formation (lined by flattened epithelium, columnar epithelium with features of apocrine cells), fibrosis, adenosis can be seen normally in pregnancy.
- **proliferative Disease without Atypia**: detected as mammographic densities. Risk for cancer is 1.5 – 2 times normal. Many entities included here**:** epithelial hyperplasia, sclerosing adenosis, complex sclerosing lesions/radial scar, Papillomas
- **Epithelial Hyperplasia**: epithelial or ductal hyperplasia is a proliferative condition. Epithelial hyperplasia is defined by the presence of more than two cell layers.
- **Sclerosing Adenosis:** occurs as an incidental microscopic finding. Diffuse microcalcifications are commonly seen in the lesion, which may mimic carcinoma on mammography.
- **Complex Sclerosing Lesion (Radial Scar):** are stellate lesions, can resemble irregular invasive carcinomas mammographically or on gross examination
- **Papillomas:** it arises more often in the central part of the breast from the lactiferous ducts (75%) but can occur in any quadrant. It is more commonly solitary, but multiple discrete tumors, usually in contiguous branches of the ductal system may occur. Nipple discharge, which may be bloody, is the most common presentation for central papillomas and less commonly of peripheral tumors. Age range is from 30 to 50 years.
- **Proliferative Breast Disease with Atypia**: risk for cancer is 4-5 times normal. Atypical hyperplasia is a cellular proliferation resembling ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) but lacking sufficient qualitative or quantitative features for a diagnosis of carcinoma in situ. Include two entities: atypical ductal hyperplasia, atypical lobular hyperplasia. Atypical hyperplasia has some of the architectural and cytological features of carcinoma in situ but lacks the complete criteria for that diagnosis and is categorized as ductal or lobular in type.