

Reproductive

Team *of* Pathology

Hazim
Jokhadar

Rawan
Al hyyan

Abdulelah
Al kapoor

Lamia
Al ghamdi

Pathology of benign breast disease



Revised by:
Maria Al ayed

9th Lecture

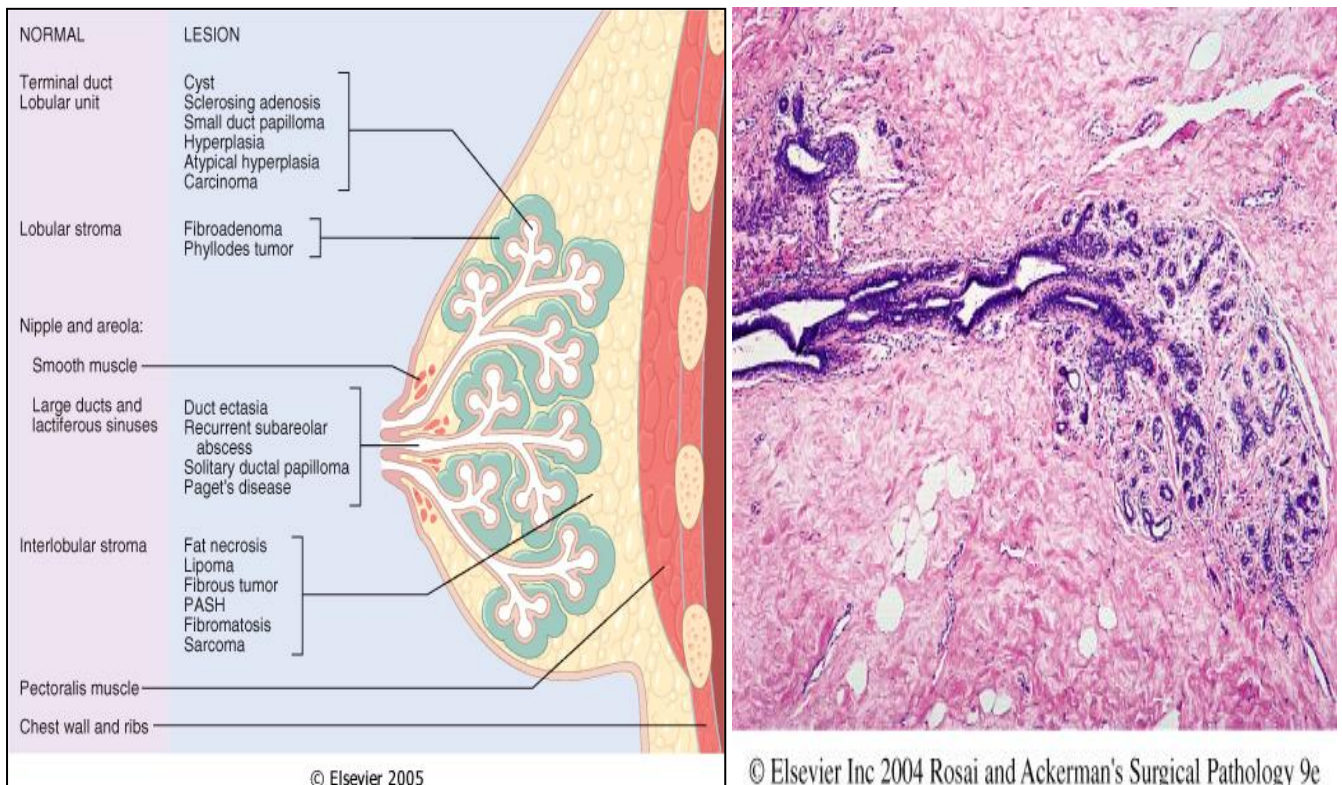
Normal Breast

- 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.
- The TDU branches into grape-like clusters of small acini to form the lobule.

1. Outer layer: myoepithelial cells, supporting the epithelium.

2. Inner layer: the epithelium (cuboidal to columnar)

The presence of myoepithelial cells indicates it is a benign condition, if absent; it is probably malignant.



Breast, 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 (harmless, due to the fluctuation in hormone levels.)
 - Noncyclical pain is usually associated with a focal site 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.**

Localized pain is a very important sign however not any localized pain means breast cancer.

Malignant masses are painless in 90% of cases, but can be painful only with the mass have grown progressively to reach the skin, muscle, fat...etc.

Fat necrosis (benign): clinical presentation is of a breastfeeding mother injured by her baby, days later she will start complaining about pain in the injured breast which is caused by fat necrosis from the

2) Palpable mass

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. (Associated with papilloma)

Milky discharge :- most of the time it is related to pregnancy or related to hormonal influence.

Bloody nipple discharge is alarming sign however 90 % of bloody nipple discharge is benign

Characteristics of Breast Carcinomas by Clinical Presentation:-

- Palpable mass
- Mammographic density
- Mammographic calcifications

The lumpy mass like nodules in the breast which is related to menstrual cycle :- is always related to benign conditions.

We have to be careful for the localized fixed mass :- which is very important presentation for cancer.

Mammographic screening was introduced in the 1980s as a means to detect small, nonpalpable breast carcinomas not associated with breast symptoms.

Screening is generally recommended to start at age 40.

Nowadays maybe 50% or more of breast cancer are detected by *Mammography*.

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**.

Tiny dot like calcifications are very important sign of early breast cancer.

Mammography detects breast cancer at the very early stages, it is recommended to do it every 5 years.

The triple test in breast :- Clinical examination , mammography and pathologic examination

e.g. you have a 50 years old patient and she has a mass lesion:-

1-clinical examination you examine this mass its looks like firm ill-defined mass lesion you send the patient directly into mammography .

2- mammography:- Check the mammogram finding you will see dense firm ill defined irregular mass lesion with calcification.

pathological examination :- You now confirm the diagnosis by pathological examination.

the final diagnosis is for pathological examination , so if the clinical examination says its benign and the radiologic examination says its benign but the pathological examination says its malignant -> we should review the histopathologic exam -> if pathological examination says its malignant (after review) -> the final diagnosis is for pathological examination ,so its malignant

Breast ,Benign Epithelial Lesions

1- Non proliferative breast changes

2- Proliferative breast disease

3- Atypical hyperplasia

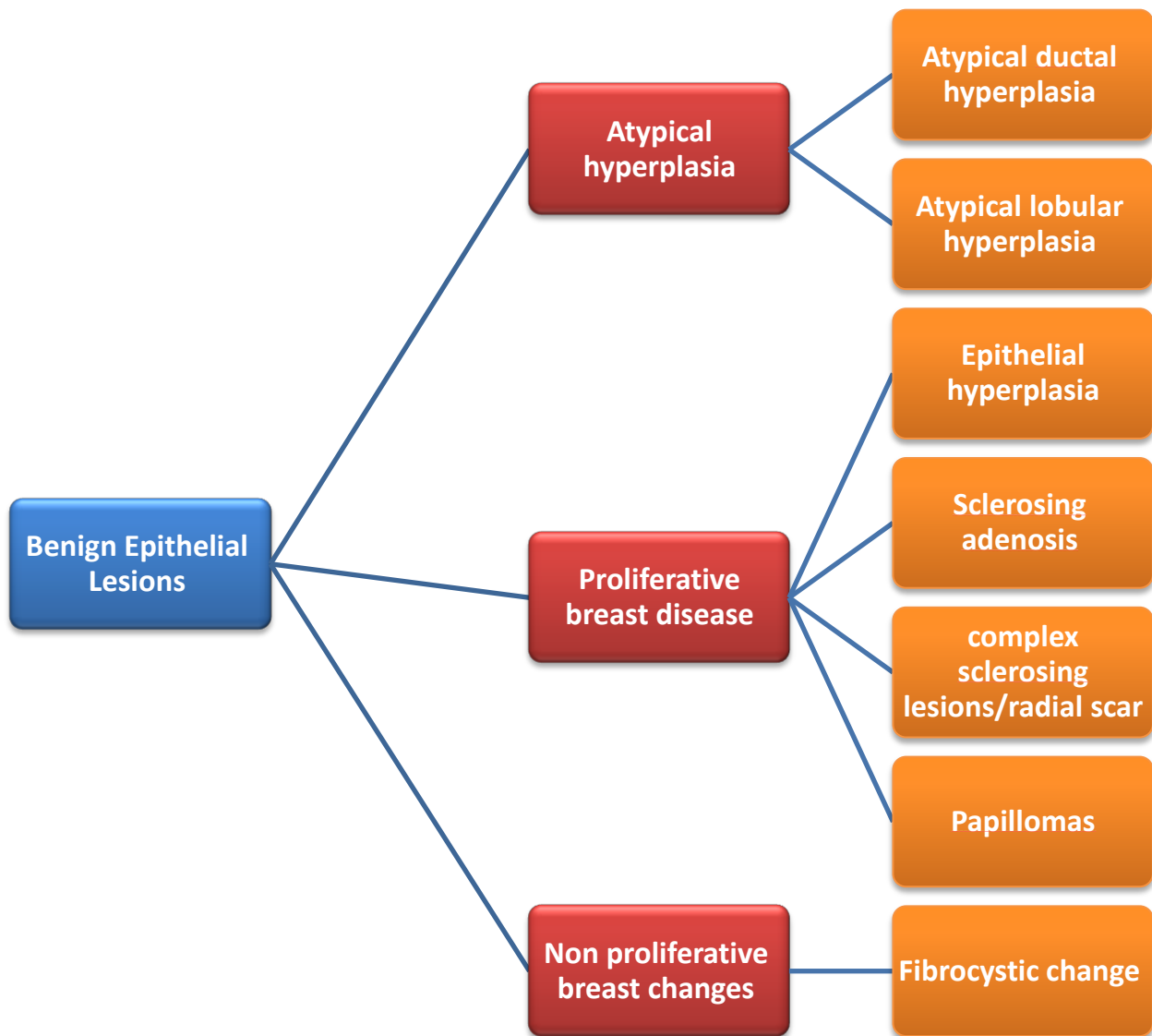
(Proliferative breast disease with atypia).

Breast disease may arise from adipose tissue, terminal duct lobular units, branching ductules, lactiferous ducts.

We classify depending on the risk for developing cancer

Non proliferative breast changes:- there is no extra risk for cancer.

The risk for developing breast cancer in the western countries: -
1 in 9 females will develop breast cancer



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 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, which are discovered by palpation. The masses vary from diffuse small irregularities (lumpy bumpy breast) to a discrete mass or masses.
- 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.

MCQ question: non-proliferative fibrocystic change has NO increased risk of cancer.

Minor proliferation; not considered as a proliferative disease.

From Dr. Sufia's slides: 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 changes

Three patterns of morphologic changes :

1- Cyst formation

2- Fibrosis

3- Adenosis .

Fibrocystic changes grow rapidly, when patients complain about a mass that have been growing progressively in a short period of time it probably is "fibrocystic change" (benign, good news)

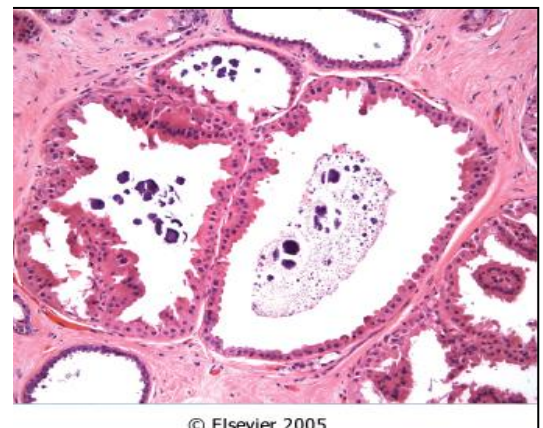
MCQ question: what are the pathological findings of fibrocystic changes?

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

- Cysts :small to big in size ,lined by benign epithelium with apocrine metaplasia

Metaplasia is not a premalignant condition; except in Barret's esophagus.

- Semi-translucent or turbid fluid
- Fibrosis : contribute to the palpable firmness of the breast
- Adenosis : Increase in the number of acini per lobule.
- Adenosis can be seen in pregnancy.



Benign Epithelial Lesions: proliferative Disease

without Atypia

Almost never palpable.

- Rarely form palpable masses
- Detected as mammographic densities.
- Incidental finding
- e.g. Large duct papilloma present in 80% as nipple discharge.
- Risk for cancer is 1.5 – 2 times normal.

Proliferation of ductal epithelium and/or stroma without cellular abnormalities that are suggestive of cancer

Many entities included here :

1- Epithelial hyperplasia

2- Sclerosing adenosis

3- complex sclerosing lesions/radial scar

3- Papillomas

Epithelial Hyperplasia.

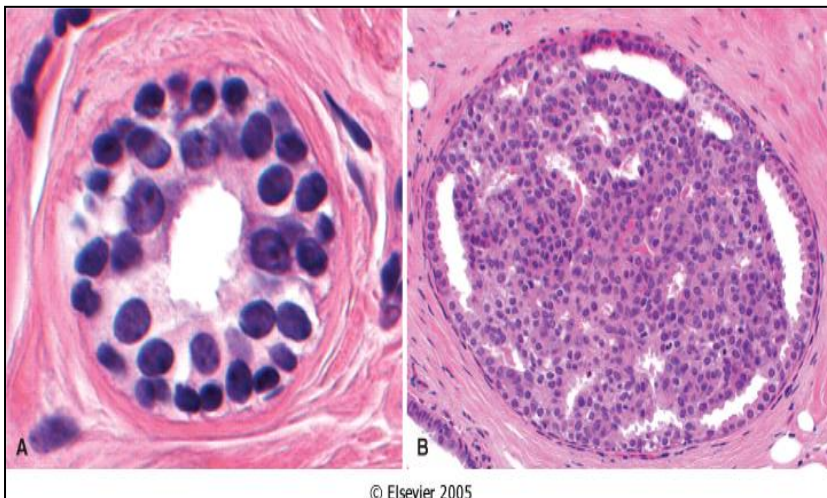
In the normal breast, only myoepithelial cells and a single layer of luminal cells. Epithelial or ductal hyperplasia is a proliferative condition in which there is an increase in the cellularity of the epithelium of the TDLU.

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.



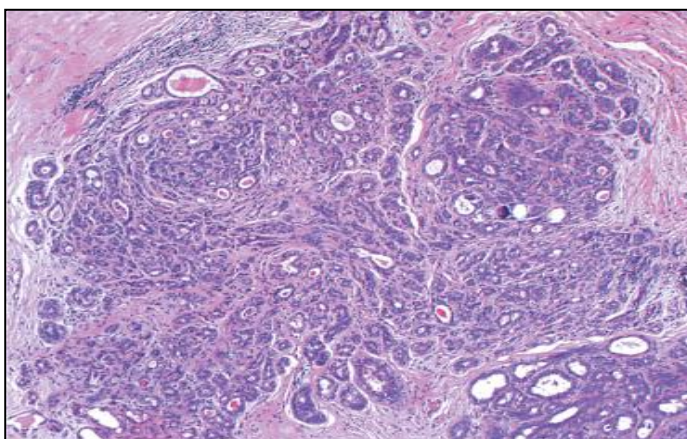
A, Normal. A normal duct or acinus has a single basally located myoepithelial cell layer (cells with dark, compact nuclei and scant cytoplasm) and a single luminal cell layer (cells with larger open nuclei, small nucleoli, and more abundant cytoplasm). B, Epithelial hyperplasia. The lumen is filled with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

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

Sclerosing Adenosis:- it present as a firm ill-defined mass lesion, clinically its looks like malignant

- Microscopically, sclerosing adenosis consists of proliferation of ductular structures and stroma with distortion of the TDLU.



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.

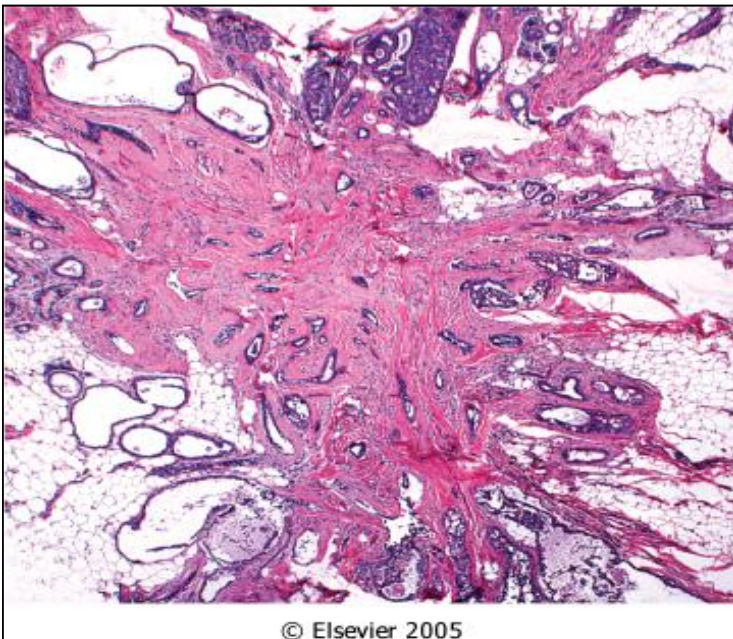
Radial scar: different concept of scars that follow inflammation (healing)

In mammography, it might be mistaken as invasive carcinoma, because of the similar growth pattern (star-like)

Complex Sclerosing Lesion (Radial Scar).

Radial scars are stellate lesions characterized by a central nidus of entrapped glands in a hyalinized stroma .

can resemble irregular invasive carcinomas mammographically or on gross examination.



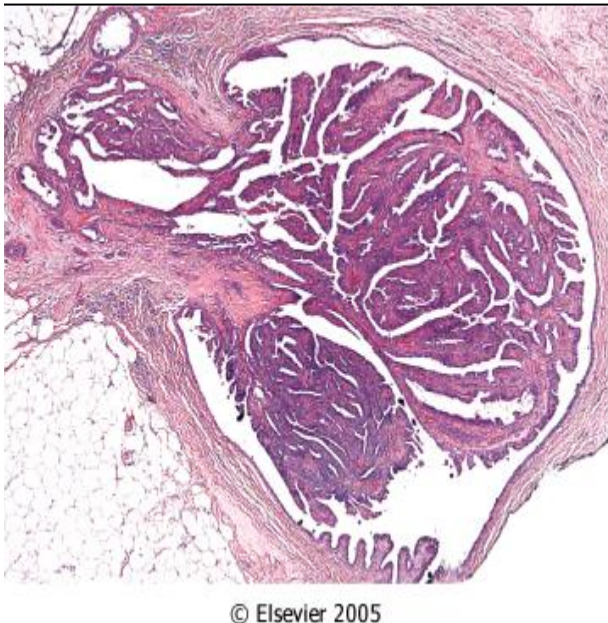
Complex sclerosing lesion (radial scar). There is a central nidus consisting of small tubules entrapped in a densely fibrotic stroma surrounded by radiating arms of epithelium with varying degrees of cyst formation and hyperplasia. These lesions typically present as an irregular mammographic density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

Radial Scar:- we have fibrosis in the center . in the periphery we have proliferation of glandular elements

Papillomas

Papillomas :- is papillary epithelial proliferation within the ducts

- 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.
- 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.

Proliferative Breast Disease with Atypia

Risk for cancer is 4-5 times normal

When we say Atypical it doesn't mean we have reached the carcinoma in situ but we are in the process of reaching carcinoma in situ

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.

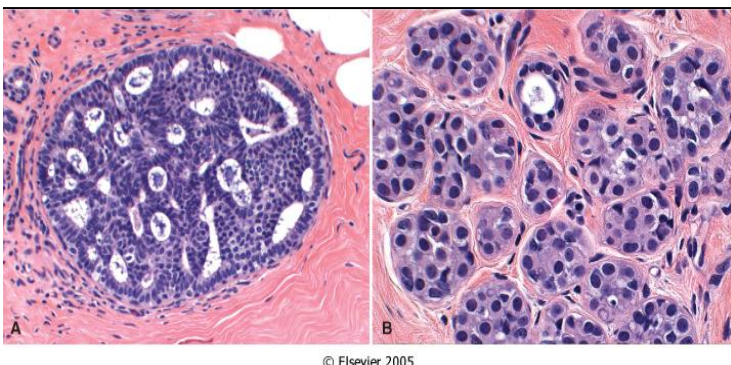
Proliferative Breast Disease with Atypia Include two entities

1 –Atypical ductal hyperplasia

In most of the time we don't see mass lesion in Atypical ductal hyperplasia or in Atypical lobular hyperplasia. Maybe we can see some densities and calcification

2 –Atypical lobular hyperplasia

Atypical hyperplasia has some of the architectural and cytologic features of carcinoma in situ but lack the complete criteria for that diagnosis and is categorized as ductal or lobular in type.



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

STROMAL TUMORS

Two basic stromal tumors are

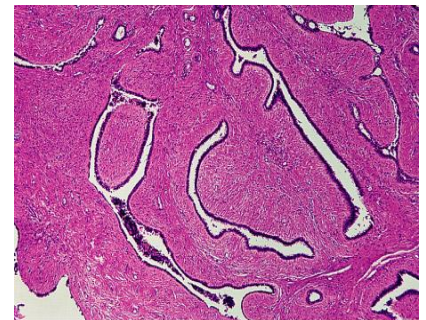
- fibroadenoma
- Phylloides tumor

Fibroadenoma

If the mass of fibroadenoma was very small in size the doctor might not remove it and leave it because it is very benign

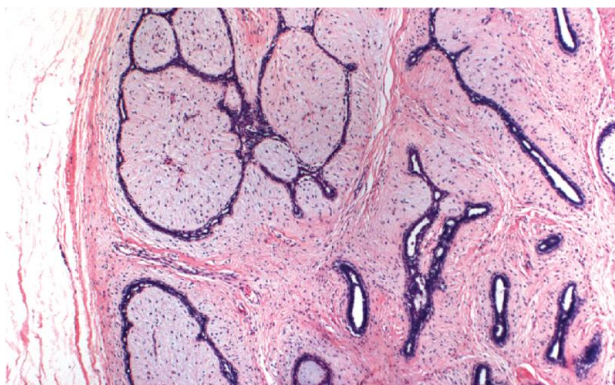
- The most common benign tumor of the female breast
- Composed of **both epithelial and stromal tissue** derived from the TDLU.
- Any age ,most common before age 30
- Usually present with a palpable mass
- Regression usually occurs after menopause.
- The tumor presents as a spherical, **rubbery nodule**, which is **sharply circumscribed** from the surrounding breast tissue and so is **freely movable** and can be shelled out.
- It may increase in size during pregnancy and cease to grow after menopause. The tumor is usually solitary but may be multiple and involve both breasts. The cut surface is pearl-white.

- Spherical nodules
- Sharply demarcated
- Freely movable
- Size vary



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- Proliferation in both glands and stroma
- Treatment: lumpectomy (only the lump is removed)
- Histologically, the tumor is composed of a mixture of ducts and fibrous connective tissue
- The tumor is **completely benign**.
- Rarely, carcinoma may arise within a fibroadenoma. The predominant type has been lobular carcinoma.



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Fibroadenoma. The lesion consists of a proliferation of intralobular stroma surrounding and often pushing and distorting the associated epithelium. The border is sharply delimited from the surrounding tissue.

Phylloides tumor

- Phyllodes tumors, **like fibroadenomas, arise from intralobular stroma**. Although they can occur at any age, most present in the sixth decade, 10 to 20 years later than the average presentation of a fibroadenoma
- Most present as palpable masses
- Phyllodes tumors must be excised with wide margins to avoid the high risk of local recurrences.
- The majority are low-grade tumors that may recur locally but only rarely metastasize. Rare high-grade lesions behave aggressively, with frequent local recurrences and distant hematogenous metastases in about one third of cases.

What is the difference between Phylloides tumor and Fibroadenoma?

- 1- In Phylloides tumor the stromal element is outgrowing.
- 2- Phylloides can be benign, boarder line or malignant (depend on the stromal element)

Summary

- **Normal Breast:-** Specialized epithelium and stroma . Six to ten major ductal systems originate at the nipple. Branching of the large ducts leads to the terminal duct lobular units.
- **Breast, Clinical Presentation:-** Pain , Palpable mass and Nipple discharge
- **Breast ,Benign Epithelial Lesion:-** Non proliferative breast changes , Proliferative breast disease and Atypical hyperplasia.
- **Fibrocystic change:-** most common disorder of the breast. Characterized by cysts, fibrous overgrowth, and epithelial proliferation . Produce palpable lumps.
- **Epithelial Hyperplasia:-** The proliferating epithelium distends the ducts and ductules. It shows two distinct cell populations, epithelial and myoepithelial cells.
- **Sclerosing Adenosis.:-** may manifest as a palpable mass that may be mistaken clinically for cancer.
- **Radial Scar:-** *we have fibrosis in the center . in the periphery we have proliferation of glandular elements .*
- **Papillomas:-** is papillary epithelial proliferation within the ducts. Nipple discharge, which may be bloody, is the most common presentation for central papillomas and less commonly of peripheral tumors.
- **Proliferative Breast Disease with Atypia:-** Include two entities :- Atypical ductal hyperplasia & Atypical lobular hyperplasia.
- **STROMAL TUMORS:-** Two basic stromal tumors are :- fibroadenoma & Phylloids tumor
- **Fibroadenoma:-** The most common benign tumor of the female breast. Composed of both epithelial and stromal tissue The tumor presents as rubbery nodule, which is sharply circumscribed, it is freely movable, completely benign.
- **Phylloides tumor:-** like fibroadenomas, arise from intralobular stroma. must be excised with wide margins to avoid the high risk of local recurrences

Questions:

1. A 41-year-old female came to the obstetrics clinic complaining of a palpable mass. She noticed that the mass have increased in size in a short period of time. Based on this information, what is likely the diagnosis?
 - A. Radial scar.
 - B. Fibrocystic changes.
 - C. Epithelial hyperplasia.
 - D. Papilloma.
2. A 47-year-old woman presented to an obstetrician, upon physical examination, the doctor palpated a mass behind the areola. After further examination the mass was found to be a subareolar papilloma. What is the cellular origin of the lesion?
 - A. Myoepithelial cells.
 - B. Adipose tissue.
 - C. Ductal epithelium.
3. A biopsy sample was taken from a breast lump of a patient. The pathological findings were Increase in the number of acini per lobule, fibrosis and cyst formation. Based on this information, what is the diagnosis?
 - A. Sclerosing adenosis.
 - B. Epithelial hyperplasia.
 - C. Fibrocystic changes.
 - D. Atypical ductal hyperplasia.
4. Which one of the following breast disease poses the highest risk of developing cancer?
 - A. Papilloma.
 - B. Radial scar.
 - C. Atypical lobular hyperplasia.
 - D. Sclerosing adenosis.

Answers:

1. B
2. C
3. C
4. C