بسم الله الرحمن الرحيم

SurgicalOncology

Seminar 1

14-20 lactiferous ducts
Fat, fibrous tissue (cooper's ligaments)
$2^{nd} - 6^{th}$ rib

60% of patients present to the clinic with mastalgia:

1. Cyclical mastalgia: very common, related to menstrual cycle, involution in 2^{nd} ½ of cycle produces pain
2. Non-cyclical mastalgia: related to change in hormones in perimenopausal period

Mastalgia → benign

Fibrocystic changes = ANDI (Aberration of **N**ormal **D**evelopment & **I**nvolution)

Cyclical mastalgia → large cyst → proliferative fibrocystic disease (along with atypical ductal hyperplasia): 8-12 folds increase in malignancy potential

Adenosis, fibrosis, sclerosing adenosis

Presentation to oncology clinic:

1- **Pain: mastalgia (most common) (not breast lump)**
2- Breast lump

Or the opposite?
"Breast pain is the second most common breast symptom for which women seek medical attention, the first being a lump in the breast. Most women with breast pain do not have cancer."
http://www.ccjm.org/content/69/5/425.full.pdf

Incidence of breast Ca: 8%

Hx: age (peak age: 53), gender, family Hx, age of 1^{st} preg. (> 35y is a risk factor for both breast & endometrial Ca)
(Endometrial Ca: obese, age of 1^{st} preg.)
Obesity: protective in premenopause, risk factor in menopause & postmenopause due to peripheral conversion of fatty tissue to sex hormones by aromatase

OCPs: risk increases in current users (Hx of previous use of OCPs is not a risk factor)
HRT: esp. if > 8 y
Alcohol strongly linked (more than smoking)
Breastfeeding: may have adverse effects?
Previous surgery on breast for benign causes: risk of Ca increases with the number of Bx

Gails model: risk of malignancy (age, family Hx, number of Bx)
Previous irradiation of chest

Lynch syndrome (HNPCC): colon, pancreas, breast, ovary, sarcoma
Li-Fraumeni syndrome: bilateral breast Ca, with sarcoma, CNS Ca (mut in p53): rare, autosomal dominant

Q: **bilateral breasr cancer + soft tissue sarcoma**? Dx: **Li-Fraumeni syndrome**

Localized abscess: (due to obstruction of a duct, ass with pain)
Common in breastfeeding females
May be due to Ca

Mets:
Mets to bone (most common): axial skeleton (thoracic vertebrae), paravertebral plexus **(Batson plexus)**: connection bet breast & vertebral col.
Bone mets can be osteoblastic (prostate: mets to lumbar vertebrae) or osteolytic (breast mets). Both may result in a pathologic fracture.

Acute spinal cord syndrome: urine retention, spastic paralysis in LL

Mets to lungs:
Coin lesion (multiple lesions)
Mets to pleura: pleural effusion, pleural nodules
Lymphatics of lung: **lymphangitis carcinomatosis** (bad prognosis)
Edema in alveoli, SOB, Sx of HF & respiratory failure (↑ mortality)

Liver mets: loss of appetite → cachectic, metallic taste, jaundice, cholestasis
(Colon Ca mets to liver: Rx by metastatectomy which increases 5-y survival), metastatectomy is not done in breast Ca
Liver mets in breast Ca are Rx by CTX

Mass:
>1 cm: palpable
<1 cm (impalpable, but pt may be able to detect masses measuring 0.8 cm)

Rough, irregular surface, indistinct borders, fixed to chest wall or skin

Skin changes: Peau d'orange (bad sign: T4) due to invasion of subdermal plexus of lymphatics → dimpling
Involvement of skin (regardless of size) → T4

Mass pulls ducts

Dimpling: when pt lifts arms
Dimpling: 1 cooper ligament
Puckering, tethering: multiple cooper ligaments

Redness: inflammatory breast Ca (T4d), another cause: ?
Ulceration: very bad prog.

Mets to skin: satellite nodules (T4)

Fibroadenoma: freely mobile, soft-firm

Fat necrosis : hard, irregular mass (border), **Hx of trauma**, on P/E & radio: may be confused with malignancy, differentiated by histopathology

Lipoma of breast: rare, soft

Fibrocystic changes: firm or hard, margins may be irregular
Nipple discharge: most common is milky discharge (hyperprolactinemia: prolactinoma)

Nipple discharge:

Uniductal: malignancy
Multiductal: duct ectasia, fibrocystic changes

Expressible: milk, duct ectasia, fibrocystic changes
Spontaneous: malignancy

Color:
Milky: most common
Clear (watery): rarest: malignancy
Bloody: common; intraductal papilloma (most common cause of bloody nipple discharge, involution, esp in pregnancy: 2^{nd} trimester) or Ca
Greenish, brownish, yellowish, bluish: duct ectasia, fibrocystic changes

Ca:
Uniductal spontaneous clear
Uniductal spontaneous bloody

Seminar 2

Breast

Triple assessment:

1) **Hx & P/E**
2) **Imaging**
3) **Bx**

Imaging:
Mammongram: above 40 y (baseline)
Normal → every 2 y
Family Hx or benign changes → yearly

Malignancy (mammographic findings):
1) Micro-calcifications
Micro-calcification → malignancy
Macro-calcification → benign entities

If single micro-calcification → not important
Pinhole grouped micro-calcifications: >5/cm^3: pre-malignant (DCIS) or malignant

2) Radio-opacity, speculated mass, irregular margin
Radio-opacity: **linear configuration → malignancy**, scattered → not important

3) LN involvement:
Preserved fatty hilum, well-circumscribed → benign
Large, all-white (fatty hilum of LN not seen) → malignancy
Matted LNs: extracapsular invasion (bad sign)

Mammogram: 3 min, cost-effective, minimal exposure to X-ray
U/S: 20 min, more costly than mammogram, better in younger individuals, malignancy: **hypo-echoic**, with irregular margins
3D breast CT: new
Breast MRI: time-consuming, costly, best **done before surgery**, done if previous results were equivocal, malignancy: multicentricity, multilocality , detects in situ component

Histopathological dx:
1) FNA: cytology (malignant, suspicious, benign, inadequate), hormonal status
2) Trucut Bx (core Bx): large gauge needle, special needle
Benign: type (fibroadenoma, fat necrosis, fibrocystic changes)
Malignant: type, hormonal status
3) Incisional Bx: for soft tissue sarcoma: longitudinal (not horizontal) incision; soft tissue sarcoma respects fascia, spreads in muscular planes, also for preservation of structures (Rx of soft tissue sarcoma: wide local excision; with safety margin -removal of NL tissue-)

Stereotactic Bx (trucut Bx under mammography, very expensive), for:

1. Focus of area of microcalcifications without a mass
2. Very small masses

Masses: > 1 cm → palpable
Malignant mass < 1 cm → breast conserving surgery:
Wire localization (U/S → tip inside mass) for very small impalpable masses
If mass can be seen with U/S → U/S-guided Bx

Histopathology:
Infiltrative/invasive ductal carcinoma (not otherwise specified: NOS): 70-75%
Invasive lobular carcinoma: 8-10% (10% of invasive lobular carcinoma is bilateral, multifocal, multicentric)
Medullary carcinoma: 3-5% (<1%?), early 50's, mimics fibroadenoma (mobile, pseudocapsule), always ER & PR –ve
Colloid (mucinous) carcinoma: can be mistaken for fibroadenoma, most express ER/PR, rarely HER2
Tubular: best prognosis (differentiated)
Inflammatory: <1% (not a certain histopathology): hotness, redness, tenderness, breast engorgement (malignancy invaded by neutrophils)
Papillary carcinoma: a type of DCIS (differentiated: good prognosis)
Phyllodes tumor: 1/3 are malignant

Sarcoma of breast: rare, bad prognosis
Lymphoma of breast: rare, bad prognosis

True story: severe pain while breastfeeding → bilateral engorgement of breast → bluish breast → ventilator → died

Rx:
Surgery
CTX: before (neoadjuvant) or after (adjuvant) therapy
RTX
Hormonal therapy

Neoadjuvant for down-staging in:
Locally advanced: T3, T4
N2 (LN matted together)
Large tumor
Breast-conserving surgery: neoadjuvant CTX with RTX: same 5-year survival as mastectomy

Surgery: Halsted operation = radical mastectomy:
Breast, muscle (pectoralis major), axillary LNs (levels 1 & 2)

Levels of LNs:
Level 1: lateral to pectoralis minor
Level 2: behind pectoralis minor
Level 3: medial to pectoralis minor (infra-clavicular, internal mammary: N3) (not removed in radical mastectomy)

Involvement of internal mammary LNs: same prognosis as stage 4 (mets)

MRM (modified radical mastectomy): same 5-year survival & local recurrence as radical mastectomy
Wide local excision = lumpectomy
Quadrantectomy: mass in upper outer quadrant
Mass above nipple: Bat-wing mastopexy

Axillary dissection doesn't affect 5-year survival. Axillary dissection is dangerous with possible injury to the nerves, veins & lymphatics. It's done for staging & Rx.

TNM: clinical vs histopathological
Sentinel LN Bx: 1st LN to drain tumor, not applicable in certain tumors, but it's applicable in breast Ca.

Indications for axillary dissection: Palpable LN, large tumor, +ve sentinel LN

Seminar 3

Breast

Axillary dissection/ clearance doesn't affect 5-year survival

Injury during axillary dissection
Motor nerves:
Long thoracic nerve → serratus anterior (winged-scapula)
Thoracodorsal nerve → Latissimus dorsi (dropped shoulder)
Med pectoral nerve → Pectoralis minor (weakness in adduction) & major
Lat pectoral nerve → pectoralis major

Sensory:
Intercostobrachial nerve (most superficial nerve in axilla, **most commonly injured nerve**): medial upper part of arm

Vascular injury: axillary vein
Lymphedema: 10% after formal axillary dissection

Axillary LNs: 60-70 (in whole body: 300-400 LN)
Axillary LNs: drain upper abdomen, upper limb, breast

LNs draining the **breast** are located **inf. to axillary vein** (20-30) (level 1, 2)
LNs draining upper limb are located sup. to axillary vein → significant lymphedema results if they're removed

Of those 20-30 LNs draining the breast: 12-15 must be removed for axillary dissection to be adequate
If all are –ve → N0
If all are +ve → N3

Clinically:
N0: no palpable LNs
N1: big, not fixed (mobile)
N2: multiple matted LNs
N3 (there's no clinical N3): CT → internal mammary LNs

Pathologically:
0 out of 12 (all –ve) → N0
< 4 (1 -3): N1
4-9: N2
≥ 10 (10-12): N3

Local invasiveness: N2 → candidate for neoadjuvant Rx

Staging for breast Ca:
Trucut Bx → Ca → investigations for mets
Bone: Bone scan
Lungs: CXR, CT
Liver: LFTs + liver U/S
} Requisites for staging

If Sx → brain CT: not a requisite for staging

Prognosis of N3 ≡ prognosis of mets
Supraclavicular lymphadenopathy ≡ mets
} Same 5-year survival as mets

"Patent blue" dye is injected in the digital space & colors lymphatics & LNs draining upper limb blue: these are not removed

Sentinel LN Bx: dye around tumor → dyes lymphatics & sentinel LN (1st LN to take the dye is removed)

Axillary clearance doesn't affect 5-year survival
Local recurrence doesn't affect 5-year survival
1ry breast tumor in contralateral breast is more likely than local recurrence

The importance of identification of benign breast disease is to differentiate them from malignancy

Hx: 25y single female, Rt upper quadrant mobile mass (2cm) for 3 months, pain increases with menses, -ve family Hx of breast Ca

1) Hx & P/E:
Hx: Hydradenitis suppurativa → skin changes, infection & obstruction of apocrine sweat glands: red, tender, hot axillary lump (hydradenitis suppurativa can also appear in perineum, genitalia which have apocrine sweat glands)

P/E: 2cm, mobile, not fixed, firm
Fibroadenoma: 20's (resembles medullar Ca of breast: 50's)

2) Imaging:
U/S (pt is young: 25 y < 40): showed lobulated structure, 3 cm, in Rt upper quadrant with regular edges.

3) Bx:
FNA: BI-RADS

BI-RADS:
0: imaging not adequate
1: NL
2: benign, no follow-up necessary
3: benign, equivocal, follow-up necessary
4: suspicious, tissue dx (Bx) necessary
5: malignant (?)

It was Bi-RADS 4

Indications for surgery for a fibroadenoma:
Large fibroadenoma, BI-RADS by U/S: excisional Bx in young age group
Fibroadenoma > 4cm, symptomatic: excisional Bx
Big painful, >2cm
Small, worrying for the patient
Strong family Hx of breast Ca
Juvenile fibroadenoma (14-15y): usually big, has malignant potential (1/1000)

Fibroadenoma → 20's

Fibrocystic disease (20 pathologic entities):
Menstrual cycle changes: involution, proliferative phase, asx
Focal adenosis
Sclerosing adenosis
Proliferative: 8?-fold ↑ risk in atypical (proliferative)

Simple cyst: very common, 2nd most common (what?), in 30's, early 40's, **Hx of sudden-onset of breast mass: 1 or 2 weeks**, P/E: very tense, may look hard
Fibrosis around cyst (part of fibrocystic disease): not regular margins, may be confused with malignancy
U/S: cystic mass containing fluid
FNA: cyst aspirate; discard unless: bloody aspirate, recurrent cyst or remnant mass in place of cyst (possibility of intracystic malignancy)

Papillomatosis: part of fibrocystic changes, cross-section in duct shows papillae, if > 1 duct is involved → DCIS (risk of malignancy)
Hyperplasia: typical vs proliferative atypical (ductal or lobular)
DCIS: pre-malignant
LCIS: ass with ↑ risk in same & other breast (marker of malignancy?), **not a pre-malignant lesion**, mostly gives rise to ductal carcinoma
LCIS → ↑ risk of **ductal** carcinoma

20 y, breast mass, -ve family Hx, Bx: LCIS → observation
60y, LCIS, +ve family Hx → bilateral mastectomy

DCIS → Paget's disease of the nipple: carcinoma in situ of nipple-areola complex, >50% ass with ipsilateral invasive ductal carcinoma

Breast abscess:
Mastitis: lactating, late 3rd trimester, bacteria from skin, or mouth of baby, redness, hotness, tenderness
Abscess is not fluctuant in breast
Don't stop breastfeeding
Rx: Abx (against staph): **cloxacillin**
Breast abscess → stop breastfeeding on ipsilateral breast, incision & drainage, Abx (if ass with cellulitis)

Accessory nipples on milk line: 8% of females
Accessory breast tissue: in axilla, enlarges with pregnancy & lactation, malignant potential same as in NL breast, removed for cosmetic reasons

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Gynecomastia:
True: development of glandular disc
False (pseudo): obesity

Related to age (senile): ↓ testosterone
Newborn: 1st 8 months (hormones of mother)
Pubertal males (disappears later)

True (glandular): related to alcohol, liver cirrhosis, drugs (digoxin, spironolactone)

Duct ectasia: part of fibrocystic disease, seen in:
Elderly: atrophy of breast tissue
Frequent breast lactation
Pathological: when bacteria causes stasis →greenish/brownish discharge (histopathological destruction of ducts)
Rx: long-course Abx (covering anaerobes), 10-20%: ductal system excision (microdocotomy)

Seminar 4

Sarcoma: malignant
Soft tissue sarcoma: very rare tumors 0.5/100,000, affect young age group

Derived from mesoderm:
Cartilage: chondrosarcoma
Bone: osteosarcoma
Bone marrow
Smooth muscle: leiomyosarcoma
Skeletal muscle: rhabdomyosarcoma
Blood
Blood vessel: hemangiosarcoma
Fat: liposarcoma
Kaposi sarcoma (in HIV +ve individuals, caused by HHV8)
Ewing sarcoma

All have same prognosis
Prognosis depends on size, differentiation (Grade)

Soft tissue sarcoma is the only tumor in which **stage** (clinical) = **grade** (histopathological)
Grade 1: good differentiation
Grade 2: moderate differentiation
Grade 3: poor differentiation
Grade 4: undifferentiated

NC ratio

Mitotic figures:
<5/HPF: good differentiation
5-10: moderate differentiation
> 10: poor differentiation

Most important prognostic factor in soft tissue sarcoma is <u>grade</u>

In the past, it was thought that tumors which have a size of < 2cm are most likely benign, & those > 5cm are most likely malignant. This is no longer the case.

Presentation: lump
2/3 of cases are in the extremities, LL>UL, thigh most common site in LL
20% trunk (presentation in this case is not a lump), mass effect (by size): ureteric obstruction → UTI/hydronephrosis, early satiety

Although most patients relate the mass to trauma, it's not related. The trauma only brings the attention of the patient to the lump.
Pt has Hx of trauma but there's no cause-effect relationship.

2 peaks: late teenage/20's & 70's

Risk factors:
1. Radiation (XRT): as for lymphoma
2. Family Hx: **Li-Fraumeni (soft tissue sarcoma + breast Ca)**

3. Immunosuppression: steroids, CTX
4. HIV: Kaposi sarcoma

Abdominal/trunk sarcoma: pressure Sx

Soft tissue sarcoma doesn't invade blood vessels or nerves. IT respects fascial planes. (circumferential invasion without pressure)

Rx in the past was by amputation. Nowadays, this is the 3rd option.

Rx:
Wide local excision (with safety margin) (2-5 cm circumferentially)
Mass on a scar is local recurrence (except for inguinal hernia region)

Ex: Hx of trauma, mass enlarging in size, not painful
P/E: hard mass, regular or irregular, no abnormal surrounding tissue
Imaging: X-ray (may reveal osteosarcoma) is –ve
CT scan (cheaper than MRI, 80 JD, pt stays in machine 1 min)
MRI (400 JD, pt spends 20-30 min in machine): better anatomy of nerves, muscle, fat & position, must be done if surgery is planned
Imaging showed encapsulated structure in the thigh just anterior to the femoral sheath

Histopathology: tissue Bx (Trucut Bx: multiple core Bx)
U/S-guided Bx, CT-guided Bx
Bx must be done from above (vertical to skin), & not from the side, because **Bx tract is included in the safety margin**

Incisional Bx → vertical incision: less chance to spread in muscle planes

Rx:
Surgery: adequate wide-local excision with adequate safety margins
Soft tissue sarcomas are radiosensitive: XRT if tumor is in retroperitoneum (close to major vessels), after de-bulking & if safety margin was not adequate.

Blue-cell tumors: very malignant (chromatin ↑):
SCLC?
Ewing sarcoma: a soft tissue sarcoma
ALL
Rhabdomyosarcoma: a soft tissue sarcoma

Is soft tissue sarcoma actually chemoresistant? No, require high-dose CTX which causes bad side-effects
CTX may be given with localization to the affected area: intra-arterial CTX, limb heating (blood is heated & returned to the limb: used when the tumor is big, inadequate safety margin & pt refuses amputation)

Mets: hematogenous → lung (Cannon-ball nodules)

Ex: 20 y, buttock mass, P/E: soft mass, histology: lipoma, when pt became 40 y, recurrence on scar?
Is there sth between lipoma (benign) & liposarcoma (malignant):
Yes, atypical lipomatous tumor → lipoma with very minimal mitotic figures, exhibits features which are benign (it never mets) & malignant (local invasion, local recurrence). It's Rx as sarcoma.

Seminar 5

Skin malignancy
Very common
Related to sun exposure: Australia → 1 in (2 or 3)
Ozone hole → UV light (UV-B: wavelength 10, 000 – 20,000 nm), UV-A is minimally related

BCC: rodent ulcer, locally invasive, rarely mets
SCC: everted edge, capable of systemic mets
Melanoma (5%): most aggressive

BCC: danger triangle (lateral canthi → mid of upper lip)
Lesion on nose or upper lip → BCC
Lesion on lower lip → SCC

BCC:
Hx: elderly, nodule: superficial, rolled edge, severe destruction, growth
P/E: "blue pearl": secretions, shiny
Site: danger triangle
Size: small
Margin: indurated
Base: fixed, hard, indurated
Regional lymphadenopathy: locally invasive (regional LN mets)
Destruction in bone

BCC subtypes:
Nodular (including rodent ulcer)
Pigmented
Superficial
...

Raised lesion "Morphea-like": in elderly (resembles malar rash of SLE) → BCC or SCC

Rx of BCC: local excision

SCC: UV light, ass with chronic ulcers (venous, diabetic/ischemic, neuropathic/dependent), chronic burns → Marjolin's ulcer

Site: any site except the danger triangle of BCC

In western countries, it affects:
Males – back
Females – leg
(Sun-exposed areas)

Regional LN mets + systemic mets → lungs & liver

Dx: punch Bx

BCC: safety margin < SCC

Head & neck: Mohs surgery → in BCC, SCC & melanoma on face (cosmetic concern): safety margin of 1 mm (through microscope)

If the mass is big → Mohs surgery + reconstruction by local flap (nasal flap, frontal flap) or FTSG

Color matching & strength (flap better than FTSG)
STSG: cosmetically not good

SCC in scalp: FTSG better than STSG
If pt is diabetic (poor vascularization): STSG better than FTSG (STSG has better "take" than FTSG)

XRT: very effective in SCC (beneficial in head & neck ≡ surgery)
If tumor is very big → XRT

Enlarged LNs → neck dissection

BCC: grow upwards
SCC: pushes into dermis (invagination of dermis)

BCC & SCC are derived from epidermis (ectoderm)

Melanoma: from melanocytes: neural crest origin (ectoderm)
Common in white/fair people (albinos: nystagmus)
Blacks have special types of melanoma (ungula/subungual melanoma)

Most common subtype of melanoma is superficial spreading melanoma which has a **better prognosis**

Nodular melanoma: very aggressive
Ungual, subungual melanoma: very bad prognosis, Rx by amputation, common in blacks

Site:
Males – back
Females – leg

Large mole > 5mm, change in color, irregular edges, ulcer, bleeding, itching, enlarging size

In-transit melanoma: satellite nodules

Melanoma: CT, extensive work-up, staging: **Breslow classification** for melanoma (Breslow's depth)

Dx: Punch Bx

Stage 4: distant mets: brain, lung, liver, small bowel **(most common tumor to mets to small bowel wall: intestinal obstr)**

Rx: XRT, CTX, immunotherapy (antibodies, this is a new modality of Rx)
Local CTX creams: 5-FU

Congenital melanocytic (hairy) nevus: pre-malignant

Keratoacanthoma: common low-grade skin tumor, resembles BCC but benign

Merkel cell carcinoma (Merkel cells are mechanoreceptors): very aggressive tumor

Tumor from hair follicle: tricholemmal carcinoma (very aggressive tumors), benign background
Tricholemmoma: benign but can transform, can't be differentiated clinically from sebaceous cyst

Hidradenitis suppurativa (HS): in axilla, genitalia, caused by obstruction of apocrine sweat glands, recurrent,
Rx: incision & drainage or, in case abscess develops, excision of skin of axilla & graft

Pilar cyst (trichilemmal cyst): common, cyst from a hair follicle

Solar keratosis (= actinic keratosis = senile keratosis): premalignant, in elderly

Campbell de Morgan spots (cherry angioma = senile angioma)

A person has an avg of 20 moles

Ex: 67 y old pt, ulcer post to knee, SOB, hepatomegaly → melanoma with mets (Stage 4)

JORDAN UNIVERSITY HOSPITAL

DEPARTMENT OF SURGERY

ONCOLOGY UNIT

BREAST CLINIC

Consultant:

Date :

Name : Age: Occupation Unit No.

Lump: Yes No R. L. Duration Weeks S. M. D. W

Pain : Yes No R. L. Duration Weeks

Nipple discharge : Yes NO R. L. Duration Weeks Colour

S.O.B.: No Mild Moderate Severe

Menarche :

L.M.P:

Premenopausal: Menopausal Postmenopausal

Menopausal symptoms

Medical History

Present Medication:

Hysterectomy: Copmorectomy

Other Operations:

Contraceptive Pill: Time Started Duration

F.H. of Breast Cancer: Yes No

Pregnancy:

Children:

Breast Feedings: Yes No

Lactational suppresstion:

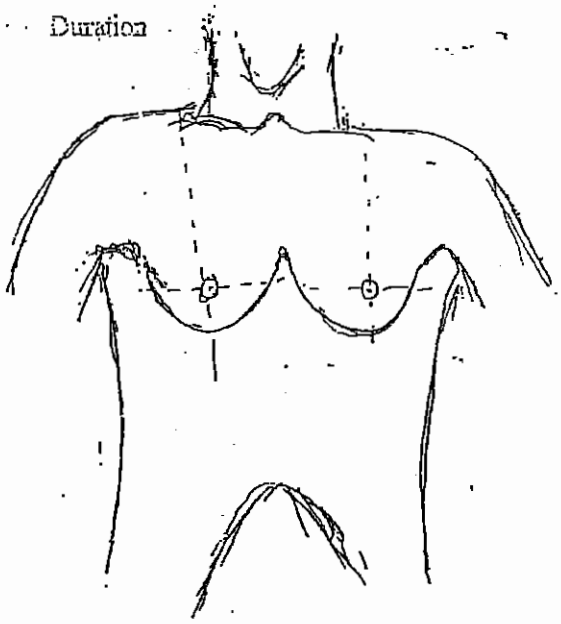
Investigations:

1- Needle Aspiration : Yes No

Result:

2- Xeromammography: Yes No

Result:



Clinical Diagnosis (Lump description)

Prob. Benign	Prop bening
Prob. Malignant	Prop. Malignant
Poss. Malignant	Poss. Malignant
Size	Size

T.N.M

Management

Final diagnosis. Stage (TNM) & Site:

INV

CXR	CBC
Skeletal Surgery	ESR
Bone Scan	Alk PO
Liver Scan	Gam. G/T
	Ca ++

Definitive Management

Pathology:

بسم الله الرحمن الرحيم

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Tumor biology

CA: abnormal purposeless growth & proliferation of cells. Usually occurs after initial stimulus but becomes independent of that stimulus.

From surgical point of view : unhealed wound.

E.g: malig. Ulcer.

Carcinogenesis : the process of malig. Changing of cells. It includes :

* initiation *promotion *progression

cells become capable of dividing by themselves without responding to orders of the body.

Characters of malig. Cells :

Morphology :

Tumor cells can be well differentiated , moderately diff. , or poorly diff.

The less they mimic the tissue of origin , the more malig. They are.

t. cells have certain microscopic characters :

* variable size * high n/c ratio
*variable staining ability
*increased nucleolus /nucleus ratio
*abn. Mitochondria

tumor cells are either abn. Cells in normal site or normal cellsin abn. Place e.g. u might find well diff. Thyroid tissue with follicles & colloid in a biopsy of deep cervical L.N here we are certain that it's a malig. Tissue coz it has spread out of thyroid.

Aberrant thyroid tissue: thyroid tissue out side the embryological line of develop. Of thyroid. It is always malig.

Behavior of t. cells :

*In contrast to normal cells, malig. Cells r loosely attached to each others .

They have decreased intracellular cements (polysaccharides & glycoprot.) &decreased desmosomes . they also have powerful electronegative charges that coz them to repel .

*movement of cells :

normal cells are motionless in the tissue but mobile in culture media until contact inhibition occurs (self control of growth)

malig. Cells move freely in tissues & culture pr

Growth & prolif. Of CA cells : growth is a continuous process in malig. Cells but its not necessarily faster than normal cells e.g. bone marrow cells .

Initial prolif. Is exponential then with time &when size increases it becomes slower due to

lack of support from the host by nutrition, bld supply &due to pressure & necrosis.
So if u find a t. with cent. Necrosis e.g. soft tissue sarcoma ,it indicates an aggressive rapid growing t.

The fact that small t. s grow exponentially & that our taget in chemo/radiotherapy is the growing cells(growth fraction) is import. In the management of t.s : we remove part of the t. so that the residual stem cells will be recruited to prolif.(G0 ⟶ G1) & compensate for the lost cells by that we inc. the growth fraction & then treat by radio/chemotherapy which becomes more effective ⟶ cytoreduction way of treatment.

Malig. Cells r usually monoclonal originating from 1 cell which had genetic alteration in the form of multiple hits making it able to survive by itself . we probably every day have some of our cells undergo malig. Transformation but they die. Another e.g. is abortion of fetus whose cells undergone malig. Transformation.

Malig. Cells r capable of production of factors necessary for their growth by oncogenes then these factors work on them by autocrine,paracrine or endocrine manner.

Benign vs malig. Ulcers:
If ur pt. Has ulcer give him the trios of treat. (clarithromycin, metronidazole & amoxicillin) For 6 wks .if it doesn't heal .it is malig. This is in case of gastric ulcers not dud. Ones ???

Cloning :
If a nucleus of fertilized frog egg is disrupted &replaced by a nucleus taken from EP. Cells of GIT of a frog it will still be able to produce a frog which means that all the genetic material is found in the nu. Of any cell but there's some kind of switch on/ switch off mechanism in diff. Cells. Malig. Cells may have switched many genes e.g. lung CA cells may be able to produce many hormones & this is responsible about the paraneoplastic synd.
Similarily malig. Cells of breast which appear in mammogram may be acting as osteoblasts &lay down bone (also extraskeletal osteosarcoma)

Oncogenes :
They r normal genes found in normal cells .they encode for growth factors or GF receptors in orderly fation . if they become mutated there will be abn. Growth of cells.
e.g. BRACA1 & BRACA2 genes & breast CA
if u do a genetic check for pt.s with a +ve family Hx of breast CA u might find changes in those genes ⟶ higher risk to breast CA .

here u might give a prophylactic antiestrogen treat. Or even do bilateral mastectomy followed bv reconstruction of breasts.

Oncogenes r found on chromosomes (2 allels) if 1 allel is damaged it will be coppied so it becomes dominent.
Tumor suppressor genes :
They r responsible for cell arrest in S or G2 phase if any mutation is detected . . this will give the chance for DNA repair or , if impossible, to programmed cell death (apoptosis).

It is import. To understand cell cycle to understand the process of carcinogenesis.
Refer to Dr. sheets.
G phases r import. For dx & ttt. Of CA
* chemotherapy ttt. Can be:
- cycle non specific
-cycle specific (nonphase specific or phase specific).

Solid tumors are formed of :
Benign part (40-50%)
Malig. Part

Benign: is the supportive tissue made of bld vessels ,lymphatics , immune cells, fibrous tissue... so if u still have a residual t. after ttt. It might be the benign part.

The malig. Part :
1. t. stem cells =clonogenic cells: resting cells called up on to work in stress conditions. They r. resistant to chemotherapy , that's why its un likely for solid t.s to be treated by chemotherapy alone. Some of the stem cells grow & prolif. Forming the growth fraction.
2. growth fraction : target of therapy.
3.dead=end cells
Doom cells: cells not capable to survive . they divide once or twice then stop & die.

Growth rate of neoplasm :
t.s don't arise over night . 2/3rd of growth is preclinical. First clinically detected size of t. is 1 gm (billion cells) which occurs after 30 doubling time.

Of the import. Characters to diff. Bet. Benign & malig. T.s is metastasis
Biology of metastasis:
It means that malig. Cells reach distant places However Local invasion is a continuous process. It is performed by mechnical pressure in the form of finger like cords or by secreting enzymes that hydrolyze the cell memb. & ECM.
Trans cavitory spread :trans celomic spread thru the peritoneal cavity e.g. krukinburg t. in ovaries came from stomach CA.
Also we have lymphatic & hematogeneus spread

Metastasis is v. selective process . metastasized cells don't seed every where . we have the seed /soil theory.

e.g. its v. rare to c mets in muscles, heart, spleen but v. common to c it in lung ,bone & liver.

Seed / soil theory :

There r prerequisites for malig. Cells to leave the primary t. , reach bld. Stream ,form thrombus & keep going until it blocks small bld vessels ,invade them ,reach tissue & induce angiogenesis . people r thinking of antiangiogenesis to prevent mets .

The end

بسم الله الرحمن الرحيم

Lecture topic: Staging of cancer
Lecturer : Dr. Jamal Masa'd

Written by : Sawsan Amireh

Staging of cancer

Staging is the clinical or pathological assessment of the extent of cancer spread. It's important in determining the approach in treating any tumor regarding the surgical, medical and radiological management. It also provides a common language between different medical centers in assessing the tumor, and by that avoiding any subjectivity of a clinician or a pathologist in evaluating the extent of any cancer. Another advantage is that it provides a baseline used in the studies and researches of cancer by making comparing different cases of different sources much easier. **Clinical staging** is a preoperative assessment, it is based on clinical, radiological and operative information and is used to determine treatment offered to the patient. While **pathological staging** is a postoperative assessment and is the most accurate one.

Note: staging can b a coasty and painful procedure to the patient, so it shouldn't be done haphazardly, but planed in a systematic approach according to the physician's knowledge in the development and progression of different cancers. Ex: it is useless to look for metastases in the spleen, muscle and cardiac tissues, knowing that tumors are not likely to seed in these tissues.

Objectives:

-Provides useful prognostic information
-Allows decisions to be made regarding adjuvant therapy
-Allows comparison of treatment outcomes between different centers.

Staging should be a very accurate procedure. We use clinical, radiological and histological measurements in grading any tumor. Sometimes the outcomes of a histological staging can be different from the outcomes of either the other two measurements. Ex: you might examine a breast tumor and estimate that its diameter is 5.5cms, giving it a stage T3, while the ultrasound report shows that its diameter is 4.5cms, giving it a stage T2.

The ideal staging system

-Easy to use and remember
-Reproducible
-Not subject to inter or intra-observer variation
-Based on prognostically important pathological factors
- Uses a common language

TNM system

Based on the anatomical extent of spread , it is usually updated every 2 years. The abbreviation stands for:
-**T:** the extent of primary tumor (size)
-**N:** refers to the extent of nodal metastases (regional lymph nodes status)
-**M:** refers to the presence or absence of distant metastases

T refers to **primary tumor** as follows:

Tx: primary tumor can not be assessed
T0: no evidence of primary tumor
Tis: carcinoma in-situ (does not involve the mucous membranes)
T1-4: increasing size and local extent of primary tumor

Note: T0 doesn't mean there is no tumor, cause sometimes a patient might present to you with signs of metastasis and lymph nodes involvement without you being able to detect the primary tumor, that's because even a tumor that is only made of a million cells is capable of metastasizing.
Note: u should be able to differentiate between carcinoma in-situ and locally invasive tumor. Exs for carcinoma in-situ: Paget disease of the nipple is usually the presentation of carcinoma in-situ in the breast, Bowen's disease in the skin, erythroplasia of kerati (squamous cell carcinoma of the glans of penis)

N refers to **regional lymph nodes** as follows:

Nx: regional lymph nodes can not be assessed
N0: no regional lymph node metastases
N1-3: increasing involvement of regional lymph node

M refers to **distant metastases** as follows:

Mx: distant metastases can not be assessed
M0: no distant metastases
M1: distant metastases present

The TNM system is generally accepted although does not record all factors (e.g. grade, contiguous organ involvement) which are prognostically important.

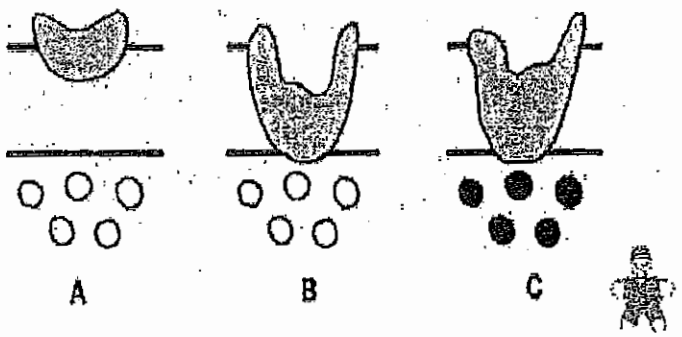
Dukes staging of colorectal cancer

It was first published in 1932 for rectal cancers, but now it is used for all rectal and colonic cancers.

Duke's A: spread into submucosa but not through muscle
Duke's B: spread through muscle but nodes negative
Duke's C: lymph node metastases present .Often divided into **C1** and **C2** dependening on the involvement of the highest lymph node.

Advantages of the Dukes classification are that it is:

-Simple and reproducible
-Accurately reflects prognosis
-Accepted worldwide



"تمت بحمد الله"

بسم الله الرحمن الرحيم

Lecture topic: Principles of cancer management
Lecturer : Dr. Jamal Mas3ad
Written by : "Mohd Amin" Ramzoon

Principles of cancer management

The objectives of surgical management of cancer are cure and palliation.

Tumors in our country are discovered a bit late. That's why palliative care is established to CONVERT a lethal disease (like breast cancer) to a chronic disease. The disease is living in the patient but the patient is coping.

WHAT is the role of the surgeon in cancer management?

- Diagnosis
- Prevention
- Treatment of primary tumor
- Resection of metastasis → improve quality of life and prolong survival
- Management of oncological emergencies
- Surgery for palliation
- Surgery for residual disease Surgery for reconstruction
- Cytoreduction
- Regional chemotherapy

FNAB (fine needle aspiration biopsy). They used to be afraid from FNA in the past, because they thought the cells from the tumor will go along the tract (made by the needle) and this will worsen the behavior of the tumor and the condition of the patient. NOW the studies proved that there is no harmful impact from using the FNA. RECENTLY the use of the FNA is becoming more common and feasible because of the emerge of GUIDED FNA, using the ultrasound or CT scan. We must give the site from where the biopsy was taken to the pathologist to in order to get the right picture.

SO the FNAB can be applied to any area in the body EXCEPT at 2 sites:

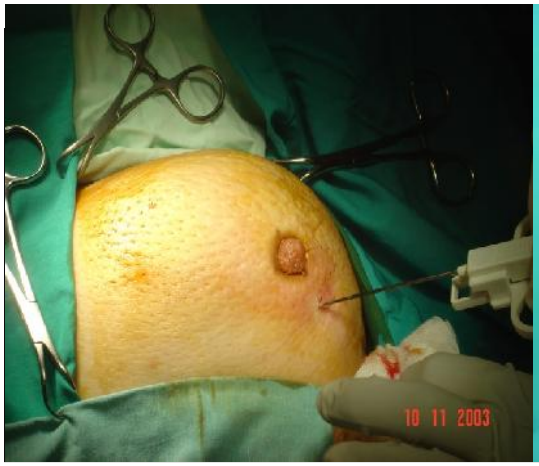
1- *PAROTID*: if we suspect a mass and in FNA it was found to be a benign tumor called Pleomorphic tumor, this tumor can propagate along the tract made by the needle.
2- *TESTIS*: to approach the testis, the surgeon should come from the scrotum. The lymphatic drainage of the testis (para-aortic LNs) is different from

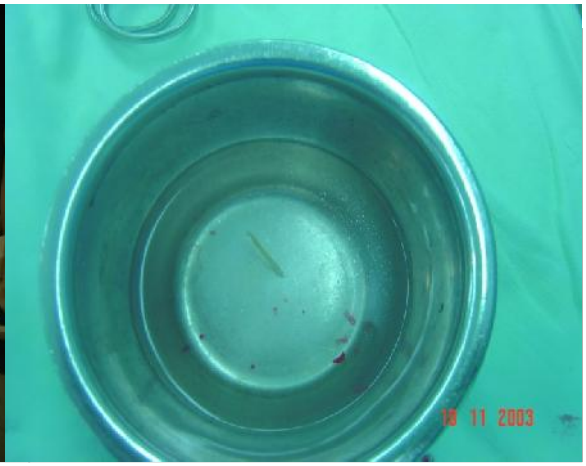
that of the scrotum (inguinal LNs). So probably while taking the FNA, some tumor cells will implant in the scrotum.

The Disadvantages of FNA:

1- It doesn't give us histological diagnosis, it gives only **cytological one**. So we can't find the stage or the grade of the tumor. I can't find if the tumor is in-situ or invasive. So we can't depend on it when there is a need to implement a major management.
2- It has a false positive and a false negative results. So if I did FNA in a suspected mass and I found it negative against my expectations, I consider myself as if I hadn't done it at all. **IT'S a good positive test but it's a bad negative test.** (false positive test can result from lab errors like fixation of cells is not good, the number of cells are not enough or the cells are dying or shrinked …etc, but this result is not critical as the false negative. The doctor are from the surgeons who don't depend on the FNA results to do mastectomy, he prefers to do tru-cut biopsy first. But he can do wide local excision.

Tru-cut biopsy gives histological diagnosis. It must be done under mammogram, CT scan or computer guidance.





OSCE:

- What are the malignant features (clinical signs)?

1- Retraction of the nipple
2- Peau'd orange

- What is the investigation done?

Tru- cut biopsy

Incisional biopsy means that we make incision through a suspicious mass, we don't remove the whole mass but part of it. Rarely used except in special circumstances where we must avoid big surgery, and when tru-cut biopsy is not suggested eg. If there is a mass in the floor of the mouth. and you

are suspicious if it's benign or malignant then you remove it with safety margin, you will remove 50% of the tongue with it and finally you discovered that it's benign (this is a bad thing!!) so you better make incisional biopsy (small peace of tissue for histopathology) **{{NOTE: in case of ulcers, you don't take from the floor because it's necrosed, you better take from the edge}}**. Incisional biopsy give us bigger amount of tissue that we can use not only for histological diagnosis, but also for responsiveness for chemotherapy and radiotherapy.

(NICE POINT): Our dear dr. said that taking incisional biopsy and leaving the tumor in its place is better than removing the tumor without safety margin then after reaching the diagnosis return back to remove the remnants of tumor with confusion that where the safety margin should be now.

Excesional biopsy (THE MOST COMMON PROCEDURE DONE) must be done with safety margin (The best oncological procedure is done when you don't see the tumor (it remains inside the safety margin and you don't see it). We don't go directly to the site of the tumor, but we go around it). The distance we take as safety margin depends on behavior **(TYPE) of tumor** (more invasive, longer safety margin) as well as the **SITE of tumor** (under the eye not like the lower limb).

Surgery for Prevention:

It means that we don't allow the tumor to come to the site.

Eg. Female patient has high incidence to develop breast cancer (family history, BRCA1 BRCA2, age …etc) we may offer her to do surgery to remove the target tissue and thus prevent cancer to occur (this approach is not agreed upon between different surgeons).

Another eg. Patient with Undescended testis has higher incidence of malignancy, if we neglect it or miss it they have higher incidence to develop cancer (this approach is also not agreed upon because some physicians say that these patients have undescended testis have this problem because of the already formed genetic abnormalit, so even if we do orchoidectomy they will have the same percentage of malignancy. Also if it's bilateral we can't do orchoidectomy)

Another eg. Is familaial adenomatous polyposis in which there are multiple familial (inherited) polyps (adenomas) that will be malignant in age of 40, so we don't wait until they become malignant to remove them, we intervene early and resect the colon. (Some say we remove the whole colon (total colectomy) and make ileostomy. Others say we do subtotal colectomy and

sparing the rectum which is not involved in this disease, also because the rectum is v. imp. in keeping the continuity of the GI tract)

Another eg. Is patients with ulcerative colitis. These patients are known to have much higher incidence to develop colon cancer more than others. We must treat these patients and follow-up them strictly (usually by colonoscopy and taking biopsies) and if they are proved to have severe dysplasia we offer them to have surgery to prevent colon cancer development.

When female patient, who is screened and found to have high incidence to develop breast cancer, is coming to you and you suggest her to do prophylactic mastectomy.

Now there are many problems that both of you must deal with:

1- Cosmetic problems (Removing the whole breast is non-human you can deal with it by doing incision removing the contents of the breast and sparing the skin, and later replace the contents by flaps, synthetic materials…whatever)
2- Psychological problems (esp. if the patient is still young)
3- The most imp. point is that YOU DON"T GARAUNTEE THE RESULTS (there is no 100% removal of the breast tissue (you can't do it)), but you decrease the risk dramatically.

YOU AS ONCOLOGICAL SURGEON MUST KNOW YOUR DIMENSIONS, LIMITATIONS, ADVANTAGES AND DISADVANTAGES. YOU MUST EXPECT COMPLICATIONS AND KNOW HOW TO DEAL WITH THEM.

Terms that you must know

The modern oncological surgery now go towards the term ADEQUATE SURGERY. In the past they used to remove the whole breast with the underlying muscles, lymph nodes and maybe the ribs in a procedure called Radical mastectomy. There were another terms like simple, total, subtotal, modified radical, but know they perform adequate surgery which can be any level between these terms according to the grade and stage of the tumor. Safety margin also depends on your expectations.

Remember destruction is easy but construction is important. In case of recurrent laryngeal cancer, they must do central neck dissection to remove the central neck compartment, where they remove larynx, pharynx, upper trachea…etc. In the past there was no reconstruction, thus the carotids will remain visible (exposed to environment) and with time they will dry and stiffen and then they will blow out. Now they have the ability to do RECONSTRUCTIVE SURGERY that go hand with hand with destruction.

WIDE LOCAL RESECTION: removing the tumor with a safety margin. Differ from tumor to another.
Eg. MELANOMA IS MAINLY TREATED BY SURGERY
Non invasive superficaial melanoma → 1cm safety margin
Invasive nodular melanoma → 3-5cm safety margin

In Mid rectum cancer treatment, they used to do abdomino perineal (AP) resection in which they remove the whole colon and anal canal and leaving the patient living with colostomy. Then they found that the most distal point doesn't descend down more than 1-2cm, so if the tumor is far from the anal canal by 5cm and the anal canal it self is 4cm, so rather than AP they can do RESTORATIVE SURGERY where they can resect the involved part with safety margin and at the same time restoring the continuity of the GI tract.

LOCAL RESECTION:
Eg. Basal cell carcinoma (BCC) in the face. Surgeons prefer to avoid deformities here. So they remove with safety margin 2-3mm, and if it happens that one of the safety margins recur later, surgeons return and do another local resection. This happens firstly due to the site of the cancer, secondly due to the less invasive behavior of BCC where I can have time to keep tissue.

RADICAL LOCAL RESECTION:
Eg. Patients with soft tissue sarcoma in their extremities just above the knee and the knee is spared. Chance of recurrence local without safety margin > local with safety margin > amputation.

Now what do you think is better as adequate surgery, amputation or compartment excision (where we remove the compartment of the extremity containing the tumor)?
The answer is compartment excision, because in amputation we can have tumor cells spreading through the compartment planes and still there is chance of recurrence. But if you remove the whole compartment we can have better results.

EN-BLOCK EXCISION:
When we remove the tumor and the whole lymph nodes drainage
Eg. Inguinal block dissection (inguinal LNs with scrotal melanoma)
Eg. Axillary block dissection (axillary LNs with breast cancer)

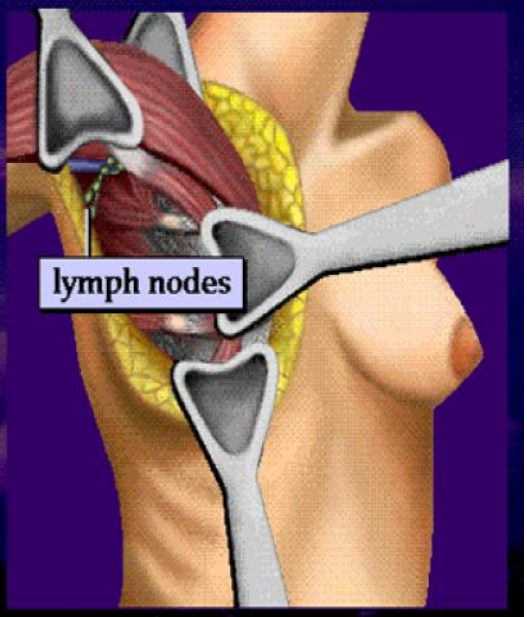
LUMPECTOMY as a term it means to remove the lump only. It's not enough for malignant tumor because it's done without safety margin. But for a benign tumor like fibroadenoma it will be enough.

Total mastectomy (Simple mastectomy)

In total mastecomy the entire breast tissue is removed.

It is similar to modified radical mastectomy except that the lymph nodes in the armpit are not removed.

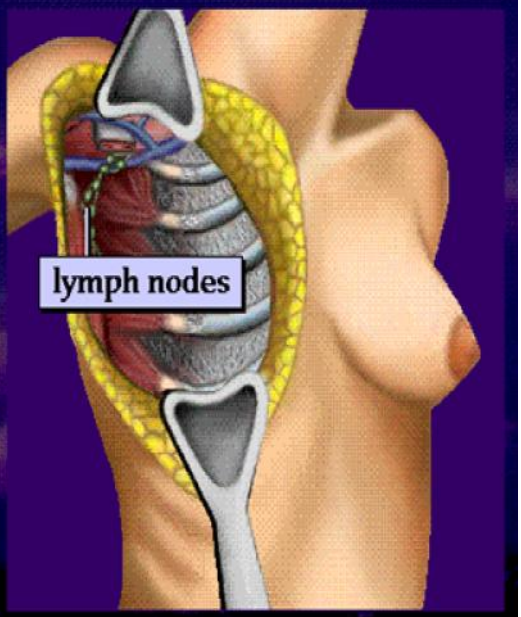
Total mastecomy is often recommended in early noninvasive cancers or when the mastectomy is being performed as a preventative measure.

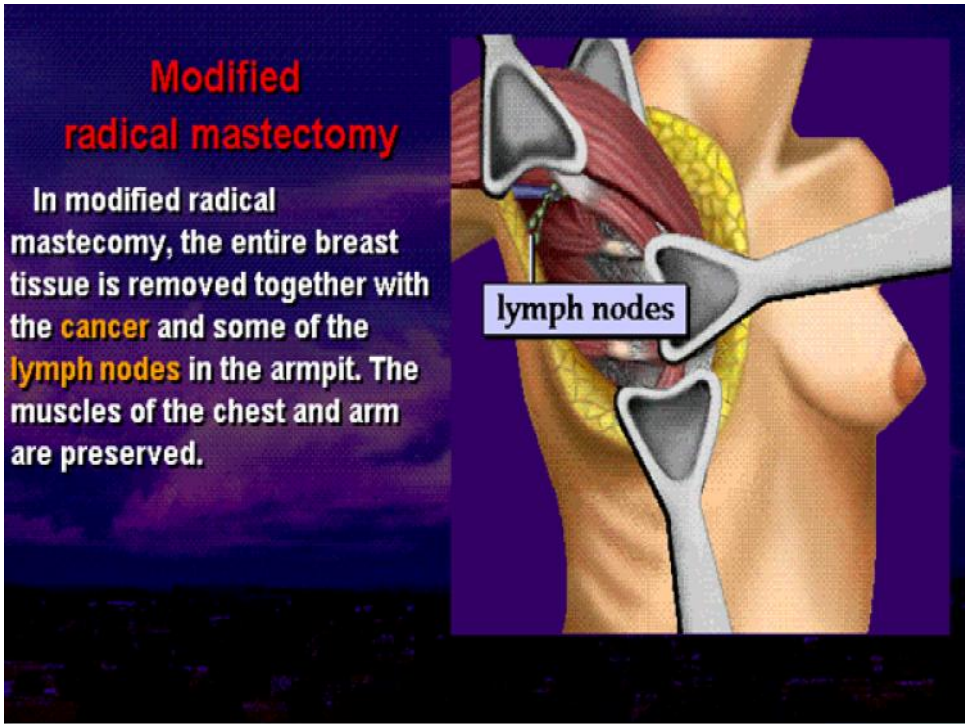


Radical mastectomy

In radical mastecomy the muscles of the chest (e.g., pectoralis major and pectoralis minor) along with the breast and lymph nodes are all removed.

Radical mastecomy is now rarely performed. It is usually reserved for very large cancers that have grown into the muscle.





Surgery for residual disease:

After Neoadjuvent chemotherapy
After radiotherapy
After inadequate surgery

Done after the response found not to be 100% or there was no response.
Complete response → 100% disappeared
Partial response → 50%-99% reduce in the size
No response

But note: If the patient receives chemotherapy and the tumor remains stable in size (appear as no response, but actually it's not), this is an indication to remain on chemotherapy.

NOTE: soft tissue sarcoma is one of the tumors that is highly vascular, we do radiotherapy first to shrink the tumor then we do surgery.

NOTE: in burkitt's lymphoma where the main line of treatment is chemotherapy, if there was a large mass, in the neck for example, we can remove it by surgery but we must start the chemotherapy as fast as possible because there will be large volume of the tumor cells that are going to be destroyed and the end product of dead cells will make many problems to the patient on the top of them is tumor rising syndrome.

NOTE: In ovarian cancer where the main line of treatment also is chemotherapy. If it's localized it's enough to treat with chemotherapy. But if the mass is large extending to the peritoneum and pelvis making multiple metastasis to the liver pancreas…etc, in the past they were think that this is incurable, but now they remove the large masses and leaving the masses less than 2cm to be dealt with by the chemotherapy. SO CYTOREDUCTIVE SURGERY TRANSFORM THE INCURABLE CANCER TO CONTROLLABLE CANCERS.

Surgery for Metastatic Disease

metastases to: **lung, brain, liver.**

Pulmonary metastases The resection of in patients with soft tissue and bony sarcomas can cure as many as 30% of patients.

Solitary hepatic .In patients with metastases from colorectal cancer, resection can lead to long-term cure in about 25% of patients

The resection for cure of solitary brain metastases should also be considered when the brain is the only site of known metastatic disease. The exact location and functional sequelae of resection making should be considered when this treatment decision.

SURGERY FOR ONCOLOGIC EMERGENCIES

Hemorrhage

Abscesses

Perforation eg. gastrointestinal Perforation of the tract after effective treatment for lymphoma

Eg. Neurological symptoms due to compression of bone metastasis on the spinal cord after breast cancer. Central nervous cancer invading the system represents another surgical emergency that can lead to preservation of function**.**

"تمت بحمد الله"

BIOLOGY AND PRINCIPLES OF RADIOTHERAPY AND CHEMOTHERAPY IN CANCER MANAGEMENT

Dr. JAMAL MAS'AD MAZEN AL-MANSOUR

RADIOTHERAPY

DEFINITION: Radiotherapy is the use of ionizing radiation in the treatment of malignancy. Radiotherapy is a way of locoregional treatment of cancer.

TYPES OF RADIATION: The radiation may be in the form of:

- X rays: these are generated from an electric machine and they are classified according to the level of penetration into:
  - ✓ superficial X rays which cause minimal penetration and are useful for superficial tumors.
  - ✓ deep (orthovoltage) X rays.
  - ✓ supra or megavoltage X rays: these are the X rays in clinical use.
- Radioisotopes:
  - ✓ α rays (little value)
  - ✓ β rays: used for superficial lesions
  - ✓ γ rays: generated by the telecobalt machine. These are the most widely used clinically.
- Fast particles: these are parts of the atom. They are of little clinical value.
  - ✓ electron: also used for superficial lesions(e.g: squamous cell or basal cell carcinoma of the skin or in breast cancer or soft tissue sarcoma in order to radiate the bed of the tumor or the scar of mastectomy and so on...)
  - ✓ neutron
  - ✓ proton

MODE OF ACTION: The mode of action of radiotherapy is to ionize the water in tissues leading to the production of free radiacals which may cause a reversible or an irreversible damage to the cells. The aim of radiotherapy is to produce an irreversible damage to the genome of tumor cells so that when they are stimulated to proliferate they will be unable to multiply. This also explains the phenomenon that wound healing is impaired in irradiated sites. This is due to the permenant damage to the cells responsible for wound healing process.

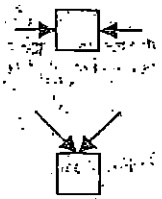
TECHNIQUES OF RADIATION:

- External:
  - ✓ Single or direct beam: the problem here is that the radiation will pass all the way from the skin to the tumor and by this it won't affect the tumor only.

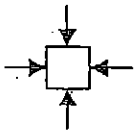
✓ Opposed pairs: This technique is used to minimize the effect of radiation on the surrounding tissues by using two beams from two different sites and at the same time concentrating the radiation in the center of the tumor. Two methods can be used:

i. direct

ii. tangentional



✓ Multiple beams with convergance: This can be used for example in the treatment of a deep seated brain tumor which can not be excised surgically. Here a single beam radiation will cause a lot of collateral damage. So the patient is asked to wear a helmet which has multiple holes from which multiple beams of radiation pass and reach the center of the tumor without causing much injury to the surrounding tissues. This is what is called the γ knife.



- Brachy therapy (interstitial therapy): small sealed source of radium is implanted in the center of a tumor. This also causes minimal surrounding tissue damage with concentrated effect in the center of the tumor. This is used in breast cancer, head and neck cancers, retroperitoneal cancers and soft tissue sarcomas. In Jordan this technique is used in the treatment of cervical carcinoma.
- Injectible form radioactive iodine in the treatment of thyroid malignancy and radioactive phosphorus in the treatment of polycythemia.

DOSE FRACTIONATION: In order to decrease the effect of radiotherapy to the surounding tissues another technique is used, **dose fractionation.** For example, instead of giving 5000 rads (50 grays[1]) over a period of 1 week they can be given over a period of 6 weeks with a dose of 200 rads daily (giving a break at the weekends). This method is also used in order to expose the cells within the cell cycle (this was written in the sheets but I didn't understand it). Hyper- or hypofractionation can be used. Hyperfraction is the use of a large number of small doses. An example of hyperfractionation is giving the dose over 6 weeks twice daily including the weekends. Hypofractionation is the use of a small number of large doses.

[1] 1 gray=100 rads

EFFECT OF RADIOTHERAPY ON NORMAL TISSUES:

- Skin and mucous membranes: the skin resembles a second degree burn, with erythema, blistering, itching, desquamation, ulceration with oozing surface and tissue destruction. It also affects mucous membranes, for example, radiation to the head and neck causes severe stomatitis and dysphagia. Radiation of the abdomen affects the GIT causing bloody diarrhea (gastroenteritis). Skin and mucous membranes are highly susceptible because they are composed of highly proliferative cells. The extent of damage caused by radiotherapy depends on the ability of the radiotherapy to produce sclerosis or thrombangutis obliterans. The late effect of radiotherapy include skin and mucous membrane atrophy, with telngiectasia and dry skin. This is why we can identify irradiated axilla from its dry appearance due to atrophy of adnexal structures. Cystitis and pneumonia may also result.
- Brain atrophy, lung fibrosis, cardiac toxicity, fistulae and strictures.
- Impaired healing
- Malignancy.

INDICATIONS OF RADIOTHERAPY:

- Priamry treatment: As a single modality. The classical example is stage I lymphoma. Also small skin tumors, e.g. basal cell carcinoma which is highly sensititve to chemotherapy.
- A part of multimodality treatment.
- Symptomatic treatment: For the treatment of symptoms. E.g. patients with a tumor and bone metastasis having severe pain. The best line of treatment of these patients is radiotherapy.

[Dr. Mas'ad presented a data show. Many photos were presented but I could not include them in this lecture. The data shows are available at the yahoogroups site for those who are interested. Here is what Dr. Mas'ad talked about them:

- Simulation room: This room has a simulation machine in it. Here the patient, his treating physician and the radiotherapist meet after having done a CT scan or an MRI and lay down the radiotherapy plan. They determine the radiotherapy field, the degree of penetration and how they can spare tissues. They may even construct a mask for the patient in order to protect the normal tissues. For example if the maxilla is to be irradiated a mask can be constructed to protect the eyes.
- Radiotherapy field: the area to be irradiated is lined out by a permenant marker (tattooing).]

CHEMOTHERAPY

INDICATIONS:

- Primary treatment: especially for tumors with high growth fraction, reaching 100% such as leukemias and some types of lymphomas.
- A part of multimodality treatment
- Adjuvant and neoadjuvant chemotherapy: **Adjuvant chemotherapy** is the chemotherapy that follows the primary treatment. For example, if a tumor has been excised surgically, adjuvant chemotherapy aims to eliminate undetected micrometastases. **Neoadjuvant chemotherapy** precedes the primary management. Here the neoadjuvant chemotherapy aims to decrease the size of the tumor. This consequently decreases the stage of the tumor **(downstaging)**. This may enable sparing of organs (conservative surgery) and it may also transform the unmanageable cases to manageable ones.

CLASSIFICATION OF CHEMOTHERAPEUTIC AGENTS:

- **According to the cell cycle:** The concept of chemotherapy depends largely on cell cycle principle. The cell cycle begins by the G_0 phase then the cells enter G_1, S, G_2, M and back to G_0 and G_1. Therefore, chemotherapeutic agents are classified to:
  - ✓ Cycle and phase non specific: these can work even on cells in G_0, such as nitrosureas and nitrogen mustard[2].
  - ✓ Cycle specific: these work on different phases of the cell cycle but do not work on G_0, such as adriamycin and cyclophosphamide.
  - ✓ Phase specific: these work in a certain phase of the cell cycle only, such as vinca alkaloids and methotrexate (MTX).

- **According to their chemical structure:**
  - ✓ Alkylating agents: these carry an alkyl group, which is an electrophilic group. Examples include cyclophosphamide, mustine, chlorambucil and ifosfamide[3]. Alkylating agents work by alkylating the DNA of cells and causing their damage in a certain mechanism such as breakage of cross linkages or prevention of seperation. Another mechanism of action was discovered recently for some of these alkylating agents other than their action on DNA. These agents cause damage to cell membranes as well by blocking the sodium potassium pump.
  - ✓ Antimetabolites: such as 5-fluorouracil (5-FU) which attacks the enzyme thymidylate synthetase, MTX which attacks the enzyme dihydrofolate reductase, 6-mercaptopurine and cytosine arabinoside.
  - ✓ Antibiotics: the most famous agent is adriamycin (doxorubicin) which is the best chemotherapeutic agent for the treatment of solid tumors. It works by inhibiting DNA and RNA. It prevents the seperation of the two strands of DNA. Adriamycin attacks a substance called cardiolipin present in the mitochondria of many cells in low amount. Cardiolipin in present in high concentrations in malignant cells, this explains its high effectiveness. Unfortunately, cardiolipin is

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[2] Nitrogen mustard is a toxic gas that was used in the chemical warfare in world war two. It was noticed that leukemic patients improved dramatically after being exposed to this gas. Further sutdies proved that nitrogen mustard can be used as a chemotherapeutic agent.

[3] Ifosfamide is one of the major drugs used in the treatment of soft tissue sacromas. It has many complications.

present in high concentrations in cardiac muscle cells as well explaining its cardiotoxicity. The toxic effect of adriamycin on cardiac muslce cells is cumulative. This means that there is a maximum dose of adriamycin that can not be exceeded.

Other chemotherapeutic agents that belong to the antibiotic family include bleomycin which is useful in the treatment of testicular and skin cancers. However, it has a very bad complication since it causes pulmonary fibrosis. Another antibiotic chemotherapeutic agent is mithramycin.

- ✓ Vinca alkaloids such as vincristine. These attack the mitotic spindle which has a role in seperating the chromosomes during mitosis. That is why they are called spindle poisons.
- ✓ New generation drugs.

PHARMACOLOGICAL PRINCIPLES:

- Anti-cancer drugs can be administered intra-arterially (regionally) where the drug is administered to the tumor's feeding artery to reach its maximum concentration in the tumor region. They can be also administered intravenously and topically (ointement). Drugs may be attached to antibodies specific for the tumor cells. A new trend is the use of **'smart drugs'** which are inactive agents that are activated only inside malignant cells[4].
- The dose is calculated depending on the surface area (m^2).
- Most anti-cancer drugs have a narrow therapeutic range (i.e. the toxic and therapeutic doses are close to each others).
- In some tumors dose escalation is feasible and in others it is not. So it is an area of controversy.[5]
- In the past continuous infusion of anti-cancer drugs was performed, recently pulse therapy is followed. In the later the drug is given in several doses every 3 weeks. By this it allows bone marrow cells which are affected (but not tumor cells) to regrow minimizing the adverse effects of chemotherapy.
- The recent trend is to use multiple drugs rather than one drug. An example is the CAF regiment for the treatment of breast cancer, where C refers to cyclophosphamide, A to adriamycin and F to 5-FU. This yields better results since each drug works in a different way to give better results.
- Chemotherapeutic agents kill tumor cells by following first order kinetics. This means that a certain dose kills a certain *fraction* of tumor cells rather than a certain *number* of tumor cells. This is called the **log cell kill hypothesis.** So if a tumor that contains 10^6 cells ($1mm^3$ in size) was treated by chemotherapy the results will be as shown in the table.

[4] An example of a smart drug is the oral anti-cancer agent xeloda (capecitabine) which is a precursor of 5-FU that is activated only inside the malignant cells.

[5] Dose escalation means increasing the dose.

course	% of original cell that have been killed since the beginning	remaining number of cells
0	0	10^6
1	90	10^5
2	99	10^4
3	99.9	10^3
4	99.99	10^2

RESPONSE OF TUMORS TO CHEMOTHERAPY:

- Tumors potentially cureable by chemotherapy:
  - ✓ Acute lymphoblastic leukemia
  - ✓ Germ cell tumors
  - ✓ Choriocarcinoma
  - ✓ Hodgkin's disease
  - ✓ Wilm's tumor
- Tumors with significant response to chemotherapy:
  - ✓ Breast cancer
  - ✓ Ovarian cancers
  - ✓ Lymphoma
  - ✓ Osteosarcoma
- Tumors poorly responsive to chemotherapy:
  - ✓ Pancreatic carcinoma
  - ✓ Melanoma
  - ✓ Soft tissue sarcoma
  - ✓ Colorectal carcinoma
  - ✓ Gastric carcinoma

SIDE EFFECTS: The side effects of chemotherapeutic agents are classified into general side effects and specific side effects.

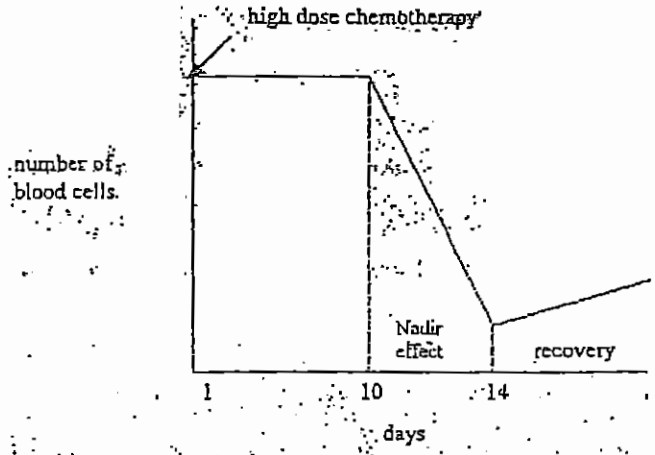
1. General side effects: these result from the cytotoxic effect of anti-cancer drugs on highly proliferative tissues in the body such as: hair follicles, bone marrow, GI mucosa and ovaries. Common examples of the general specific effects include:

✓ Allopecia: due to the toxic effect on hair follicles. This is a continuous reminder of the patients and their relatives of the disease.

✓ Nausea and vomiting: due to the central effect of anti-cancer agents on the chemoreceptor trigger zone (CRTZ). Allopecia and nausea and vomiting are the most annoying side effects.

✓ Amenorrhea: due to the toxic effect on the ovaries. In women approaching menopause amenorrhea caused by chemotherapy may be premenat and cause early menopause.

Low blood cell count: due to the toxic effect on bone marrow. Here comes the role of pulse chemotherapy in minimizing the effect on bone marrow. See the figure.



2. Specific side effects:
   - ✓ Pulmonary fibrosis: bleomycin
   - ✓ Renal failure: cisplatin. That is why good hydration is required.
   - ✓ Hemorrhagic cystitis: Cyclophosphamide and ifosfamide. The hemorrhagic cystitis actually results from their metabolite acrolein. Acrolein can be chelated from the body by a substance called MESNA (mercaptoethane sulfonate). Thus administration of MESNA with cyclophosphamide or ifosfamide reduces their toxicities.
   - ✓ Cardiomyopathy: adriamycin
   - ✓ Hepatocellular damage: MXT.
   - ✓ Skin pigmentation: 5-FU.

Breast examination

Before you start the routine physical examination (inspection, palpation, & (L.N) Lymph node examination. Make sure of the following;

1. Privacy of the atmosphere.
2. the presence of good illumination.
3. witness, if the examiner is ♂.
4. exposure of the upper half of the body (to the waist)

Breast examination should be done with the patient in both the sitting & supine position. Care must be taken all the time to be gentle.

Inspection

(A) The breast should be inspected initially while the patient in the sitting position with the arms relaxed

- inspect both breasts to compare.
- inspect for

- Size, Shape, & symmetry

if a size discripancy is noted, Its chronicity should be determined. Many women's breasts R identical in size & the finding of small discripancies is rarely a sign of malignancy. Differences in breast size that R of recent onset or progressive in nature, However, maybe due to both benign & malignant disease & require further evaluation.

Look at any abnormality or bulge in breast contour. Alteration in the breast shape in the absence of previous surgery R of more concern.

- Skin changes Inspect for Scars, dilated veins, ulceration, erythema, edema (peau d'orange), discoloration, nodules, puckering tethering or retraction of the underlying skin

- Nipple & Areola

→ Should include symmetry & Changes. Remember the 7D's (Destruction, Depression, Discolouration, Displacement, Deviation, Discharge, & Duplication)

* Depression = Retraction or inversion
* Duplication = the presence of accessory nipple along the mammary line. or ectopic tissue in the axilla

* about the nipple you may see
  - eczematous changes ⟶ as in Paget's Disease.
  - bilateral inversion & displaying transverse slit pattern ⟶ duct ectasia
  - colour ⟶ change with age
    ↘ darkens during Pregnancy.
* In the areola, you may see Montgomery's tubercles; These R_normal finding - small nodules in the corrugated skin of the Areola.

Ⓑ After inspection with the arms relaxed, The patient should be asked to raise her Arms to allow a more complete inspection of the lower half of the breasts

→ this may exaggerates asymmetry & skin tethering
But if the patient is > 60 yrs old, it is a punishment. So do it as fast as possible

Ⓒ Inspection is completed with the patient contracting the pectoral muscles by pressing her hands against her hips.

→ this may reveal a previously invisible swellings.

Ⓓ Inspect the axilla, arms, & supraclavicular fossa (enlarged LN - dil. veins - arm lymphedema

Palpation

according to students with Dr Jamal
(supine - with her hand behind her head - tilting to the opposite side)

Position the breast is palpated with the patient ~~sitting up at 45°~~
(In my notes the Dr said; In supine position with a pillow under her neck)

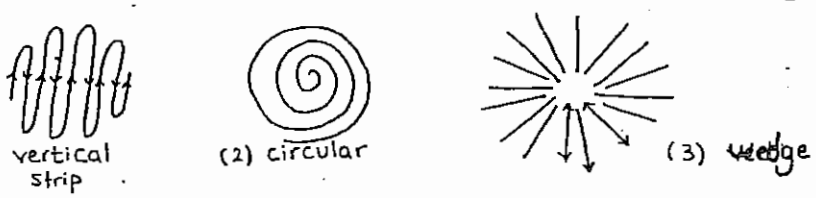
- In patients with large breasts, it maybe necessary to tilt herself to the opposite side (to enable the examiner to palpate her breast against the chest wall)
- when the patient elevates her arm, Part of the upper outer quadrant & the axillary tail will enter the axilla so we ~~lose~~ loose the chance of examining that part, while the medial part will be stretched & thinner so it will be palpated better.
  i.e when examining the Medial part ⟶ arm above the head.

when examining the lateral part ⟶ the arm should be beside the patient

How to feel?

- using the palmar aspect of the fingers (Middle 3 fingers) & not with the palm of the hand - Fingers R more sensitive-
- pinching is bad. Pinching breast tissue between fingers always results in the perception of a mass & is a common error of inexperienced examiners & women attempting self examination.
- palpation should be against hard object (chest wall).
- It is better with the wrist flexed or at rest but not extended.
- with gentle rolling (topography) & dipping (consistency) with variable pressure.

Where to start & where to end? ⇒ there are many patterns :-



(1) vertical strip (2) circular (3) ~~wedge~~

- The breast tissue is then systematically examined. Whethe the examination is done using a wedge pattern or vertical strip pattern is unimportant, provided that the entire breast is examined. But studies have shown that Vertical strip is the best.
- The whole breast area should be examined (2^{nd} - 6^{th} rib & endge of sternum - midaxillary line). Remember that we R examining the breast Area not the breast mount.

Palpate the following

whole breast area, Nipple, Axillary tail, & the Axilla (for LN)

- begin with the normal side or face the patient & feel both breasts
- feel the texture of the breast, it is enormously variable more than any other organ, depending on age, parity, body mass & hormonal activity

So the texture of the breast maybe → quite soft & apparently featureless
→ firm & fibrous, with easily palpable nodules (= normal lobules)
→ (or) engorged & tender (in menstruating woman)

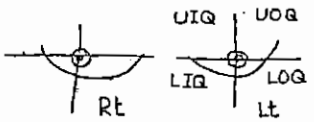
because the breast is glandular tissue, this will give it nodular feeling on palpation. This is more apparent in premenopausal women.

- Don't forget palpating the subareolar area. This area has no glandular tissue.

- feel the axillary tail → this is maybe obvious in a slim woman with firm breast tissue.
  ↓
  occasionally may seem to be separate from the main breast & so presents as an apparently axillary swelling.

Notes

- If you find any lump, ascertain its site, shape, size, surface, edge & consistency, as with a lump in any other area of the body. All this should be described in the medical record.
- It is very important to register what you find & you should draw the topography for future reference
- even if you still cannot feel the lump that patient can feel, take the symptom seriously & arrange further investigations or reexamination.



Nipple

- by gentle squeezing the inverted Nipple maybe everted (if not everted, there is likely underlying disease)
- by gently pressing the areola around the base of the nipple, observe if any discharge (red, white, creamy yellow or watery)

Axilla For LN examination

The axillary lymph glands form 3 sided pyramid, whose Apex is in the narrow gap between the first rib & the axillary vessels

- the right axilla is examined with the physician's left hand while the patient flexed right is supported by the examiner's Right hand. this allows the pectoral muscles to be relaxed & access to the axillary space. (Lt axilla → opposite
- Do the following to examine each group of LN's

* LN of the central & medial side of axilla → by sweeping the tip of your fingers across & from the top to the base of the axilla to catch the glands against the chest wall
* Apex of the axilla → Push the tips of your fingers upward & inwards. explain to the patient that you must push firmly & this may cause discomfort
* axillary tail → Move anteriorly against the edge of pectoralis minor & downward behind the edge of pectoralis major
* Subscapular LN → posterior wall of the axilla.
* lateral aspect of the exilla

-4-

* Finally palpate supraclavicular fossa & the neck

General examination

Check

- the Arms → for swellings or any neurological or vascular abnormalities
- the Abdomen → hepatomegaly, ascites.
- lumbar spine → pain or restricted movements

the END

That's all I could do for a subject with no cassette & with poor little notes (the lecture was not recorded). So I had to create something from nothing. Most of the informations R from BROWSE (b17rf).

Good luck in the exams.

Thanx

Your Sister;

Alaa Abu-hijleh

ادعولنا

من كلمات المفكر الاسلامي "الشهيد سيد قطب "
الذي أعدم بعد رفضه الاعتذار عن كتاب ألفه
بعنوان "معالم على الطريق"

"ما احوج المسلمين اليوم إلى من يرد عليهم إيمانهم بانفسهم وثقتهم بماضيهم ورجاءهم في مستقبلهم ...وما أحوجهم لمن يرد عليهم إيمانهم بهذا الدين الذي يحملون اسمه ويجهلون كنهه ،ويأخذونه بالوراثة اكثر مما يتخذونه بالمعرفه...إن الاسلام دين عقيدة استعلاء ،من أخص خصائصا أنها تبعث في روح المؤمن بها احساس العزة من غير كبر ،وروح الثقة في غير اغترار ،وشعور الاطمئنان في غير تواكل . وأنها تشعر المسلمين بالتبعية الانسانية الملقاة على كواهلهم ،تبعية الوصاية على هذه البشرية في مشارق الارض ومغاربها ،وتبعية القيادة في هذه البشرية وهدايتها إلى الدين القويم والطريق السوي،واخراجها من الظلمات إلى النور بما آتاهم الله من نور الهدى والفرقان ..."

بسم الله الرحمن الرحيم

Written by: Saba' A. Jarrar
Lecturer: Dr. Jamal Mas'ad

Surgery
Breast Diseases

> Presentation of breast diseases include:
1. breast pain.
2. breast discharge.
3. breast mass.

> Breast pain:
- Called mastalgia or mastodenia.
- It is of two types:
    1. Cyclical: related to menstrual cycle.
    2. Non-cyclical: not related to menstrual cycle.

▪ Cylical mastalgia:
- Some ladies don't notice the relationship between mastalgia and the cycle but if you dig deep in the history you can find the relation.
- The majority of patients coming to the breast clinics due to mastalgia, have cyclical related mastalgia.
- Premestrually, the breast is sometimes edematous, enlarged, tender, with some nodularity, (ya3ni there is an abnormality in the examination). These are physiological changes, they start a week or so before menses, and usually they decrease with the onset of menstruation, however, the residual masses could stay for a while, so when pt come after menstruation with a mass {it is not a real mass (the real mass is the one that is not related to cyclical changes)} the course of treatment is to assure them after exduding the presence of a real mass by the examination, the ultrasound or mammogram if the pt is >35yrs. If there is no real mass, we will wait, the mass either will disappear on its own (like the cycle related mass (physiological)), or it will be removed by surgery, or it is aspirated if it is a cyst.
  We wait for 2-3 cycles, if the mass persists, it should be investigated properly.
- This is repeatable, it occurs every 1, 2 or 3 months.
- The exact etiology and pathogenesis are not known.
- It has a relation with the hormonal climate of the pt. The most important hormone that is incriminated in this abnormal physiology is prolactin, sometimes it is one of the precursors of prolactin.
  Most of these pt's have normal prolactin level, but there is an increase in the sensitivity of the breast to prolactin or there is a decrease in the threshold to the normally circulating hormone.
  If prolactin is high, we should investigate why it is high (most of the time it is due to pituitary adenoma) to treat it.
- Some of ladies are heavy smokers, drink a lot of coffee, and eat lots of chocolates and sweets. These sources contain caffeine which originates from xanthine which is one of the substances in the prolactine synthesis pathway.

These ladies, after being diagnosed properly, should be assured that there is nothing to worry about, and they should decrease the uptake of xanthine derivatives.

- There are remedies to treat this condition, but these remedies are not effective in all pt's, we do stepwise plan for management, most of them should not use a drug.

  Some are given:

  - ✓ pyridoxine (vitamine B6)
  - ✓ evening prebrose oil: this contains essential fatty acids
  - ✓ sea weeds: it was used and it was ineffective in our pt's.
  - ✓ danazol: it was used in the past, it is a weak testosterone, it was successful but it had lots of side effects including hirsutism. Nowadays, it is used for endometriosis.
  - ✓ Antiprolactin e.g. palmedin, which is effective.
  - ✓ Oral contraceptives, especially progesterone.

  But these hormones relieve the breast problems but cause other problems.

  - ✓ Tamoxifen which is used in cases of malignancy.

Note from a question: simple analgesics can be used but usually they don't work. But they may help.

- Acyclical mastalgia:
  - may be caused by
  - ✓ huge breast, improper use of bra which is used for lifting the breast, heavy breast may induce back pain or kyphosis.
  - ✓ referred pain: due to osteoarthritic changes in the cervical spine, in this case the pain is in the breast, shoulder and arm...
  - ✓ abscess, infection or inflammatory process in the breast, e.g. periductal mastitis or lactational mastitis.
  - ✓ Thrombosis in the vessels in the breast area (Mondor's disease)
  - ✓ Osteoarthritis in the costochondral junction (Tietze's syndrome).

- Breast cancer can present with pain or an abscess, there may be central necrosis. In patients with breast abscess, it is drained and a biopsy is taken to exclude malignancy.
- These problems represent 50% of breast problems.
- The remaining 50% are:20% of breast problems represent breast cancers, 20% gross cyst, 5% fibroadenoma, 5% periductal mastitis, fat necrosis, sclerosing adenosis and chronic abscesses.

> How to distinguish between breast cancer, breast cyst and fibroadenoma?

age: fibroadenoma is in younger age group (2nd and 1st decade), breast cyst is in 3rd or 4th decade, breast cancer is in > 4th decadebut there are cases younger than that.

- Breast cyst: it is a big mass that is discovered early (appears and felt within 1 week), its size is as an egg, it is painful if the cystic pressure is high. Upon examination, it is ildefined mass but movable (less than fibroadenoma and more than breast cancer), we need to do fine needle aspiration. Usually the cysts are aspirated, but there are indications to remove the cyst, which are:
  - ✓ Recurrence.

- ✓ Incomplete removal after complete aspiration
- ✓ If there is solid component (either by clinical examination or ultrasound)
- ✓ Bloody con tents.

Fibroadenoma may mimic medllary carcinoma of the breast. In patients less than 20 years, if the fibroadenoma is less tan 1 cm, it may disappear spontaneously, but you should first confirm that it is fibroadenoma.

By this we have finished talking about breast diseases.

Diagnostic tools of breast cancer

There is the triple assessment:

- ✓ clinical assessment.
- ✓ mammograghy.
- ✓ Fine needle aspiration or true cut biopsy.

In some cases you may go in further investigations, e.g. when the mammogram is negative: it is –ve in 15% of breast cancer cases, also it is –ve if the patient is young (the breast is dense), so it is done to patients > 35 years.

We do MRI to patients whose mammogram is –ve or in case of recurrence.. in MRI we depend on the physical appearance of the mass and the pattern of dye.

Biopsy: fine needle aspiration, true cut biopsy, mammotom.

Staging of breast cancer

- Common organs of metastasis are investigated, which are bone, liver and lung.
- In some guidelines: CT scan is done for the brain, neck, chest, abdomen and pelvis. But this is not cost effective and the yield is not that much.
- International guidelines: we do:
  - ✓ Chest x-ray: high kilo-voltage x-ray.
  - ✓ Liver function test (LFT): if LFT is abnormal, especially the alkaline phosphatase, LDH and γ-GT, you do ultrasound.
    Some do ultrasound and alkaline phsphatase at the same time.

CT scan is only done if there is a puzzling tissue that appears in ultrasound or LFT.

- ✓ Bone scan:
  - It shouldn't be done routinely in the assessment of patients with breast cancer.
  - In stage I or II, you need to do 300-400 bone scans to demonstrate metastasis. Ya3ni, if the tumor is in stage I, the bone scan will be -ve, but it is done once as a base line and future comparison.
  - It is technetium phosphate scan; technetium is a radioactive material, it is reacted with phosphate which will be uptaken by the bone then it is detected by gamma camera (the area where technetium and phosphate are precipitated will emit radiation which will be collected by gamma camera on a computer and an image is constructed.

It is +ve in areas with increased vascularity which increases in cases of metastasis, inflammation, trauma, and osteoarthritic changes. So the bone scan is quite sensitive (any change in the bone will demonstrate increased activity of technetium in that area).

Bone scan is sensitive but not specific

Changes in bone scan appear 6 months before x-ray[1]. In this case the patient has no history of trauma or fracture at the site of increased activity; also the bone metastasis occurs in axial skeleton and in more than one site, so there will be increased activity in the ribs, cervical spine, hip, proximal femur or shoulder

✓ PET scan:

It is positron emission topography scan. Positron is a radioactive material that depends on the presence of glucose, glucose is needed for all active tissues including the malignant tissue. It is recent and can demonstrate metastasis and recurrence, and it is good for monitoring the response to the treatment.

✓ Tumor markers:

- They are important in diagnosis of breast cancer.
- They are : $CA^{15.3}$, CEA.
- They are important in monitoring the response to treatment and in detection of recurrence of the tumor.

Management of breast cancer

- Surgical management:

It is the first management.

In the late 19th century, a surgeon called Holstred (not sure about the spelling) put the Holstredian theory which implies that breast cancer starts at a certain site, then it enlarges then enters the lymphatics around the lesion. He said that the best way to attack it is to remove the breast, lymphatics and all the L.N's that might be invaded, so he removed the breast, pectoralis major (because sometimes there is breast tissue and lymphatics in the pectoralis fold) and axillary L.N's and also he removed lymphatics in the rectus muscle, 60-70% of patients (patients with T of 1 or 2cm) lived.

This way continued until the 40's, there was recurrence of the disease. At the end of 1975, a surgeon called Bernard Fisher (not sure about the spelling) who did extended radical mastectomy; he removed supraclavicular L.N's internal mammary L.N's but there was recurrence and distal metastasis. Also it caused high morbidity, inability to use the arm, lymphedema and localized cachexia (at the side of pectoralis). So they decided to preserve the pectoralis major and do modified radical mastectomy (MRM), then they compared the results of MRM and radical mastectomy, they have the same results.

Then it was said that we should do simple mastectomy without removing the axillary L.N's then we apply radiotherapy.

Then they did the conservative therapy to conserve the breast and avoid the psychological problems due to mastectomy.

---

[1] Sensitivity: the ability to identify correctly those who have the disease.
Specificity: the ability to identify correctly those who do not have the disease.

Then Fisher said that the tumor at the time of metastasis is large and contains a lot of cells ($10^9/cm^3$) and some of them will detach very early, sometimes the disease is will controlled in the breast but there is metastasis, so some said that patients shouldn't be given chemotherapy only, because if it is used alone and we removed the breast there will be residual cells so the breast cancer, unlike lymphoma, is not 100% responsive to chemotherapy.
Fisher conducted a study to compare between radical mastectomy, MRM with axillary dissection and MRM without axillary dissection but with radiation. He found that the results are the same. Then he compared between MRM and breast conserving surgery, he found that the 5 year survival and tumor recurrence are the same. So it is not necessary to do mastectomy for every patient because wide local excision followed by radiotherapy gives the same results.
It took time to convince people not to do mastectomy, between 1970-1980, only 10-15% of American surgeons accepted this.
Breast conserving surgery has certain criteria.
Nowadays, the surgeon shouldn't do mastectomy without offering the patient reconstruction process (prosthesis, flaps, ...)

Should we give radiation to the patient who underwent mastectomy?
The recommendations say that, if the tumor is large (> 5cm) or a part of a tumor is left (no safety margins) or there are > 4 axillary L.Ns involved, radiotherapy should be done.
So if the incidence of local recurrence is 7% and with radiation it becomes 3%, there is a gain of 4%, ya3ni, we should irradiate 100 ladies to give advantage fc 3 ladies.

In breast conserving surgery, every patient who underwent this surgery should have radiation, and if there is contraindication of radiation then it is not necessary to do breast conserving surgery.

In our hospital, we have 2 policies:

- Doing wide local excision without radiation.
- Doing wide local excision with radiation (as the general recommendations)

In patients without radiation, the local recurrence rate is 30-40% (very high), in patients who received radiation it is 7-10%. But the local recurrence will not affect the survival, and the radiotherapy is costy and cause morbidity, pneumonitis, also it may cause cardiomyopathy if it was in the lt side.

According to studies in some hospitals, in old age group, if a big part of the breast is removed with good safety margins, there is no need for radiation.

Now, surgery and radiotherapy alone are not enough, there is a systemic part of the disease so we should use systemic treatment which is chemotherapy, hormonal therapy or both.

According to guidelines; premenopausal patients with +ve L.N. should receive chemotherapy, or if T>1cm they should receive chemotherapy regardless of nodal status.

In patients with T<1cm and –ve L.N., premenopausal and +ve estrogen receptors (ER), we may use hormonal therapy.
Nowadays, the use of chemotherapy is decreasing. In postmenopausal lady, +ve ER and –ve L.N., she should be given hormonal therapy.
If ER is –ve or L.N. were +ve, we should use chemotherapy.
Finally, breast cancer is a very important issue and its incidence is increasing. In developing countries, 60% of breast cancer cases come in an advanced stage

"There is no compulsion for man to accept the truth. But it is certainly a shame upon the human intellect when man is not even interested in finding out as to what is the truth! Islam teaches that God has given man the faculty of reason and therefore expects man to reason things out objectively and systematically for himself. To reflect and to question and to reflect."

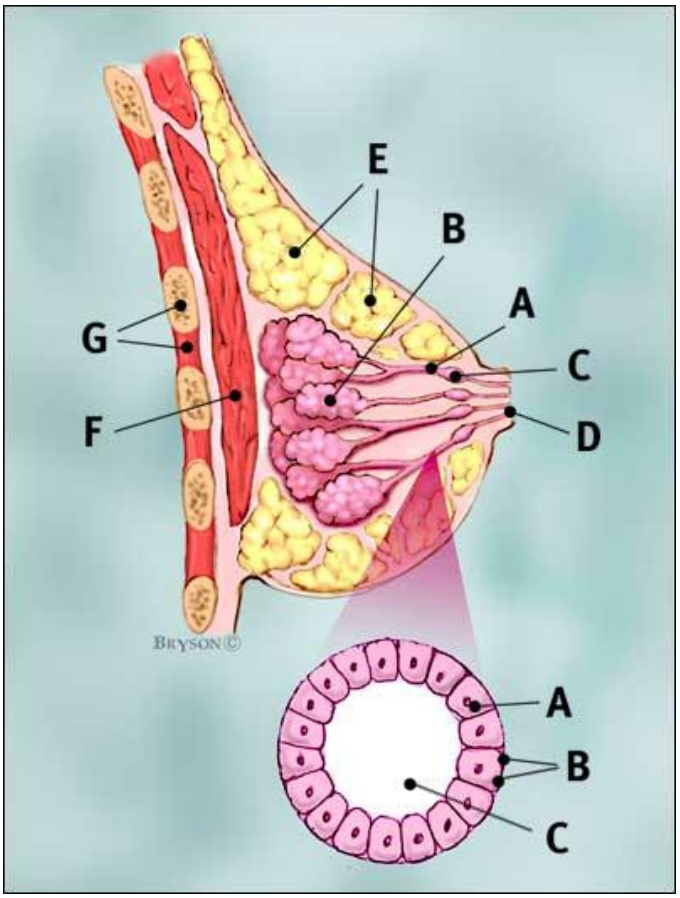
— Maurice Bucaille, a French surgeon

بسم الله الرحمن الرحيم

Lecture topic: Breast diseases
Lecturer : Dr. Jamal Masa'd
Written by : Mohammad Ghalib Riziq

Breast Diseases

*** Breast anatomy:**



Breast profile:
A ducts
B lobules
C dilated section of duct to hold milk
D nipple
E fat
F pectoralis major muscle
G chest wall/rib cage

Enlargement:
A normal duct cells
B basement membrane
C lumen (center of duct)

The breasts are between the second and sixth ribs and are composed of breast tissue, skin, and subcutaneous tissue. The breast tissue is composed of parenchyma and stroma. The parenchyma is composed of 15-25 lobes, and each lobe contains 20-40 lobules. Each lobule consists of 10-100 alveoli. Fifteen to 25 lactiferous ducts provide separate drainage to the corresponding lobes. Before opening at the nipple, these ducts become dilated, forming the lactiferous sinuses.
The breast tissue is enveloped superficially by the superficial pectoral fascia and deeply by the deep pectoral fascia, with the 2 layers connected by fibrous bands called Cooper suspensory ligaments.

The lymphatic drainage of the breast is unidirectional, from the superficial to the deep lymphatic plexus. The lymph then flows centrifugally to the regional lymph nodes after traveling through the lymphatic vessels of the lactiferous ducts. 97% of this flow is collected in the axillary lymph nodes, while only 3% goes to the internal mammary nodes.
Axillary lymph nodes are divided into apical lymph nodes, interpectoral (Rotter) lymph nodes, axillary vein lymph nodes, central lymph nodes, scapular lymph nodes, and external mammary lymph nodes.

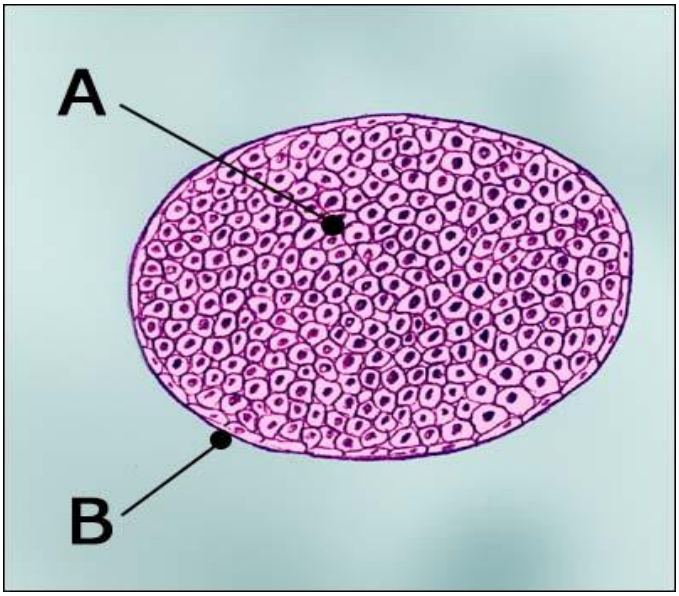
*** Breast Diseases:**
The single most important factor in the personality of any breast cancer is whether it is non-invasive ("in situ") or invasive. This will determine your treatment path and, to some extent, your expectations for results.

- **Non-invasive (or "in situ") cancers** confine themselves to the ducts or lobules and do not spread to the surrounding tissues in the breast or other parts of the body. They can, however, develop into or raise your risk for a more serious, invasive cancer.

- Invasive (or infiltrating) cancers have started to break through normal breast tissue barriers and invade surrounding areas. Much more serious than non-invasive cancers, invasive cancers can spread cancer to other parts of the body through the bloodstream and lymphatic system.

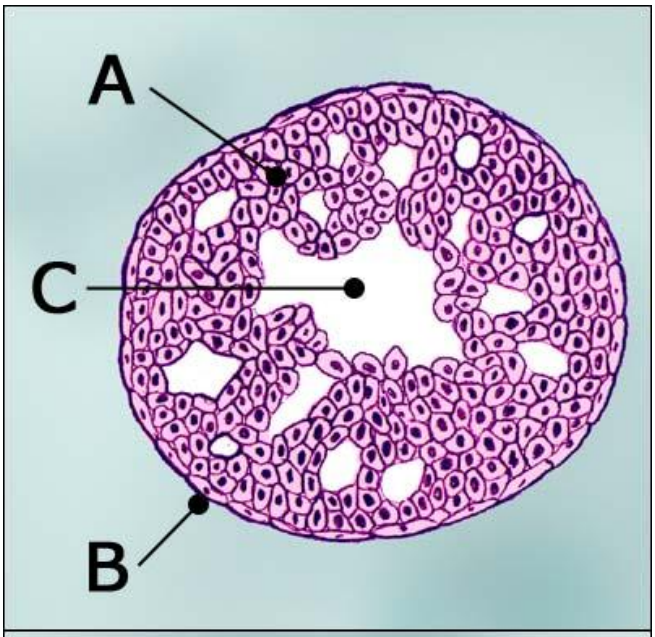
*** Non-Invasive Cell Growth Subtypes:**
Because cancer is essentially an uncontrolled growth of cells, doctors pay a lot of attention to *how* the cancer cells grow. "Non-invasive" breast cancer (also called "in situ" breast cancer) stays within the ducts or lobules of the breast and does not spread to the surrounding tissues of the breast or other parts of the body. Non-invasive cancer is grouped into four subcategories, based on how the cancer cells grow relative to each other, within the center of the milk duct.

1- "SolidSolid": There is wall-to-wall cell growth
- **A** cancer cells
- **B** basement membrane



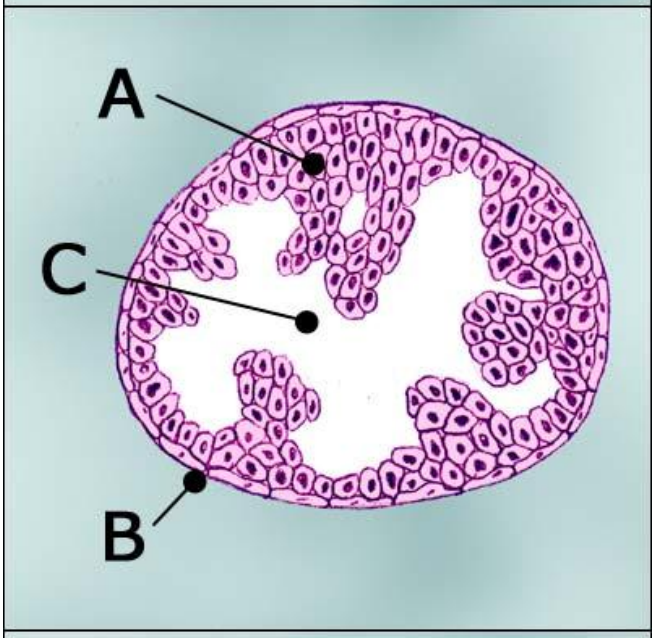
2- "Cribiform": There are holes between groups of cancer cells, making it look like Swiss cheese.

- **A** cancer cells
- **B** basement membrane
- **C** lumen (center of duct)



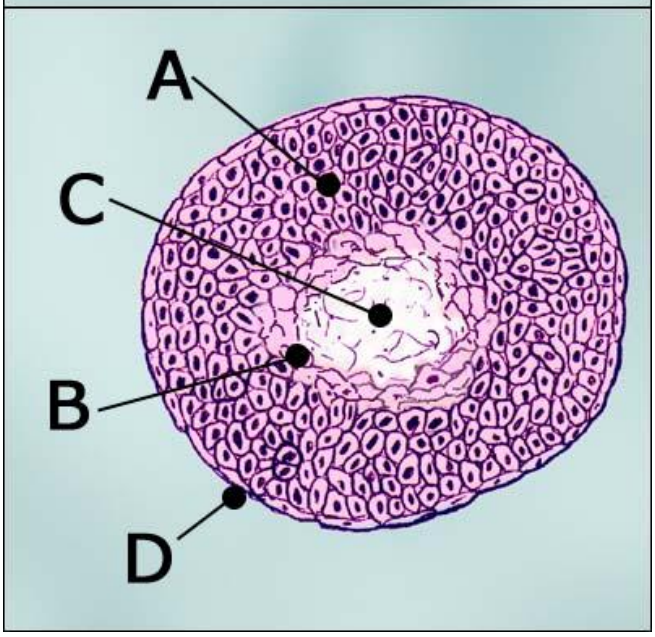
3- "Papillary": The cells grow in fingerlike projections, toward the inside of the duct.

- **A** cancer cells
- **B** basement membrane
- **C** lumen (center of duct)



4- **"Comedo":** There are areas of "necrosis," which is debris from dead cancer cells; this indicates that a tumor is growing so fast that some tumor cells wither and die because there's not enough blood supply to feed all of them.

- **A** living cancer cells
- **B** dying cancer cells
- **C** cell debris (necrosis)
- **D** basement membrane

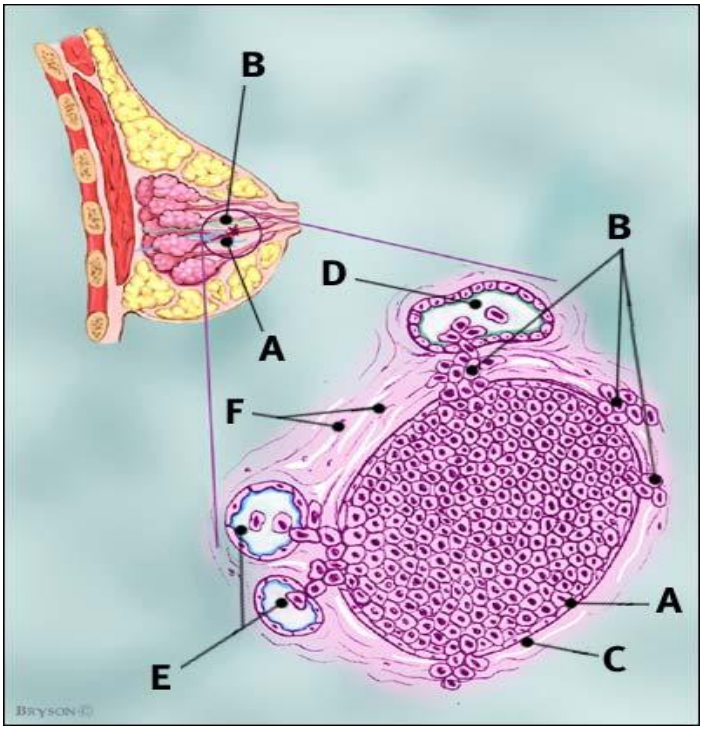


*** Vascular and Lymphatic Invasion**

- Normal breast with cancer cells invading the lymph channels and blood vessels in the breast tissue.
- **A** blood vessels
- **B** lymphatic channels

Enlargement:

- **A** normal duct cells
- **B** cancer cells
- **C** basement membrane
- **D** lymphatic channel
- **E** blood vessel
- **F** breast tissue



The pathologist will also check to see if cancer cells have broken into the normal lymphatic channels and blood vessels within the breast. These are the "highways" that connect breast tissue to other parts of the body, bringing in nourishment and removing the waste products of cell life. If cancer cells are found in the lymph channels or blood vessels, it means that cancer may have traveled to areas beyond the breast.

*** Ductal Carcinoma in situ (DCIS)**

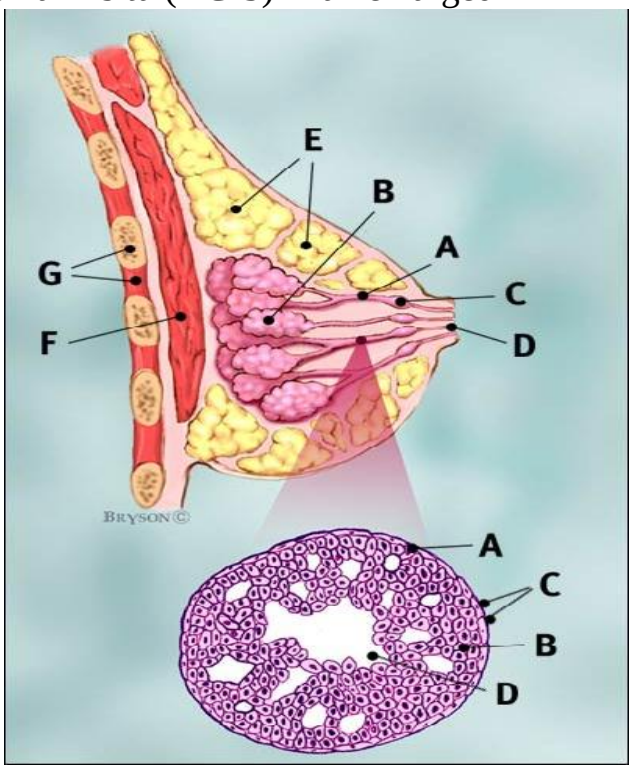
- breast with non–invasive ductal carcinoma in situ (DCIS) in an enlarged cross–section of the duct.

Breast profile:

- **A** ducts
- **B** lobules
- **C** dilated section of duct to hold milk
- **D** nipple
- **E** fat
- **F** pectoralis major muscle
- **G** chest wall/rib cage

Enlargement:

- **A** normal duct cells
- **B** ductal cancer cells
- **C** basement membrane
- **D** lumen (center of duct)



Radiation therapy important after DCIS surgery. Although DCIS itself isn't life-threatening because it hasn't started to invade normal tissue, doctors still take it seriously because it is associated with an increased risk of invasive cancer in the future.

Ductal carcinoma in situ, or DCIS, is the most common kind of non-invasive breast cancer. It is *ductal* because the cancer is confined to the milk ducts—which are the "pipes" that bring milk from the lobules to the nipple. *Carcinoma* refers to any cancer that begins in the skin or other tissues that cover internal organs—such as breast tissue.

In situ or "in its original place" means that the cancer has not spread to any surrounding tissues.
DCIS is generally detected by a mammogram. Cancer cells inside the ducts appear on the mammogram, and may appear along with tiny specks or calcifications—the buildup of material left from dead cancer cells.

*** Lobular Carcinoma in situ (LCIS)**

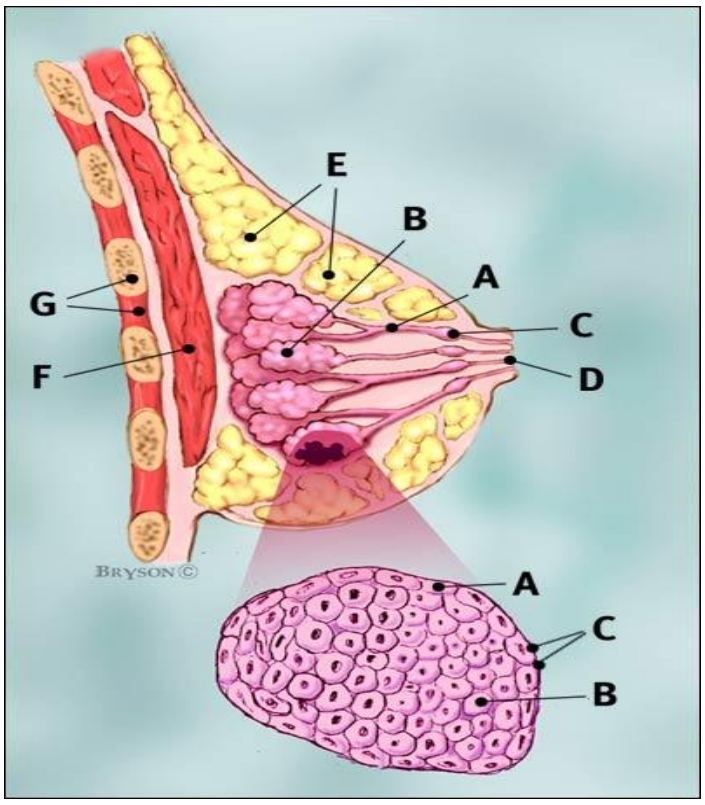
- Normal breast with lobular carcinoma in situ (LCIS) in an enlarged cross–section of the lobule.

Breast profile:

- **A** ducts
- **B** lobules
- **C** dilated section of duct to hold milk
- **D** nipple
- **E** fat
- **F** pectoralis major muscle
- **G** chest wall/rib cage

Enlargement:

- **A** normal lobular cells
- **B** lobular cancer cells
- **C** basement membrane



Lobular carcinoma in situ, or LCIS, is generally considered to be a pre-cancerous condition ?!!. It is *lobular* because the cancer is confined to the lobules—which are the glands that actually make milk. *Carcinoma* refers to any cancer that begins in the skin or other tissues that cover internal organs—such as breast tissue. *In situ* or "in its original place" means that the cancer has not spread to any surrounding tissues.

*** Invasive Ductal Carcinoma (IDC)**

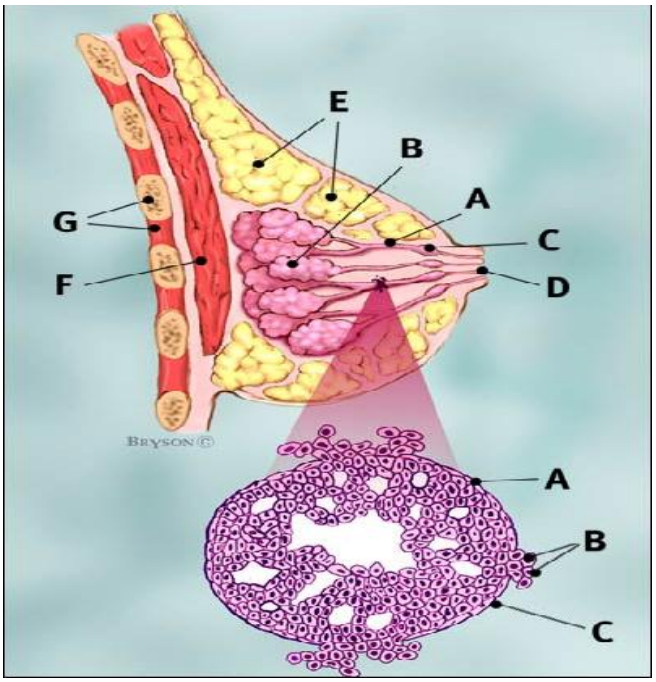
- Normal breast with invasive ductal carcinoma (IDC) in an enlarged cross–section of the duct.

Breast profile:

- **A** ducts
- **B** lobules
- **C** dilated section of duct to hold milk
- **D** nipple
- **E** fat
- **F** pectoralis major muscle
- **G** chest wall/rib cage

Enlargement:

- **A** normal duct cells
- **B** ductal cancer cells breaking through the basement membrane
- **C** basement membrane



Invasive ductal carcinoma, or IDC, accounts for about 80% of all breast cancers. *Invasive* means that it has "invaded" or spread to the surrounding tissues. It is *ductal* because the cancer began in the milk ducts—which are the "pipes" that bring milk from the lobules to the nipple. *Carcinoma* refers to any cancer that begins in the skin or other tissues that cover internal organs—such as breast tissue.

*** Invasive Lobular Carcinoma (ILC)**

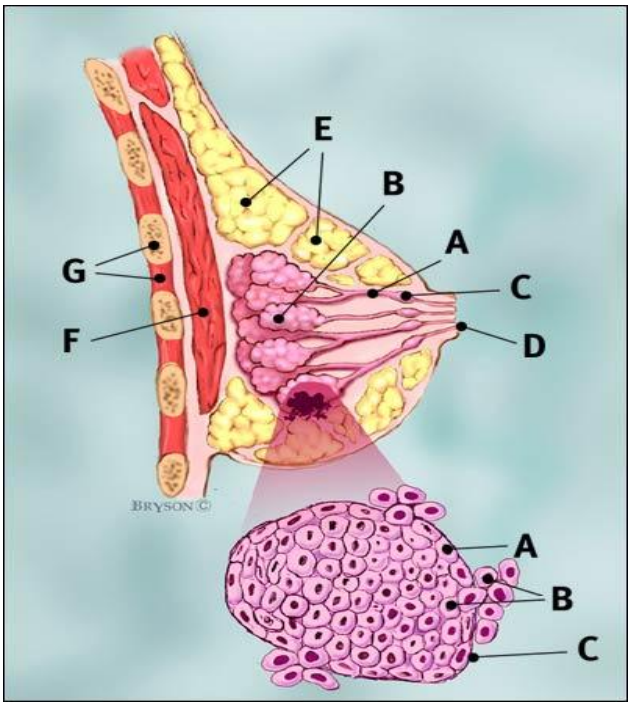
- Normal breast with invasive lobular carcinoma (ILC) in an enlarged cross–section of the lobule.

Breast profile:

- **A** ducts
- **B** lobules
- **C** dilated section of duct to hold milk
- **D** nipple
- **E** fat
- **F** pectoralis major muscle
- **G** chest wall/rib cage

Enlargement:

- **A** normal cells
- **B** lobular cancer cells breaking through the basement membrane
- **C** basement membrane



Invasive lobular carcinoma, or ILC, accounts for about 10%–15% of all breast cancers. *Invasive* means that it has "invaded" or spread to the surrounding tissues. It is *lobular* because the cancer began in the lobules—the glands that actually make milk. *Carcinoma* refers to any cancer that begins in the skin or other tissues that line or cover internal organs—such as breast tissues.

"تمت بحمد الله"

((بسم الله الرحمن الرحيم))

Do'a Z. Ashour
Dr.Jamal Mas'ad

Breast Cancer

- Most important problem in the breast, it's 2nd leading cause of death after cardiovascular disease.
- All over the world breast CA is the most common type of CA in ♀ except in certain areas.
- 560 breast CA case/y in Jordan & this is a high no. according to the no. of population.
- At 1979 in America the no. of breast CA cases was 182000, mortality was 4300. In UK the no. of the breast CA was 45000, mortality was 18000. Which means it is a heavy burden & affects the life of the population.
- The seriousness of breast disease is related to CA & we should distinguish it from other things.

Physiological importance of breast:

- It's the organ of lactation & the organ of feminity. Loosing the breast will cause loosing the lady herself image, even it's important from the cosmetic point of view to have breast with good shape. Any mutilation or surgery will affect the psychology of ♀.
- The remove of the breast will lead to cosmetic, psychological & even social problems; many ladies after mastectomy face social dissociation & divorce.

Breast CA is important for the lady, her family & the society.

Basic Anatomy:

The breast extends from the 2nd to the 6th rib, protruding part of the breast is called breast mount but breast area is between 2nd & 6th rib. With repeated pregnancy & lactation, the breast will be tossed, so sometimes the breast is found between 4th to 6th .On P/E of breast, I won't examine the breast mount but examine the breast area including the breast mount.

I can't palpate breast in sitting position because we can't examine the breast mount, but if the patient is in the supine position I'll examine the breast area.

The breast extends from the edge of the sternum to the anterior axillary line.

Breast is composed of ducts & glands. The nipple has 15 to 20 openings, they will open into a duct then to the lactiferous duct then to the main duct, that will open in acini, these acini are lined by cuboidal cells or tall columnar cells during pregnancy & lactation, also lined by myoepithelial cells which allow the sinus to contract.

Icroscopic types of breast CA:

- Ductal CA: infiltrating or in situ type
- Lobular CA: infiltrating or situ type:
- NOS CA: if we look to the tumor cells under the microscope we can see that there are just malignant cells not making any structure. So it's called not other wise specified.
- Papillary CA: malignant cells forming papillae.
- Colloid CA: malignant cells secreting mucous.
- Medullary CA: malignant cells like NOS type but there is vacuum spaces in between (Swiss cheese appearance) infiltrated by lymphocytes which means that the body is trying to exert a response against the tumor. The prognosis of that tumor is better than NOS type (all the differentiated types have better prognosis than NOS type).
- Adenoid cystic CA: like the NOS type but infiltrates the nerves.
- In situ CA: includes solid, cystic & comedo type. Comedo is a bad type of in situ because there is no good vascularity, the tumor is growing faster than neovascularisation.

Breast is composed of compartments that are embedded in fat and separated by fibrous tissue which is connected to Coopers ligament.

NOS type will be hard because tumor cells most probably worked as fibroblasts producing collagen leading to desmoplastic rxn, which induces the hard feeling of the breast. This fibrous tissue will contract leading to traction of Coopers ligament that is attached to skin leading to skin dimpling, puckering or tethering. If this desmoplastic rxn occurs in the area deep to areola-nipple complex will cause nipple retraction.

Tumor will be ill-defined with limited mobility because the fibrous tissue is anchoring the tumor to the surrounding. Mammographic findings of malignant mass will be very dense star shaped or satellite lesion

Lymphatic Drainage of Breast

We have 2 main lymphatic plexuses:

1. Sub-areolar lymphatic plexus
2. Sub-pectoral lymphatic plexus

Parts of the breast will drain to sub-areolar plexus then ultimately will drain to sub-pectoral plexus then to the LN which are mainly axillary or internal mammary.

If there is a tumor probably it will invade lymphatics, so lymphatic reserve that drains the breast will be affected leading to breast enlargement manifested in the form of edema.

There are adenexial structures in the skin that are anchored down to the dermis. When there is edema these adenexial structures will not float on the surface of the skin but will remain stretched down leading to peau'd orange appearance.this appearance is very important for the staging of the disease.

Blood supply of breast

1. Inter coastal artery.
2. Lateral thoracic artery.
3. Internal mammary artery.

Note: its important to know

1. Breast boundaries.
2. Why tethering occur.
3. Mechanism of peau'd orange.

What the normal feeling of the breast?

Breast goes into stages: before puberty it's flat in ♀ &♂, after puberty there will be difference & there is involutional changs in the breast after menopause, changes during pregnancy & location.

The most common cause of breast clinic visits is the monthly changes on the breast, which are physiological and should be appreciated by the lady.

What is the presentation of the Breast CA?

1. The common presentation is the presence of the breast mass, our main objective is to know if it's benign or malignant.
2. Pain: malignant process is usually painless, but malignancy can come in the form of an abcess or inflammatory CA which is painful. Probably adenoid cystic CA is painful.

3. Nipple Discharge: it's a rare presentation of breast CA. Usually bloody stained discharge is due to duct papilloma but could be due to duct CA.

Normally the breast secrets fluids, scanty in amount, pass unnoticed, it decrease & increase with physiological changes, the lady will notice this secretion as a dryness on the areola or as a yellowish stain on the pra, this fluid is scanty, serous, yellowish, not watery but with viscosity & surface tension.

We have to elicit the risk factors of any patient in the Hx:
1) Age. 2) Gender. 3) Family Hx. 4) Previous surgeries in the breast...etc
The most important risk factor from the clinical point of view is family Hx.

Physical Examination of The Breast:

There should be:
- Private atmosphere.
- Good light.
- Witness esp. for male doctors.
- Exposure of the upper part of the body.

Examination is done in 2 positions:

A) Sitting Position.
B) Supine Position.
We should start by inspection: symmetry, areola-nipple complex, the size of the breast, any changes on the breast (redness, scar, edema, dilated veins, puckering, peau'd orange).

The breast in a young lady is conical in shape, areola-nipple complex at the level of deltoid insertion, 18- 20 cm from the sternal notch.

If the breast is big, patient's hands are beside her we can't see more than 40% of the breast. If the patient elevates her arms above her head we'll expose lateral side of breast, if we can't see the lower part we have to elevate it & see it.
If we suspected that certain area has tethering or puckering we can ask the patient to lean forward to accentuate some questionable sites.

Palpation: in sitting position we palpate supra clavicular L.N., infra clavicular L.N., and axillary L.N.
There are different ways to examine the axilla:
1) We put 2 fingers above the elbow, put arm on arm, put fingers of the other hand on the apex of the axilla, press on the chest wall & move downward; by

this we can palpate apical & central part, then I put my hand behind the anterior axillary fold. (Which is formed of pectoralis major).

We should examine it against counter pressure; by this we examined the anterior group.

2) Put your hand on the shoulder of the patient, patient's hand on your shoulder then palpate the axilla.

3) Examination of axilla from behind as a special maneuver.

*The classical way is the first.

Palpation of the breast:

The golden standard of examination that we have to be relaxed, the patient have to be relaxed, and the examination should be against firm structure.

If the patient is in the supine position & the breast is large it'll fell apart.

The most common site of breast CA is the upper outer quadrant so we have to concentrate on it.

If the breast is small & it is on the chest wall there is no need to make any maneuvers.

If the breast is not on the chest wall we have to ask the patient to lean to the opposite side leading to the falling of breast on the chest wall. This maneuver is good to examine the lateral part of the breast while the arm is on her side.

When the patient elevate her arm two things will happen:

1) Part of the upper outer quadrant and the axillary tail (tail of Spence) will enter the axilla so we loose the chance to examine that part.

2) The medial half of the breast will be stretched, so it will be thinner & palpated better.

→ when we want to examine the medial half of the breast the arm should be above the head with a pillow below the patient while she is leaning to the opposite side.

→ when we want to examine the lateral part of the breast the hand/arm should be beside the patient.

→ Examination should be with the palmer aspect of the fingers without flexion, if we feel a mass that is different from the rest of the breast we can do tactile discrimination (which means palpation until you can discriminate 2 points as 2 points).

→ the breast is not a soft tissue but glandular structure with fibrous and fatty elements.

→ there is physiological nodularity of the breast, so if there is a mass on this background of nodularity you have to distinguish it.

→ if you distinguish a real mass this is called a dominant mass which is felt by any person without any doubt, sometimes there is created masses due to wrong P/E, sometimes there is something in between so you can't say if it's a real mass or not but the area is abnormal in it's consistency.

→ if you need you can milk the areola (not squeeze because it's painful and traumatic) in order to demonstrate the discharge.

Characteristics of any mass:
1) Consistency 2) Dimensions 3) Mobility 4) Fluctuation
5) Skin over the mass, etc.

Pit fall:
Normally when the breast is examined there is an area with a firm tissue & other lacking this sensation. Usually around the areola there is no breast tissue so the breast tissue near that area will be felt as a mass with boundaries.

→ Due to the heaviness of the breast & its pivot movement there is a sort of fat necrosis in the infra mammary ridge which leads to indurations, tenderness & firmness.

Case:
50-year-old ♀ patient feeling a mass in her breast for 3-month duration, painless. Her mother & sister developed breast CA. She is obese, alcoholic, married at 35 of age, her first delivery at 40 years of age; she used OCP, early menopause with hormonal replacement therapy. Before her marriage she had done a Bx & she was told to have atypical epitheliosis in the breast.
So usually patients of breast CA are ♀, obese, old, nulli para or old primigravida, alcoholic, used OCP & hormonal replacement therapy, she has strong family Hx, and she has large ill-defined mass with limited mobility.

Differential Diagnosis of Mass in The Breast:

1) **Fibro adenoma:** it is the most common solid tumor, usually comes after puberty but commonly in the second & third decade of life, it is well circumscribed mass, freely mobile with lobulated surface.
→Medullary CA can look exactly like fibro adenoma but it comes in older age groups, can come as well circumscribed mass. It has good prognosis due to the infiltration with inflammatory cells, this tumor has estrogen receptor negative.

2) **Fat Necrosis:** present with hard, ill-defined mass with limited mobility. The commonest cause leading to fat necrosis of breast is the diagonal strap.
→Many ♀ having RTA will be treated for their injuries without examining the breast, after 2-3 months she feels that there is a tumor in her breast which is due to fat necrosis.

3) Fibrocystic Disease: there is nothing called fibrocystic disease that is used properly. It is considered as physiological exaggeration, some books call it abnormal physiology. The majority of patients having fibrocystic disease have physiological changes but there are certain types that are pathological. **Tumor Adenosis** is a part of fibrocystic disease that is presented with hard ill-defined mass with limited mobility, even in the Bx it is not easily differentiated from malignancy.

4) Peri-ductal Mastitis: which is a part of duct ectasia, some times it can be present with hard ill defined mass with limited mobility especially centrally behind the areola, some time with peau'd orange and retraction of the nipple.

5) Abcess: if the abcess is miss Dx and treated with antibiotics which doesn't remove the pus but arrest the inflammatory process, this is called "chronic abcess", when we use antibiotics it is called " anti pioma".

D. Dx. Of a mass in the breast is:

1. **Fat necrosis.**
2. **Anti pioma.**
3. **Peri ductal mastitis.**
4. **Sclerosing adenosis.**
5. **Abcess.**
6. **Fibro adenoma.**

→If I want to Dx breast CA I have to do triple assessment:

1. Clinical examination.
2. Radiological examination.
3. Histological investigation.

→In the previously mentioned case we give it 5/5 depending on clinical basis.
→The next step for that lady is to do mammogram; if the result was that there is star shaped lesion with calcification and disturbed architecture and the size was 3*2 this is also given 5/5.
→After that I do FNA; if the result says that it is strongly suggestive of malignant cells we also give it 4/5.
→The score given to the Hx &P/E + Radiological investigation + FNA =
5/5 + 5/5 + 4/5 = 14

- If the score is 12 – 15 it is a malignant mass.
- If the score is 10 – 12 it is highly suspicious of malignancy.
- If it is < 8 it is a benign lesion.

There are certain difficulties during investigation:

→mammogram can miss 15 – 20 % of lesions due to:

1. The mammogram is not done in proper way to have the whole breast in the view and the tumor is outside this view.
2. The density of the breast is high, the tumor will look white and the breast tissue is white so the tumor will not appear.

→some times we do U/S.

→some times we do MRI which is very helpful to Dx malignancy, not only in its shape but also in the pattern of the material or the dye that is given which will produce special curve for malignancy and special curve for the benign lesions.

Mother in Law Curve for Malignant Lesions: the dye will appear very early and will continue then disappear very late.

→MRI is not used as a routine for investigating breast CA.

The End

بسم الله الرحمن الرحيم

Lecture topic: Breast imaging
Lecturer : Dr. Jamal Masa'd
Written by : Moa'th Al-Hamad

Breast imaging

1) Breast mammogram:

- The breast can be imaged with mammography, ultrasound or MRI
- Mammography is the most sensitive of breast imaging modalities
- Sensitivity is reduced in young women due to the presence of increased glandular tissue
- For symptomatic patients, imaging always performed as part of triple assessment
- Mammography is a useful adjunctive diagnostic measure when used in patients with clinically suspicious or high-risk breasts. About 25% of breast cancers diagnosed in mass screening programs are detected by mammography alone. A negative mammogram should not dissuade biopsy of a suspicious mass.
- Diagnostic mammography
  A diagnostic mammogram is used to evaluate clinical symptoms (eg, focal pain, lump, nipple discharge) or an abnormality detected on a screening mammogram. The study may involve additional or spot compression views or a combination of views that eliminate overlapping shadows or include parts of the breast not completely visualized on standard mammograms. Margins of masses and areas of microcalcification may require magnified views.
- After analysis, the radiologist may recommend ultrasound or an interventional procedure. In the presence of an

obvious clinical carcinoma, a mammogram is still worthwhile to evaluate the extent of disease and to look for occult carcinoma in the other breast.

- To "standardize mammographic reporting" and "help clinicians understand disposition of their patients," the American College of Radiology has developed a Breast Imaging Reporting and Data System (BIRADS) lexicon and five assessment categories. Category 0 means the assessment is incomplete. Category 1 (negative finding), category 2 (benign finding), and category 3 (probably benign finding, short interval follow-up suggested) are considered negative. Category 4 (suspicious abnormality, biopsy should be considered) and category 5 (highly suggestive of malignancy, appropriate action should be taken) are considered positive, and some form of biopsy needs to be performed for these two assessments.

- Digital mammography
  Digital mammography requires an x-ray source and an electronic detector to generate the image, which can be reviewed on a high-quality monitor. Several of the newer mammography units can be adapted for digital imaging in the future. The image capture process (detector) has not yet been refined for full-field technology, and at present the image has to be produced on a transilluminated film. Theoretically, more information could be manipulated at digital viewing stations and transmitted to other stations locally or worldwide. Ultimately, hard-copy film and the need for film libraries could be eliminated. Although computer-aided detection and diagnosis may enhance diagnostic acumen, clinical trials are needed to determine if digital mammography can outperform conventional mammography .

- See below for more details about mammographic features of breast Ca.

2) Breast U/S:

- Ultrasound is useful in the assessment of breast lumps
- Complements mammography and is able to differentiate solid and cystic lesions
- Also able to guide fine needle aspiration and core biopsies
- Can be used to assess tumor size and response to therapy
- In the diagnosis of malignancy it has a sensitivity and specificity of 75% and 97% respectively
- Cysts and solid lesions have typical appearances

Ultrasound image showing dark irregular mass

- Ultrasound reflects the acoustic characteristics of breast tissue and is well established as an ancillary technique for evaluating breast lesions. However, it is operator-dependent and requires optimal technique, and findings must be correlated with the mammogram whenever possible. Ideally, the study should be performed by a radiologist with expertise in mammography.

- Because it is a nonionizing technique, ultrasound is particularly advantageous for evaluation of palpable masses in young, pregnant, or lactating women. It can differentiate cysts from solid masses seen on mammography or found on palpation. Because taut compression is not required for ultrasound, it can be useful in evaluating a painful, inflamed breast to determine if a focal, drainable abscess is the problem. Also, ultrasound can be helpful when no mammographic abnormality is seen in a clinically suspicious area of the breast.

- If results of mammography and ultrasound are both normal in a woman with a palpable, suspicious mass, a biopsy of the mass should always be done, regardless of the imaging results. A palpable mass not seen in dense parenchyma is suitable for ultrasound evaluation. However, ultrasound does not visualize all solid masses (or malignant tumors), nor can it consistently show microcalcifications.

- Ultrasound is also helpful for determining whether lesions incompletely visualized on a mammogram or palpable masses that cannot be included on a mammogram are cystic or solid. The mammographic features of certain solid masses may suggest a benign lesion and allow the radiologist to assign it to a short-term follow-up category. On the other hand, if certain features are characteristic of malignancy, biopsy is recommended.

- Clinical studies evaluating possible future uses for breast ultrasound technology and research into three-dimensional breast ultrasound are under way. The utility of ultrasound in the detection of clinically and mammographically occult breast cancer is also being studied. Until the results of these clinical studies are available, ultrasound screening is not advocated for routine clinical use.

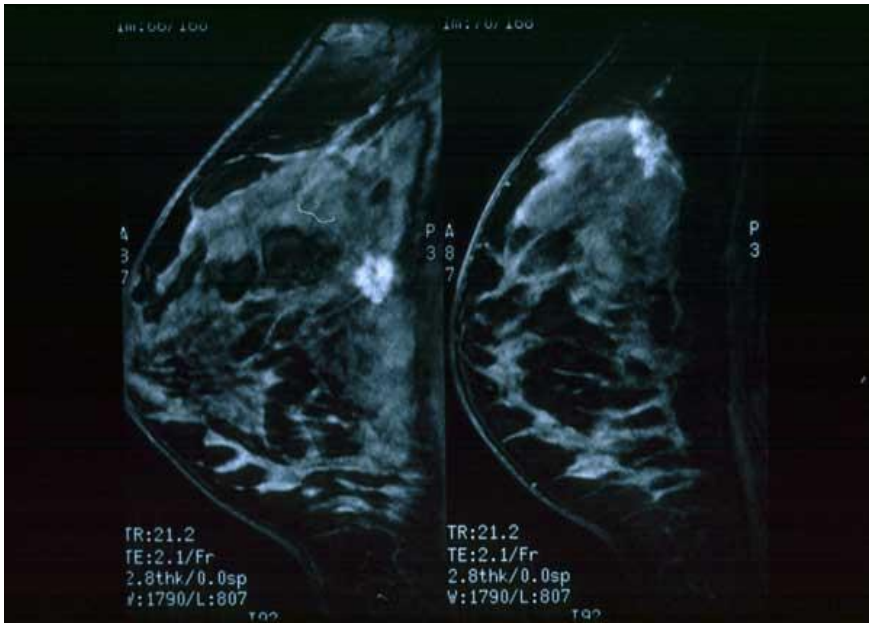
- Solid lesions have internal echoes

- Malignant tumours have:
  - ✓ Hypoechoic areas interspersed between brighter echoes
  - ✓ Irregular edges
  - ✓ Cast: hypoechoic shadows
- Benign tumours have:
  - ✓ Isoechoic or hypoechoic patterns
  - ✓ Smooth well defined borders
  - ✓ Cast: no hypoechoic shadows

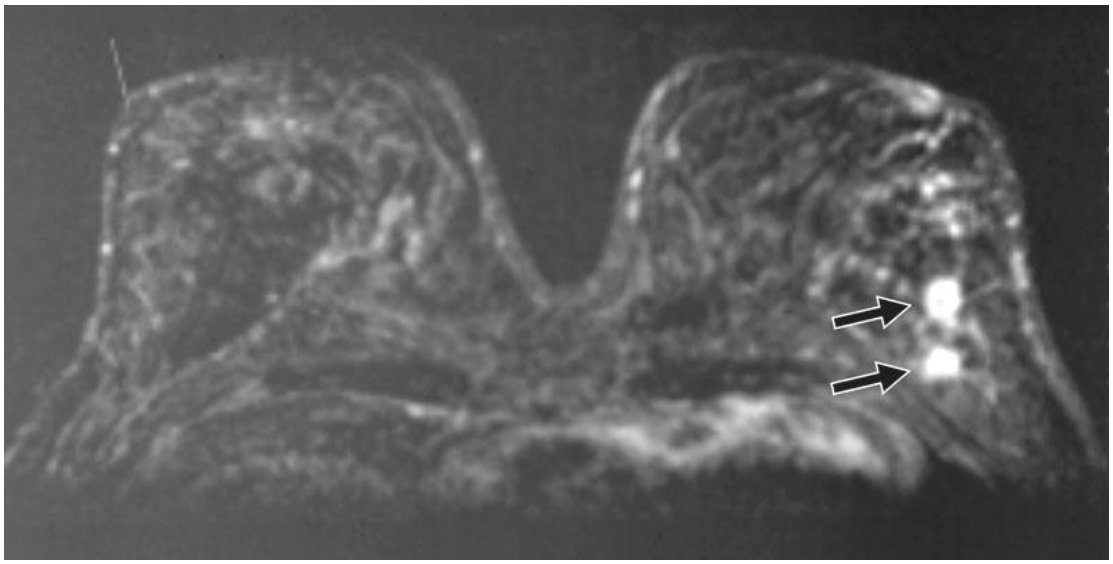
3) Magnetic resonance imaging:

- MRI is a nonionizing imaging technique with multiplanar capability. Breast imaging requires a dedicated breast coil and demanding technical standards for optimal results. Also, intravenous contrast medium (gadolinium) is needed to evaluate kinetic and architectural features of breast masses.
- Virtually all breast cancers enhance on MRI studies, probably because of tumor angiogenesis. Therefore, normal findings exclude invasive carcinoma with a high degree of certainty. When signs suggest a high probability of malignancy, sensitivity is 85% to 90% and specificity is 70% to 90%.
- As a supplement to mammography, MRI can detect and define breast cancer preoperatively and thus guide appropriate surgical planning. In patients with metastatic disease, breast MRI may reveal primary tumors not seen on mammograms or with ultrasound studies or detected with clinical breast examination. MRI also is useful for differentiating tumor recurrence from postoperative and radiation scarring if the study is done some time after therapy (usually after about 18 months). The integrity of breast implants can be assessed more accurately with MRI than with breast ultrasound.

- Before clinical applications of breast MRI can be fully implemented, MRI-guided breast biopsy and needle localization must be developed. Until then and until the cost and accuracy have improved, <u>breast MRI is not recommended for routine clinical use</u>. Its role in high-risk breast screening and in patients with dense breasts has yet to be studied, given that microcalcifications are <u>not</u> consistently demonstrable with this technique

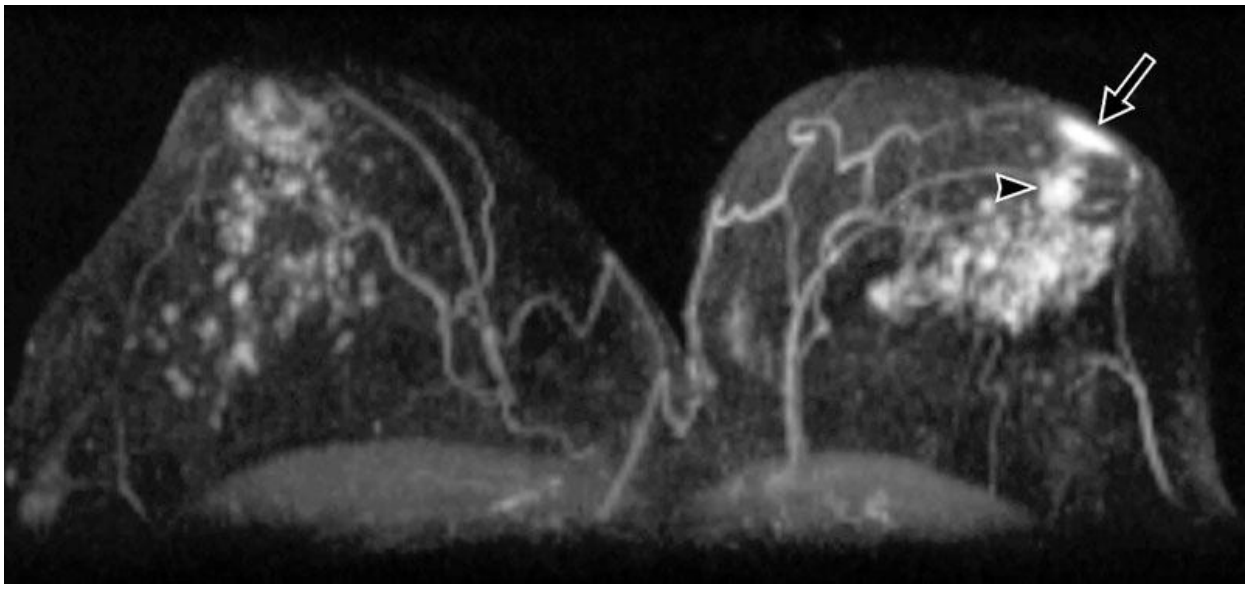


MRI scan of the breast reveals two discrete areas of abnormality, which proved to be cancer.

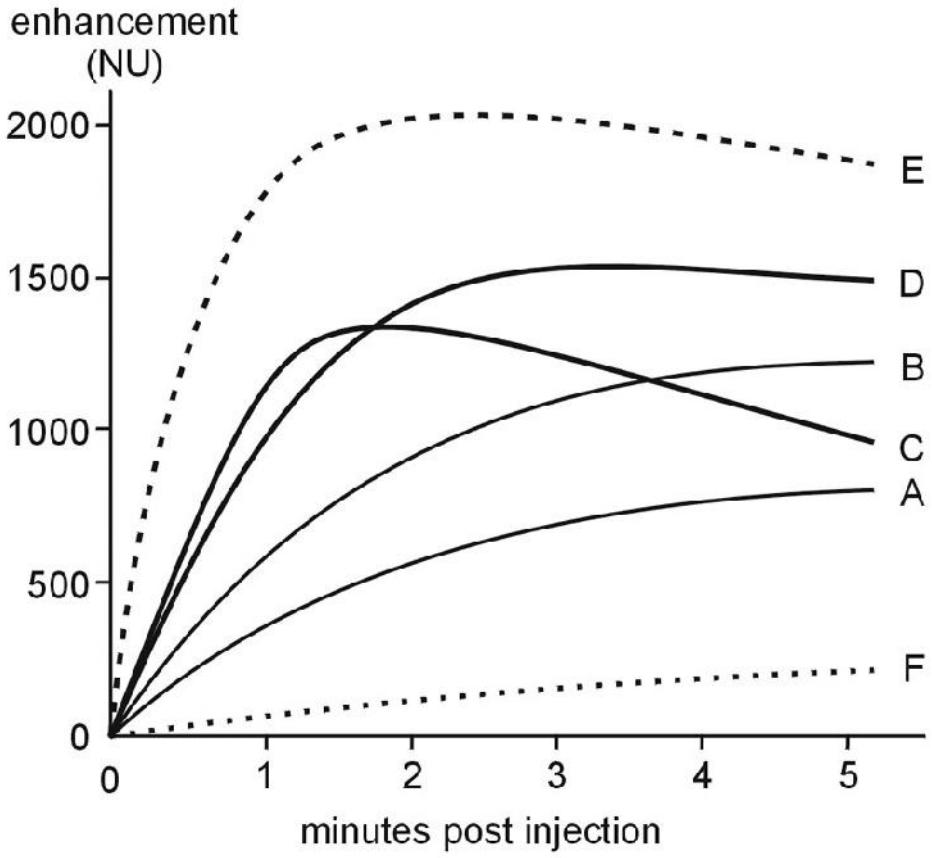


Forty-four-year-old patient who underwent breast conserving surgery of the left breast 2 years prior to the current examination. The follow-up mammogram showed dense breast parenchyma but no suspicious areas. On MRI three focal, rapidly enhancing lesions were seen in the left breast, two of which are seen on the scan (arrows). On ultrasonography,

two hypoechoic lesions were seen. On microscopy of the mastectomy specimen two invasive foci of lobular carcinoma measuring 1.0 cm each and one measuring 0.5 cm were found and, in addition, several smaller foci of invasive and noninvasive lobular carcinoma.



Paget’s disease of the nipple on MRI



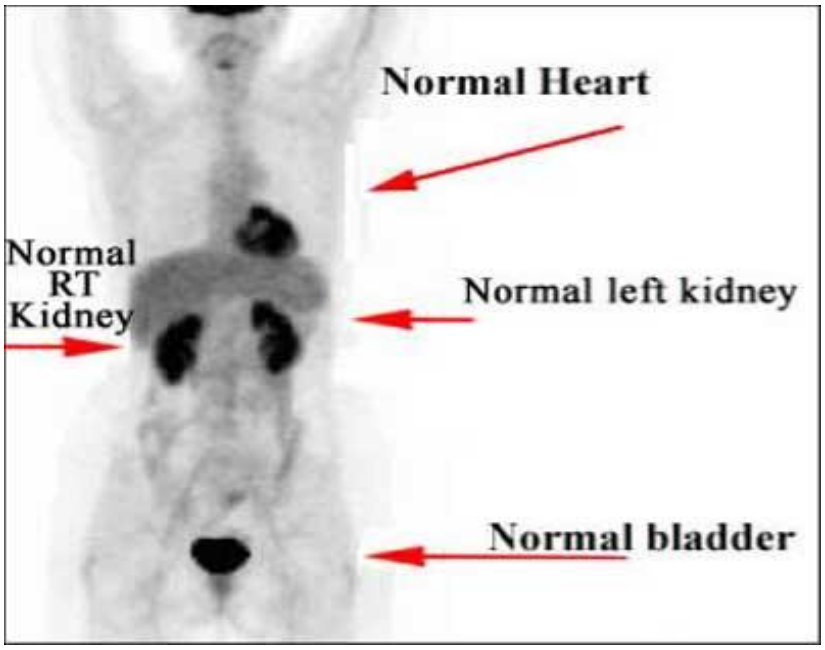
MRI, breast

Enhancement curves for carcinomas. About 90 % of all caricnomas enhance according to the patterns represented by curves marked C, D and E. NU = normalized units

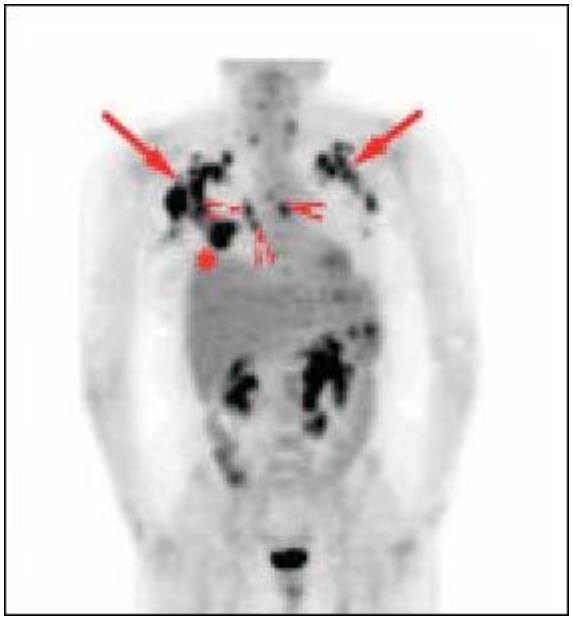
4) PET scan:

- Positron emission tomography with 18-fluorodeoxyglucose (FDG-PET) has been evaluated for diagnosis, staging, restaging, and monitoring therapy response in patients with breast cancer. Although the current data suggest that FDG-PET may have limited diagnostic utility in detecting small primary tumors, staging the axilla, and detecting blastic osseous metastatic lesions, PET has superiority over conventional imaging in detecting distant metastases and recurrent disease and in monitoring therapy response.
- The aggressive accumulation of the glucose analogue FDG in breast cancer relative to the surrounding tissue is a manifestation of the raised metabolic rate seen in many carcinomas. The radionuclide is short-lived and needs to

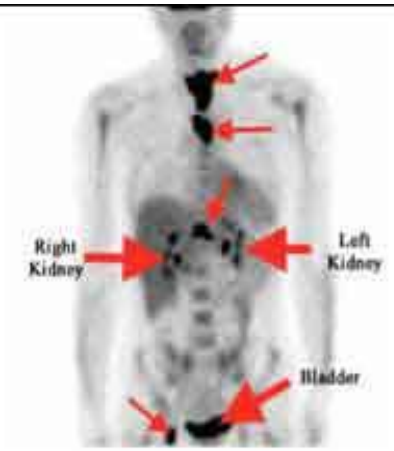
be produced using a cyclotron. Also, the tracer needs to be injected intravenously. Lesions smaller than 1 cm are typically not detected. Although primary and metastatic breast cancer and breast cancer recurrence can be imaged with FDG, to date practical considerations limit its use.

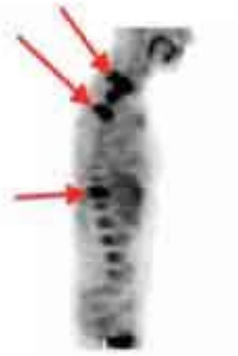


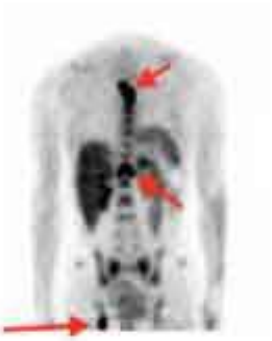
Normal PET Scan.



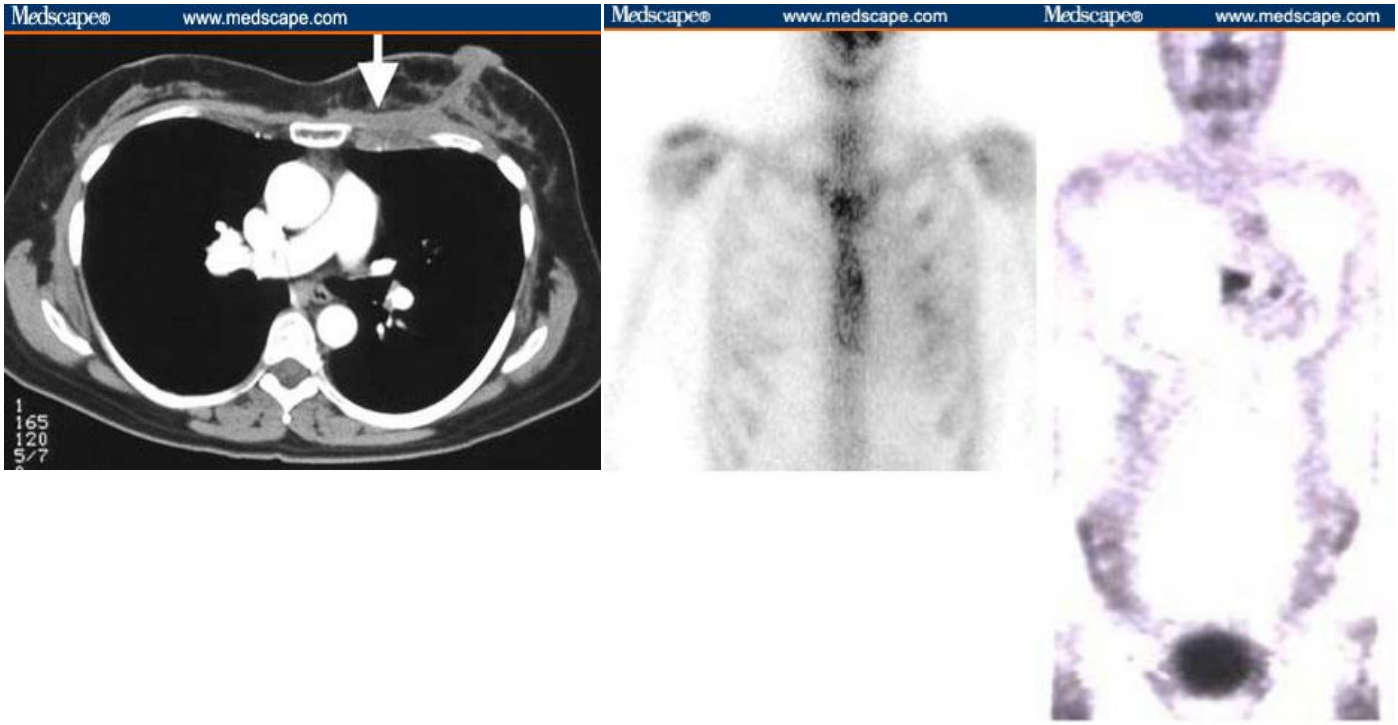
PET scan showing abnormal lymph nodes.



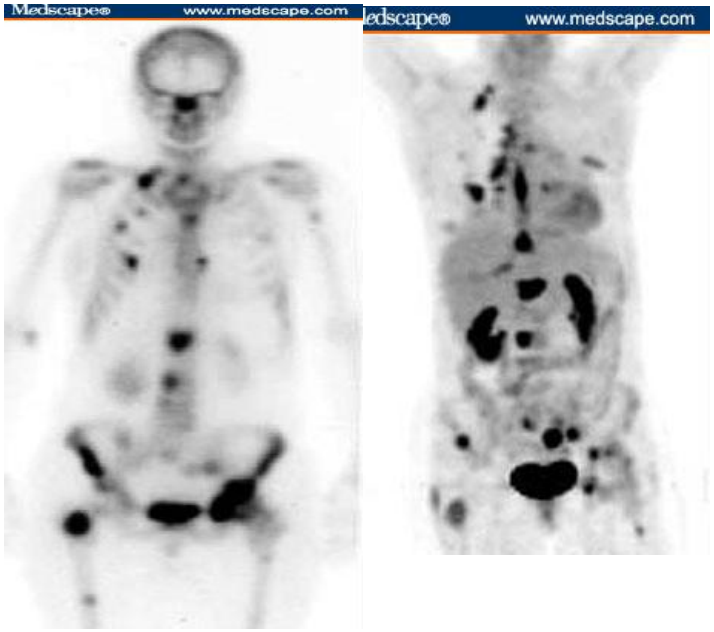




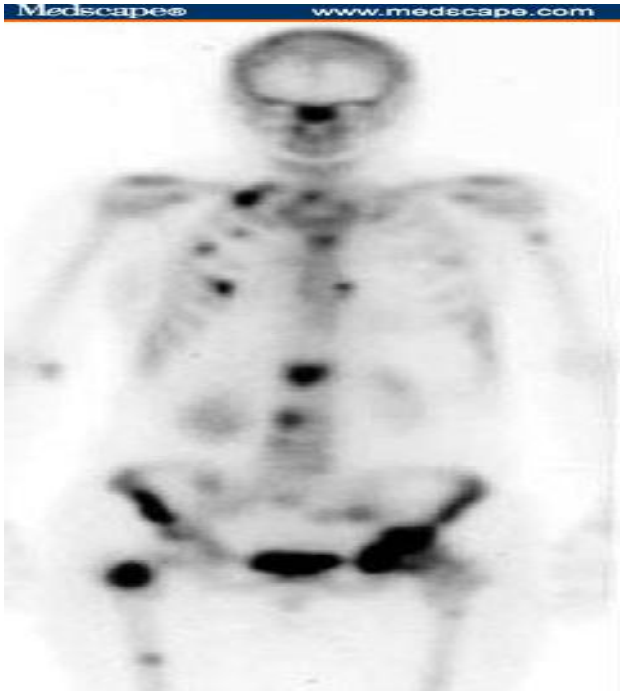
PET Scan in patient with breast cancer that has spread to bones.
Thin arrows show abnormal sites of uptake in spine and lower right pelvis.
Thick arrows show normal PET scan apperance of right & left kidney as well as bladder



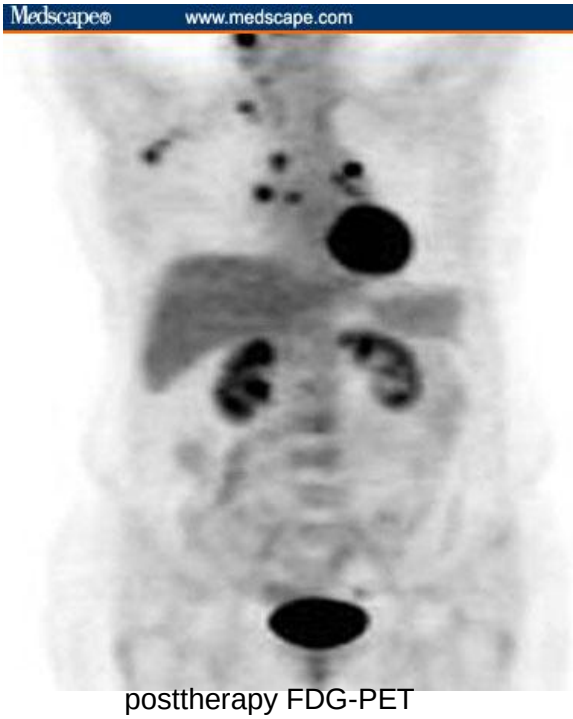
A 46-year-old woman with history of left breast cancer initially treated with lumpectomy and radiation therapy. (a) Follow-up computed tomogram shows irregular soft tissue density in the left breast. Post therapy changes cannot be distinguished from possible local recurrence. (b) Bone scintigraphy was negative. (c) FDG-PET demonstrates hypermetabolic anterior chest wall recurrence.



A 57-year-old woman with history of metastatic left breast cancer. (a) Bone scintigraphy shows widespread osseous metastases. (b) FDG-PET shows extensive soft tissue metastatic lesions in addition to a similar distribution of osseous metastases as seen on bone scintigraphy.



pretherapy PET demonstrate extensive metastatic nodal disease of the neck, axilla, and mediastinum



posttherapy FDG-PET

5) Nuclear Medicine or Single Photon Emission Computed Tomography:

- Scintimammography using technetium Tc 99m sestamibi (MIBI).
- This agent is the only agent to receive FDA approval for breast cancer detection.
- Uptake of MIBI appears related to angiogenesis, and the degree of mitotic activity
- Does not appear to be affected by breast density
- lower sensitivity in smaller tumors, imperfect specificity

6) Bone scan:

Perform a bone scan if any of the following conditions are present:

- Advanced local disease
- Lymph node metastases
- Distant metastases
- Bony symptoms

Mammographic Features of Breast Cancer

<<Note: it is recommended that you download the electronic copy of this lecture to have mammograms of better quality>>

Mammography is unchallenged as a screening test for the early detection of breast cancer. No other imaging technique matches its ability to find small cancers. Some of these criteria are extensively accurate. They are divided into major signs of malignancy (conventional signs) and supporting signs of malignancy (indirect signs).

Major Signs:

1. Spiculated Margins:

Spiculated margins are a true diagnostic feature of malignancy. Strands of tissue are seen radiating out from an ill-defined mass, producing a stellate appearance (Fig. 1a,b). This appearance is pathognomonic of breast cancer. Spiculations represent retraction of tissue strands towards the tumor due to fibrosis - as a result of desmoplastic response. Sometimes, only the spiculations are seen (Fig. 1c).

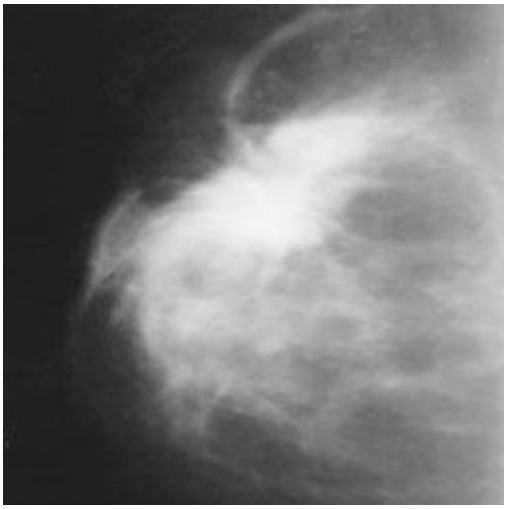


Fig 1a: Mass with spiculated margins

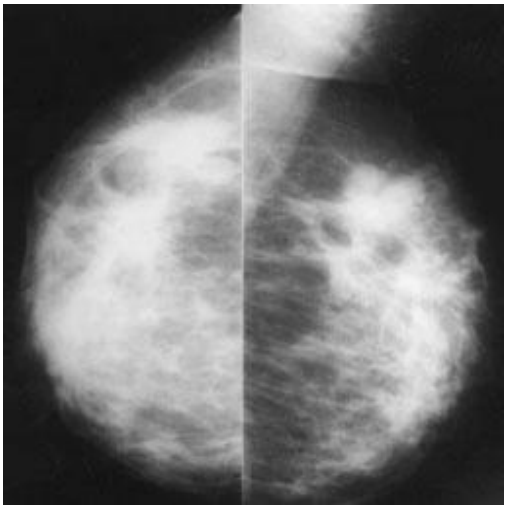


Fig 1b: Multiple SOLs with spiculations.

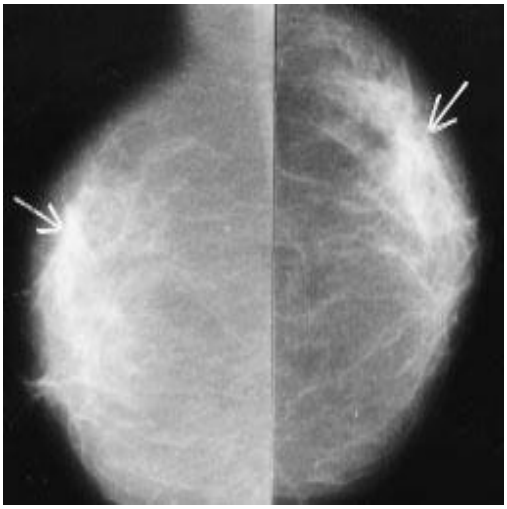
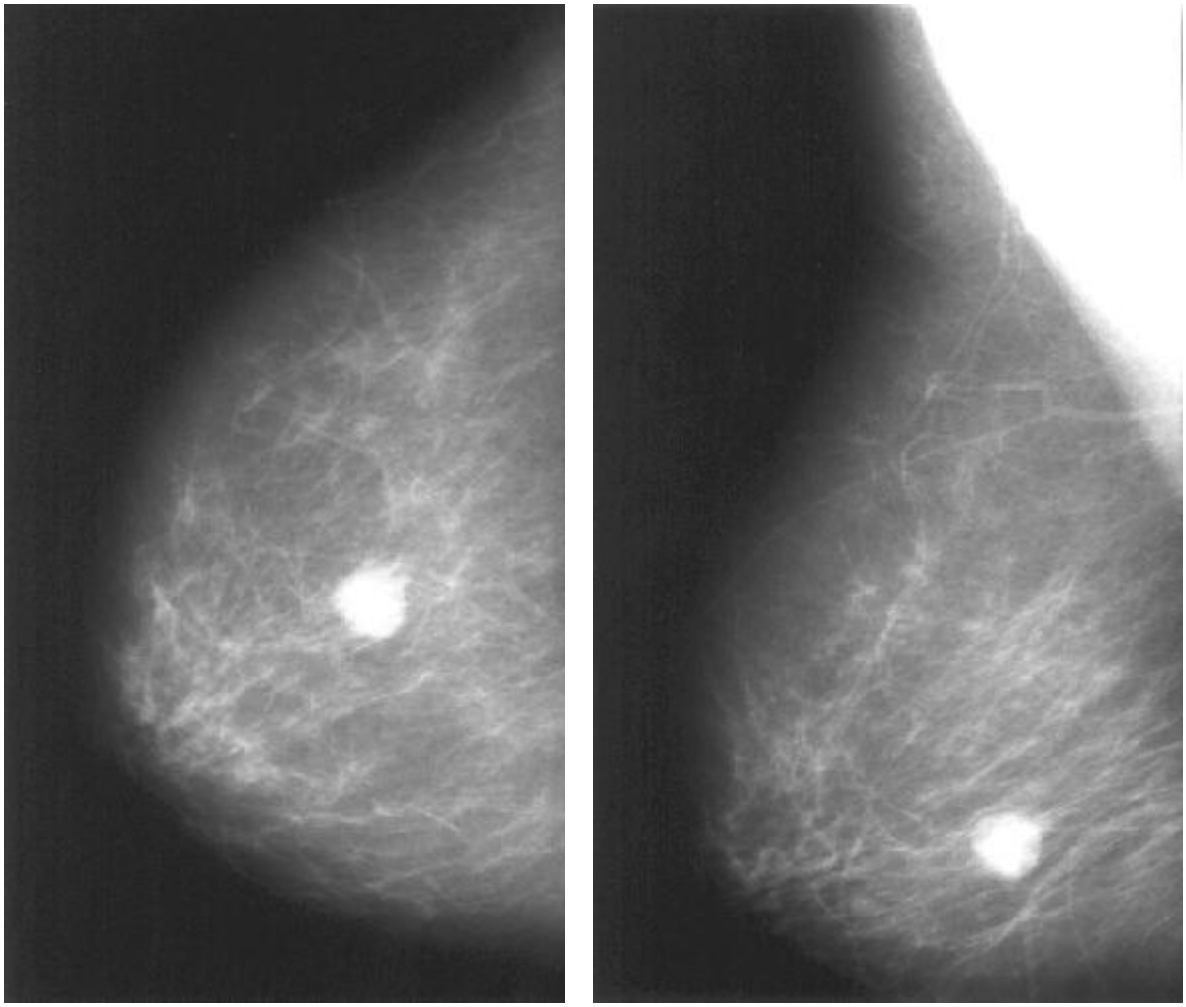


Fig 1c: Only spiculations seen, no definite mass lesion seen



speculated masses

2. Clustered Microcalifications:

Mammography is the only technique capable of detecting microcalcification (Fig 2a). Microcalcification, even when found in isolation they indicate the presence of early stage breast cancer. Five or more calcifications, each measuring less than 1mm, in a volume of one cubic centimeter, define a 'cluster'. The possibility of malignancy increases as the size of individual calcification decreases, the total number of calcification per limit area increases (Fig. 2b, 2c). It is the distribution and morphology of the calcifications, which defines their significance.

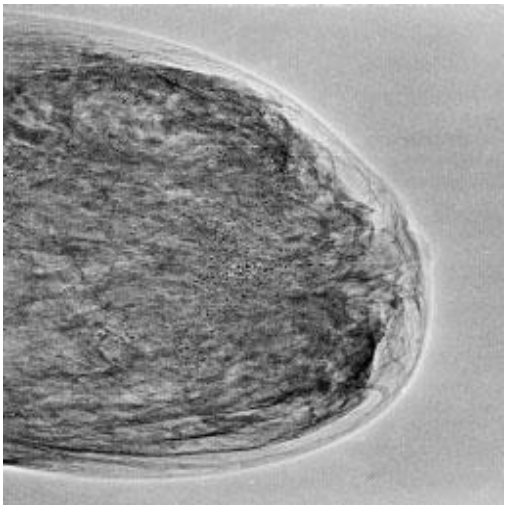


Fig 2a: Microcalcification seen on a xeromammogram

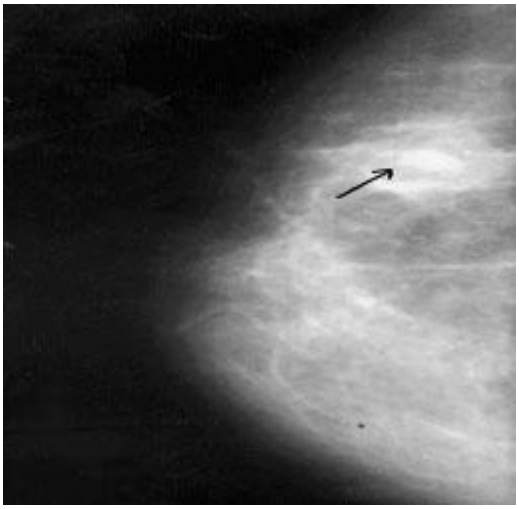


Fig2b: 'Clustered' heterogeneous calcifications.

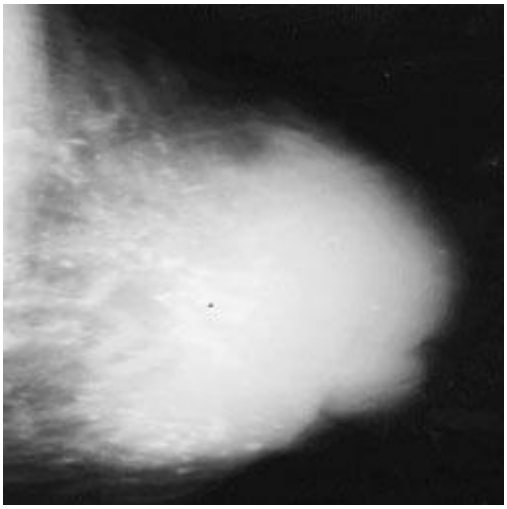


Fig 2c: Microcalcification – heterogeneous in size and shape.

Supporting Signs of Malignancy

These indirect signs, though non-specific, signify enough risk to warrant intervention.

1) Poorly Defined Mass

Most breast cancers are seen as poorly defined masses, without any mammographic features more suggestive of malignancy (Fig 3a). Circumscribed masses with margins that are mostly well defined with only a portion ill-defined, are also managed as other ill-defined masses (Fig. 3b). There are a sizable number of benign breast masses whose margin appears to be poorly defined, and therefore are difficult to differentiate

from malignancy resulting in the need to biopsy in order to detect early cancer.

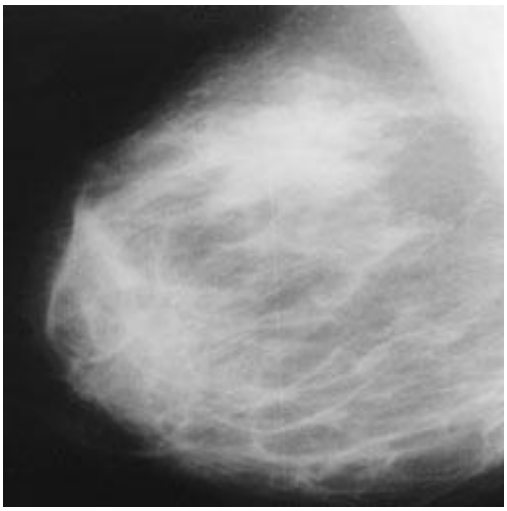


Fig 3a: An ill-defined mass in the right breast.

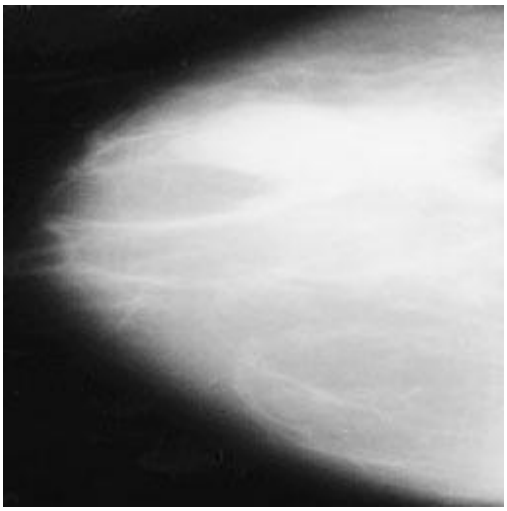


Fig 3b: Mass with an ill defined posterior margin.

2) Microlobulation

Lobulations are usually associated with fibroadenomas. Increased number of lobulations, measuring few millimeters should be suspected for malignancy (Fig. 4a, 4b).

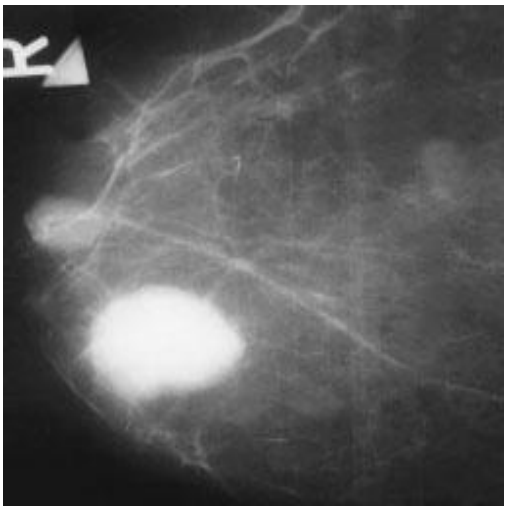


Fig 4a: Mass with microlobulations.

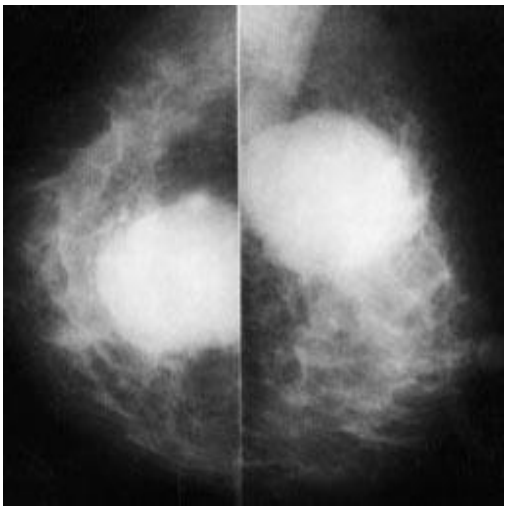


Fig 4b: Mass with microlobulations, antero-inferior margin.

3) Architectural Distortion

Breast cancer does not always produce a mammographically visible mass. Sometimes it produces just a localized cicatrization (Fig 5a,b). If previous surgery and trauma to the breast can be excluded, there is high likelihood that the distortion is because of malignancy. Invasive carcinoma distorts the interface between breast and normal parenchyma due to desmoplastic response of host tissue to the malignancy.

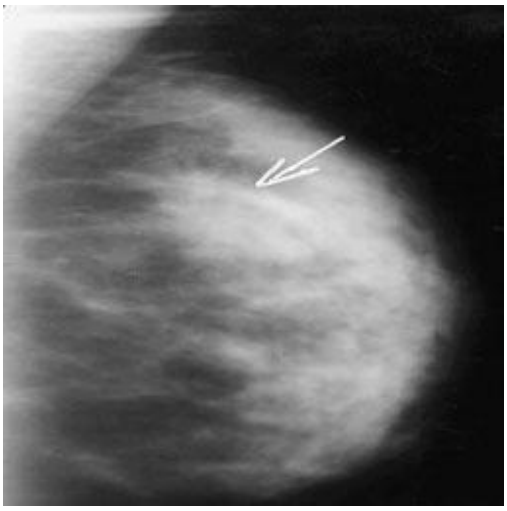


Fig 5a: Architectural distortion seen in the cranial aspect of the breast.

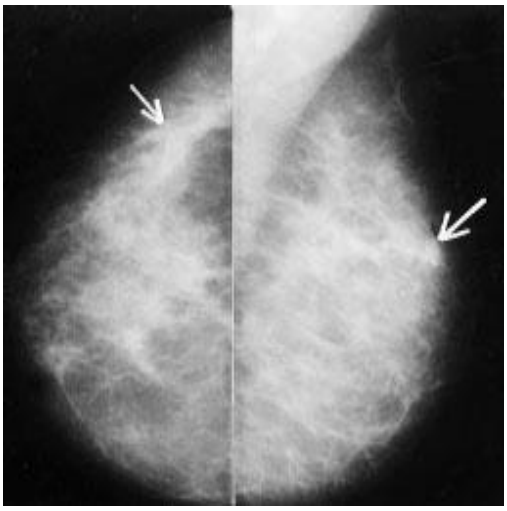


Fig 5b: 'Cicatrization' seen in upper outer quadrant of the breast.

4) Asymmetric Density

Asymmetric density is the three dimensional area in which the density is greatest at the centre and fades towards the periphery trying to form a mass (Fig 6 a,b). In this situation, it is helpful to to view the mammograms of both breasts side by side (Fig. 6a*, 6b*).

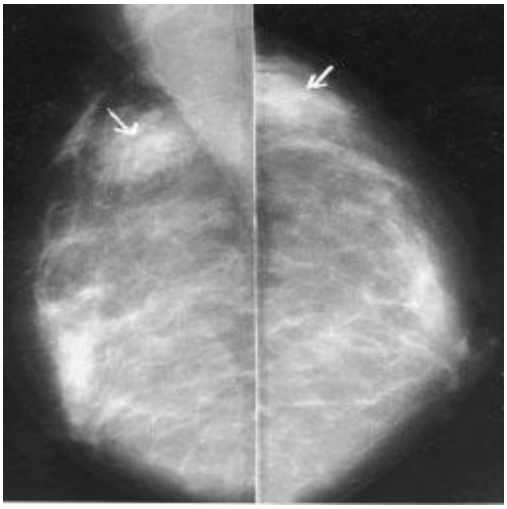


Fig 6a: Asymmetric density, upper-outer quadrant of the breast.

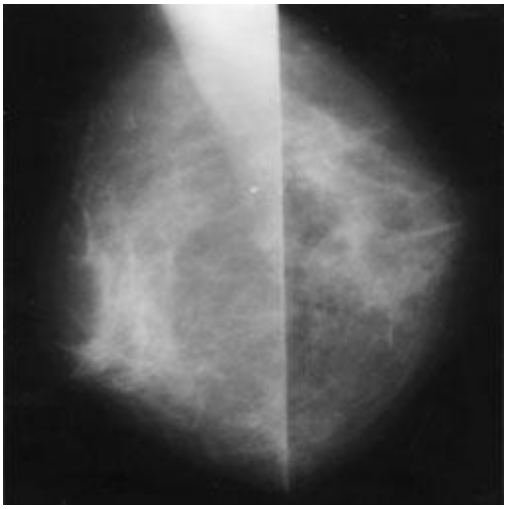


Fig 6a*: Mammograms of other breast for comparison.

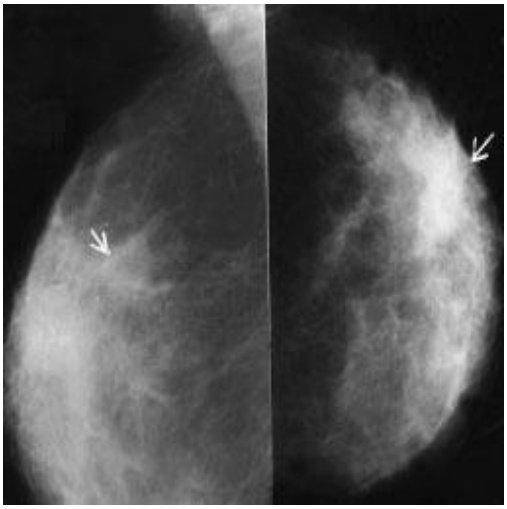


Fig 6b: Asymmetric density seen in the parenchyma.

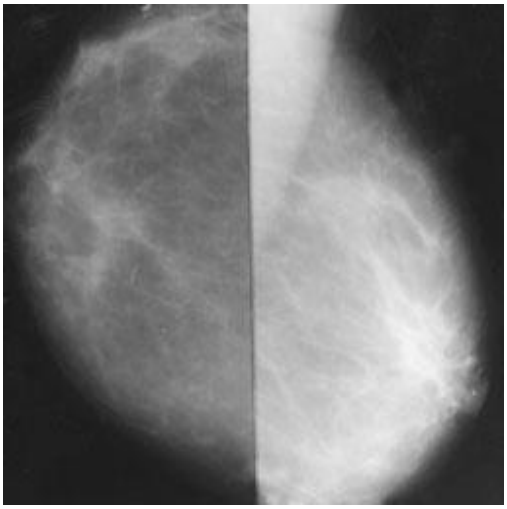


Fig 6b*: Mammograms of other breast for comparison.

5) Nipple Retraction

Nipple retraction "over a short period of time " is suspicious of an underlying cancer (Fig 7 a,b) .

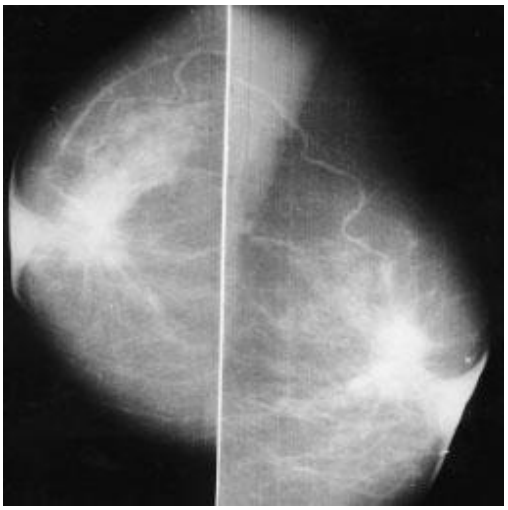


Fig 7a: Retraction of nipple in three months duration.

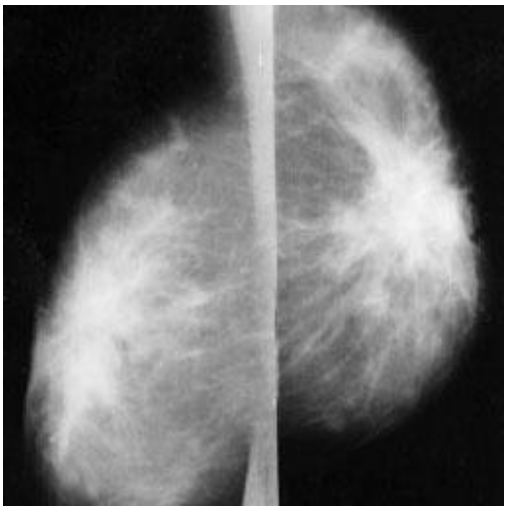


Fig 7b: Retraction of the nipple caused by underlying spiculated mass

6) Enlarged Axillary Lymphnodes

Demonstration of large nodes is non-specific sign of malignancy. Involvement of the nodes(s) indicates worsening of prognosis (Fig 8).

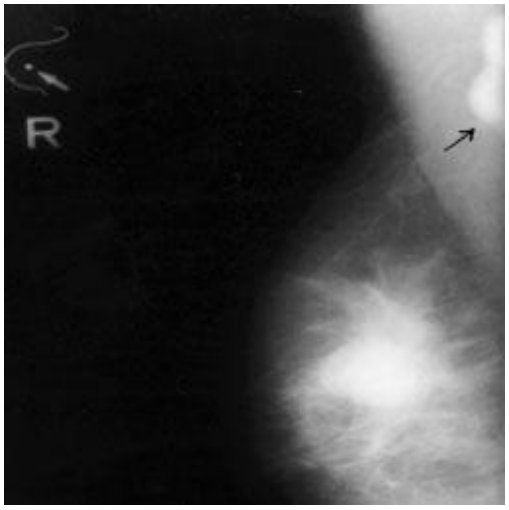


Fig 8: Enlarged node (malignant on FNAC) in a case of carcinoma of the breast .

Table 1: TNM staging system for breast cancer[1]

Stage	Tumour status*	Node status†	Metastasis status‡
0	Tis	N_0	M_0
I	T_1	N_0	M_0
IIA	T_0	N_1	M_0
	T_1	N_1	M_0
	T_2	N_0	M_0
IIB	T_2	N_1	M_0
	T_3	N_0	M_0
IIIA	T_0	N_2	M_0
	T_1	N_2	M_0
	T_2	N_2	M_0
	T_3	N_1	M_0
	T_3	N_2	M_0
IIIB	T_4	N_0	M_0
	T_4	N_1	M_0
	T_4	N_2	M_0
IIIC	Any T	N_3	M_0
IV	Any T	Any N	M_1

*Tumour status: Tis = carcinoma in situ; T_0 = no evidence of primary tumour; T_1 = tumour ≤ 2 cm in greatest dimension; T_2 = tumour > 2 cm but not > 5 cm in greatest dimension; T_3 = tumour > 5 cm in greatest dimension; T_4 = tumour of any size with chest-wall extension, ulceration, peau d'orange or inflammatory breast cancer.

†Node status: N_0 = no regional lymph-node metastasis; N_1 = metastasis in movable ipsilateral axillary lymph node(s); N_2 = metastases in ipsilateral axillary lymph nodes fixed or matted, or in clinically apparent ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph-node metastasis; N_3 = metastasis in ipsilateral internal mammary lymph node(s) or in ipsilateral supraclavicular lymph node(s).

‡Metastasis status: M_0 = no distant metastasis; M_1 = distant metastasis.

بسم الله الرحمن الرحيم

Maha Naim Al-Said
Dr Jamal Masa'd

Skin lesion

SCC: squamous cell carcinoma, BCC: basal cell carcinoma, tu: tumor, malig: malignant, ben: benign, carc: carcinoma, Dx: diagnosis, DDx: differential diagnosis, Hx: history, Bx: biopsy, usu: usually, esp: espicially, ttt: treatment, pt: patient, vls: vessels, #: number, FU: florouracil, grp: group, thru: through, bt: between, BK: the name of a family affected by the disease

-]The commonest non pigmented/ non melanotic skin tumor that are confusing in Dx:
  1. SCC, malig.
  2. BCC, locally malig.
  3. keratoacanthoma, ben.
- Pattern of growth is very important:
  To reach 1cm in diameter SCC needs 3-6m, BCC needs up to 12-18m, while keratoacanthoma needs 2-3w.

BCC

-It is a locally malig lesion (not carc in situ)
-It is called a rodent ulcer coz it invades & infiltrates downward to the bone & brain.
-It is the commonest skin tu that occurs in fair, outdoor workers, living in tropical areas who expose to UV light (UV light impairs local immunity in the skin & it has a carcinogenic effect, so we see BCC in Australia but in Scotland the incidence reach 1/10 that of Australia coz there is no sun most of the year).
-It usu occurs in exposed area of the body; esp the area above a line drawn from the angle of the mouth to the ear lobule, but below this line is the area of SCC (there is some exception).

- Types:

1- Nodular: there is no break in the epithelium, shiny, pearly white, and leash of vls creeping from adjacent skin or there is telangectasia. It will end by ulceration but usu it tends to heal.
2- Ulcerative: beaded edge (rolled), shiny, filled with granulation tissue, infiltrating.
3- Pigmented form: it is one of the DDx of melanoma, shiny, leach of vls, rolled edged ulcer.
4- Papule scarely tissue/morpheic/atrophic (not elevated) /geographical BCC.
ttt: difficult to Dx exise with a safety margin.

Treatment:
1) X ray electron beam a session every day for 2-3w. It is sensetive to radiotherapy coz it is a cutaneous lesion.
2) Exision under local anasthesia with a safety margin of 0.5-1cm. Sometimes it comes in areas as nasolabial region esp in old age, that will induce cosmotic problems such as cartilage & eye necrosis if radiotherapy is used.
3) mofs
4) 5-FU topical application (virabameel is the trade name)
*Indications: a) multiple #.
b) Pt is not fit for surgery.
c) Morpheic type.

Example on it is Xeroderma pigmentosum: it is a genetic problem, the pt here is liable to skin tu.

SCC

1) Nodular: not shiny, fungating occurs in the teeth's technician coz of X-ray exposure.
2) Fleshy form
3) Ulcerative: a) typical: with everted edge.
b) Marjoleen ulcer: which developped in pt with:
1. chronic osteomylitis
2. Long standing venous ulcer.
3. Old burn or scar.
4. Irradiated area

** ttt of which is exision with a safety margin larger than BCC safety margin not by

radiation in order not to damage the skin.

Keratoacanthoma

-It is a rapidly growing tu, has a steady course, resolves spontanously within 12-18m but no body will wait unless he is sure about the Dx but it is sometimes difficult to Dx it clinically & histologically so u need to exise it although it has no malig potential.

-It has a rolled not beaded edge, with a higher shoulder than BCC.

- It has a keratinous material (not granulation tissue)

❖ Pigmented non melanotic skin lesion:

1. BCC
2. Hystiocytoma/Hystiocytosis: increase sclerosing to the angioma, its color is similar to the skin but as the # of non obliterated vls increase it appears more pigmented.
3. Pyogenic granuloma: it is a wet shiny lesion that look like a granulayion tissue, occurs in response to long standing infection on the face & the dorsum of the hand.

→ If can't Dx it clinically take a Bx.

❖ Seborrhoeic keratosis: non melanotic skin lesion, brownish in color rough surface occur in older age grp, it looks as if it is sitting on the skin not coming out of it. The pt comes complaining of that these warts stick to his cloth. Most of the time occurs at the back.

❖ Bowen's disease/Erythroplasia of keratocyte: it is an infective erythematous skin lesion that occurs mostly in the groin, anal area & glans of penis. It is a carc in situ (malig cells don't invade surrounding tissue). To Dx it take an exisional Bx.

>>>Exam question: all of the following is carc in situ except: Pajet's disease, erythroplasia of keratocyte, Bowen disease, Hunshiston frade, BCC.

Naevi

- Naevi: pig lesion thru the neural crest these naevi migrate along the nerve to reach their disteny at the junction bt the dermis & epidermis.
  - Freckle: increase production of melanin
  - Lentigo: increase # of melanocytes.
- It could be nodular or flat. If its size is 2-3mm in diameter, or it is multiple & present in many sites this is considered normal & the malig potential is negligible.

** Types: 1) junctional: normally the melanocytes present in the basal layer of the epidermis, & when they stay around the junction bt the epidermis & dermis they r called junctional naevi. At the age of puberty there is no need to worry if there is a junctional activity but if the age is 40-50 yr we should worry about its malig potential.
2) Compound naevi.
3) Intradermal naevi.

- Naevus of spit/Juvenile melanoma: it is an ugly nodular lesion that presents at the line of maturation occurs in young age grp 10-12yr old may has a junctional activity; it is not a melanoma & has no malig potential.
- Congenital naevus خلقي: could be small or large ($100cm^2$) or giant ($>100cm^2$ with a high chance of malig so we exise it down to the subcutanous tissue). This naevus continue to grow as the child is growing without problem. if the child stop growing but the naevus continue its growth this will be a big problem.
- Dysplastic naevi/BK mole: they r large multiple lesion with a high malig potential. It is difficult to exise them so we observe them & do comparasion.
- Halo naevus: there is a halo around it, coz some of the naevus disappear due to immune response or spontanous resolution of melanoma.(most of immune therapy research is carried on melanoma so IL &INF r used as active vaccination against melanoma)

Melanoma

- Phases:

1. Superficial spreading melanoma: u can see it but can't feel it, then it may become nodular
2. Acral lentigo.
3. Hunshiston trade (care in situ)
4. Nodular: either de novo or on top of superficial spreading melanoma

It is a flat lesion, if it is 3-4mm in diameter it is considered a benign lesion but if it is 6-7mm in diameter this is a crucial situation.

- Indication of removing any lesion is its size (not if it becomes itchy, more pig, ulcerated or bleed), coz melanoma has a horizental &vertical growth.
- Melonoma is quite low in Jordan.
- It is associated with a satellite lesions present within 5cm of the 1° tu that is called intransient metastasis this occurs as the malig cells migrate thru the lymphatic vls to reach the L.N, they r arrested inbt the L.N & the 1° tu & peirce the lymphatics (it is difficult to manage).

Ttt: exision with a safety margin which depends on the size; it is 2-2.5cm in nodular type &1cm in superficial spreading melanoma.then either close the defect primarily or use a graft or a flap.(if the pt is under a spinal anaesthesia we take the graft from the other limb in order not to induce intransient metastasis).

Tumor thickness is important in the prognosis (Clarck & Breslow &clays classification)

Survival of stage I melanoma

thickness	5 yr	10 yr
<0.8	>95	95
0.8-1.6	85	75
1.6-3.6	70	60
>3.6	40	30

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من صالح دعائكم

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