Breast

1) CARCINOMA BREAST

- m/c & deadliest malignancy affecting women globally ✓
- Each year 1.7m women are affected & 1/3 out of 9t dies ✓

Epidemiology

* 4-7 times higher incidence in Europe & USA
* Rare : < 25 years ✓
* ↑ses incidence after 30
* Starting from 1980s – ↑ed incidence due to ° Mammographic screening & post-menopausal therapy.
* Risk of death has declined in older women

RISK FACTORS

Table 23.2 Risk Factors for Developing Breast Cancer

Risk Factors	Relative Risk[a]
1 Female gender 2 Increasing age >30 3 Germline mutations of high penetrance 4 Strong family history (>1 first-degree >1 relative, young age, multiple cancers) 5 Personal history of breast cancer 6 High breast density	>4.0
1 Germline mutations of moderate penetrance 2 High-dose radiation to chest at young age 3 Family history (1 first-degree relative)	2.1–4.0
1 Early menarche (age <12 years) 2 Late menopause (age >55 years) 3 Late first pregnancy (age >35 years) 4 Nulliparity 5 Absence of breastfeeding 6 Exogenous hormone therapy 7 Postmenopausal obesity 8 Physical inactivity 9 High alcohol consumption	1.1–2.0

[a]Relative risk is the likelihood of developing invasive carcinoma compared to women without any risk factors.

6 :- >4

3 :- 2.1 - 4

9 :- 1.1 - 2

RF RF m/n

PATHOGENESIS

Sporadic & familial

i) **Sporadic** breast cancers :

- Predisposed by excessive / imbalance of estrogen & environmental factors
- ↑ estrogen ⇒ physiological proliferation with the help of GF ⇒ ductal hyperplasia
- These proliferating cells can accumulate & acquire mutations in PIK3CA pathway
  ⇒ ER+ atypical ductal hyperplasia.

ii) **Familial** breast carcinoma

- Predisposed by BRCA1 & BRCA2 genetic mutations
  - Mutations in BRCA2 & PIK3CA ⇒ atypical hyperplasia, DCIS ⇒ invasive carcinoma (LA)
  - 2nd pathway ⇒ amplification of HER2 gene
  - 3rd pathway ⇒ mutations in BRCA1 & TP53 gene.

(i) BRCA-2, PIK3CA
(ii) BRCA-1, TP53
(iii) Amplification of HER2

Classification

i) CARCINOMA INSITU (non-invasive)

→ Ductal carcinoma is
→ Lobular carcinoma is
} presence of tumor cells within the ducts / lobules

a) Ductal carcinoma is

→ Atypical hyperplasia of ductal epithelium → filling of ducts with tumor cells (ductal epithelial cells)

cf - palpable mass, nipple discharge (30%)

→ MORPHOLOGY

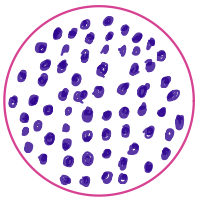
Gross : * Small, poorly defined focus to 2-5 cm diameter mass
* on cut section, → shows cystically dilated ducts containing cheesy necrotic material

Histologically :

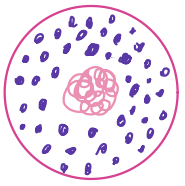
SPCC

(4) types of pattern

* Solid pattern - filling of ductal lumina with tumor cells

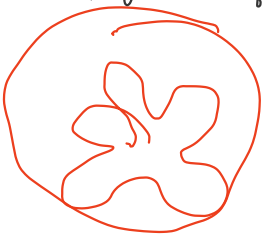


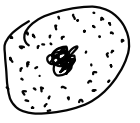
* Comedo pattern - centrally placed necrotic debris surrounded by tumor cells.



Sol

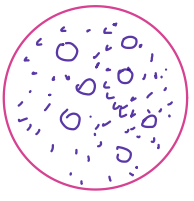
* Papillary pattern : intraductal papillary projections of tumor cells





Solid
comedo
papillary
cribriform

* Cribriform pattern : neat punched out fenestrations in the intraductal tumor

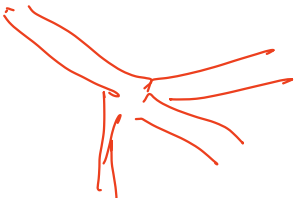


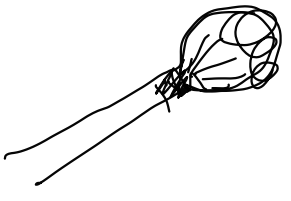
•) lobular CIS

* not palpable or grossly visible tumor

morphology : gross ↑

- m/s : filling up of terminal ducts & ductules or acini by mostly uniform cells which are loosely cohesive

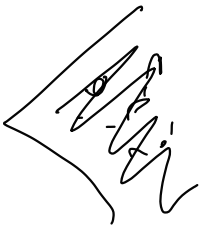




2) Invasive breast carcinoma

o Invasive carcinoma of no special type (NOST)

- Classic BC
- m/c histologic pattern (80%)
- hard consistency due to dense collagenous stroma (desmoplasia) very hard
- m/c - left breast (upper outer quadrant)
- morphology:
  - * gross - Irregular, hard mass
    c/s - grey white to yellowish with chalky streaks ✗
  - * morphology - lacks a regular & uniform pattern
    - → Anaplastic tumor cells arranged in tubules, sheets, nests, cords or as individual cells.
    - → infiltration of tumor cells into stroma & fat
    - → Pleomorphic cells with hyperchromatic nuclei, prominent nucleoli, numerous mitotic figures.



o Invasive lobular carcinoma

- More frequently bilateral ✓
- mutated CDH1 gene → loss of cohesion of tumor cells & diffuse infiltration

morphology:

gross → well defined scirrhous mass to a poorly defined area of induration that may remain undetected by inspection as well as palpation

m/s → 2 distinct features ✓

Single file arrangement in stroma

* Pattern - A characteristic single file linear arrangement of stromal infiltration by tumor cells.

* Tumor cytology - small & regular with very little pleomorphism & infrequent mitoses

Other histologic types of BC

i) Invasive carcinoma NST with medullary pattern

- 3-5% of all BC
- better prognosis ✓
- morphology:

gross → large, well circumscribed, round mass, soft & fleshy

c/s - hemorrhages & necrosis

m/s → 2 distinct features

* Tumor cells: large, pleomorphic tumor cells, ↑ cytoplasm, large nuclei, Anaplasia, Atypical mitoses

lymphoid component in stroma

* Stroma: loose CT stroma is scanty & usually has prominent lymphoid component. (+)

ii) Tubular carcinoma

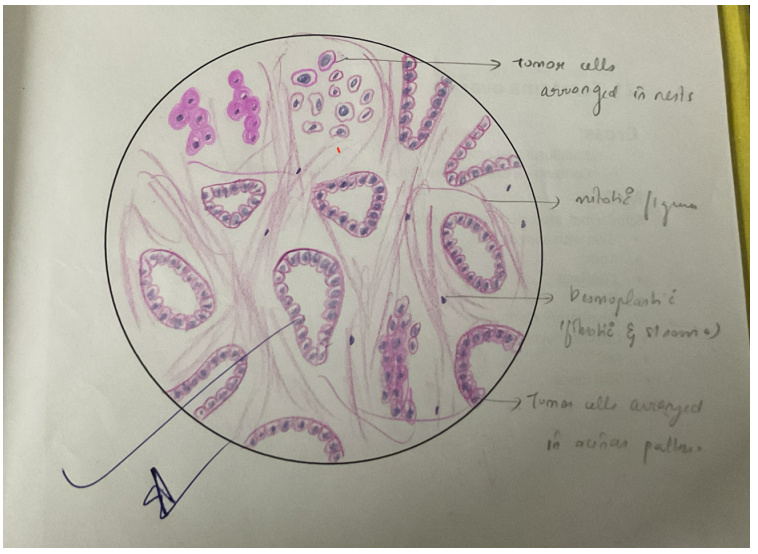
- comprises about 2% of invasive ductal carcinoma
- small, ill-defined, gritty nodules
- well formed tubules present.

iii) mucinous

- 2% Tumor cells floats in large pools of extracellular mucin

iv) Cribriform carcinoma

v) Papillary carcinoma



Molecular classification of BC

1) Luminal A
- ER +
- PR +/-
- HER2 -
- Tubular, mucinous, lobular, papillary
- Osseous metastasis common
- Good prognosis
- Lower relapse rate

2) Luminal B
- ER +
- PR +/-
- HER2 +/-
- IDC-NOS
- Osseous metastasis common
- Intermediate prognosis

HER2 positive
1) ER +/-
2) PR +/-
3) HER2 +
4) IDC-NOS
5) Osseous metastasis common
6) Worse prognosis

Triple negative / Basal
1) ER -
2) PR -
3) HER -
4) IDC with medullary features
5) Visceral & brain metastasis
6) Worst with early relapse

worst prognosis
↳ because metastasis to brain & viscera.

Prognostic factors

Prognostic Factors	Comments
Elements of AJCC 8th Edition Staging	
Distant metastasis (M)	Metastasis beyond regional lymph nodes is the most important prognostic factor.
Regional lymph nodes (N)	Nodal metastasis (including the number of involved nodes) is the second most important prognostic factor.
Tumor (T)	Size, involvement of skin (e.g., ulceration or dermal metastases), invasion into chest wall, and presentation as inflammatory carcinoma are important features.
Histologic grade	Survival diminishes with higher histologic grade.
Expression of ER, PR, and HER2	Survival is highest for the most favorable combination (high ER and PR and absent HER2) and is lowest for the least favorable combination (absent ER, PR, and HER2).
Other Prognostic Factors	
Lymphovascular invasion	Tumor cells seen in vascular spaces at the periphery of carcinomas are a poor prognostic factor.
Special histologic types	Some histologic types of cancer are strongly correlated with very favorable survival (e.g., tubular, adenoid cystic).
Response to chemotherapy	The degree of response is a strong prognostic factor for TNBC and HER2 cancers, but not the majority of luminal cancers.
Gene expression profiling	The most important clinical value of these assays is to identify patients with antiestrogen-responsive cancers who do not need chemotherapy.

Fibroadenoma breast

- Benign biphasic tumor of fibrous & epithelial elements
- m/c benign tumor
- Yf : solitary, freely mobile

Gross → small, solitary, well encapsulated, spherical/discoid mass, Encapsulated mass

C/S → firm, grey white, slightly myxoid, slit like spaces formed by compressed duct

M/S → 2 types of patterns

* Intracanalicular : stroma compresses the duct :. they are reduced to slit like cleft lined by ductal epithelium
* Pericanalicular : encircling masses of fibrous stroma around the patent/dilated ducts
  - fibromyxoid stroma +ve