Pathology of the breast

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Structure of tutorial

- Predominantly breast cancer
- Anatomy of breast
- Types of lumps in breast
- Features of benign and malignant lumps
- Clinical assessment, symptoms and signs
- Genetic and hormonal factors
- “Carcinoma in situ” and carcinomas
- Aetiology, risk factors and epidemiology
- Staging and management
What is the structure of the breast?

Name 5 types of benign breast lump that may be confused with cancer
• Paired glands between 2nd and 6th ribs
• Covered with skin
• Lie on the pec major muscle between two fascial layers which are connected by suspensory ligaments (of Cooper)
• Hierarchical structure, alveoli, lobules, lobes, ducts, sinuses, nipple
• Glands and stroma surrounded by fat
• Blood from subclavian
• Lymph drainage to axilla (97%) and int mammary
95% of breast lumps are either:

- Carcinoma of the breast
- Cyst
- Fibroadenosis (fibro-cystic disease)
- Fibroadenoma
Other breast lumps

- Skin lumps (benign and malignant)
- Thrombosis of the superficial veins of the breast or chest wall (Mondor’s disease)
- Lipoma
- Abscess
- Fat necrosis
- Duct papilloma
- Sarcoma (rare)
- TB, rib tumour
Fibroadenoma
Fat necrosis
Implant rupture
Name 3 features of benign lumps and 3 characteristics of malignant lumps

Name 5 clinical signs on examination related to breast cancer (other than a lump)
Clinical History

- Duration Sx, presentation, pain etc.
- Previous breast disease or breast trauma
- Menarche / menopause
- Parity, breast-feeding.
- Medications (OCP, HRT)
- Family history
Clinical Examination

- Chaperone
- Inspection of breasts
- Patient sitting up, fully exposed
Clinical examination

- Any previous mastectomy scars, Bx sites.
- Nipple tethering/retraction/inversion/discharge.
- Peau d’orange, skin reddening.
- Paget’s disease of the nipple.
- ?? ulceration.
- And usual, signs of metastatic disease
Clinical examination

If a mass is felt note:

- Site, size, shape, surface, surroundings
- Consistency, ?transillumination
- Tenderness
- Fixation, tethering, mobility
- Single or multiple lesions

**Benign** - painful, smooth, regular, no skin dimpling or nipple retraction, cyclical changes

**Malignant** - painless, hard/irregular/fixed
Clinical Examination

- When examining axilla, support the weight of the ipsilateral arm
- All four quadrants + axillary tail
- Is there matting of LNs?
Clinical Examination (4)

• Don’t forget to examine the liver.
• As well as the other major systems.
Nipple retraction
Dimpling/Tethering
Peau d’Orange
Paget’s disease of the nipple

Almost invariably sign of underlying invasive cancer or DCIS
Paget’s disease of the nipple
Nipple discharge (1)

- 1. Blood-stained:
  - Duct papilloma
  - Intraduct carcinoma (DCIS)
  - Paget’s disease
  - Invasive carcinoma (unusual)
Nipple discharge (2):

- 2. Serous: early pregnancy
- 3. Yellowish, brown, green: fibroadenosis (duct ectasia)
- 4. Milky: galactorrhoea after lactation, also hyperprolactinaemia (e.g. from pituitary adenoma/drugs)
- 5. Purulent: breast abscess
What happens at the one-stop breast clinic?

How are asymptomatic lesions picked up?
Triple assessment

- Clinical examination - lump and regional nodes
- Imaging (ultrasound <35 yrs, mammogram >35 yrs)
- FNA or biopsy
  - C1=inaadequate
  - C2=definitely benign
  - C3=probably benign
  - C4=probably malignant
  - C5=definitely malignant
Screening

• Started in 1989
• 50-69 year olds invited for mammogram every 3 years
• If abnormal, further assessment by FNAC or core biopsy
• Common exam question - Wilson criteria for a screening test
Name 5 factors known to increase risk of developing breast cancer (excluding genetics)

Name 3 factors with a protective effect against developing breast cancer
Breast Carcinoma

- Britain has highest breast cancer mortality
- Increasing in incidence.
- Uncommon in <30s.
- Disease of ‘Western world’
  (Incidence higher in N America / Europe vs Asia and Africa)
Breast carcinoma: risk factors

- Advanced age
- Born in N Europe or N America (esp if white and high social class)
- Previous breast/endometrial/ovarian carcinoma
- Pre-existing proliferative disease
- Chest wall irradiation
- Family history (any first degree relative)
- Early menarche, late menopause.
- Nulliparity
- First child over 30
- Postmenopausal obesity
- High unsat fat diet, physical inactivity
Breast carcinoma: protective factors

- Age at first period >15 years
- Breastfeeding more than 1 year
- Unsaturated fat rich diet
- Physical activity
Pathogenesis

- Genetic mutations
- Hormonal influences
- Environmental influences
Name 3 genetic factors or inherited syndromes conferring an increased risk of breast cancer
Genetic factors

- As with all cancers, breast ca is the result of multiple genetic changes or mutations
- Hereditary breast cancers represent a small proportion (around 10%)
- Mutations in BRCA1 and BRCA2 responsible for ~ 40% inherited cases
- BRCA1 ~80% risk at 80 yrs
- BRCA2 25-30% breast ca risk in female carriers, also increased risk of male breast ca and other cancer types
- Li Fraumeni syndrome
- Cowden disease, Peutz-Jehgers, Muir-Torre
Name 3 cellular mechanisms involved in breast carcinogenesis

What is the clinical significance of HER2 and c-erbB2?
Mechanisms of breast carcinogenesis

- Loss of cell cycle and growth control, hyperplasia, dysplasia
- Oestrogen receptor lost in a third of breast cancers and a third of ER+ve recurrences
- No apoptosis when hormones limiting
- Loss of cell adhesion molecules
  - E-cadherin lost early in lobular carcinoma
- HER2 encodes epidermal growth factor receptor (EGF-R), abnormal oncogene product c-erbB2
Morphology

- Ductal carcinoma in situ (DCIS)
- Lobular carcinoma in situ (LCIS)
- Invasive ductal carcinoma
- Invasive lobular carcinoma

90% of carcinomas are DUCTAL, lobular carcinoma
~1%, all other types have much better prognosis
Terminal Ducto-Lobular Unit
DCIS

- Solid-type DCIS
- Comedo-type (comedo-carcinoma)
- Cribriform-type
- Papillary

- May be associated with microcalcification
- Usually associated with a mass. May be multifocal (rarely bilateral)
DCIS
DCIS (2)
DCIS (3)
Paget’s disease of the nipple
(+ HMWCK immunohistochemistry)
INVASIVE DUCTAL CARCINOMA
Tumour Grade (Histological)

- Modified Bloom-Richardson system:
  - TUBULES (1-3) +
  - PLEOMORPHISM (1-3) +
  - MITOSES (1-3)

- Grade 1 = 3-5
- Grade 2 = 6-7
- Grade 3 = 8-9
Invasive lobular cancer (lobular carcinoma in situ)
LCIS
LCIS (2):
INVASIVE LOBULAR CARCINOMA
Tubular carcinoma has a better prognosis...
Colloid / mucinous carcinoma

As

Does

Mucinous

Carcinoma
What are the management options for breast cancer?

Give three contra-indications to breast-conserving surgery
Treatment of breast carcinoma:
surgery

- Breast conserving surgery (BCS)
- Wide local excision (WLE)
  +/- axillary sampling (at least four nodes)
  or axillary clearance

- Contra-indications to BCS
  - Pregnancy
  - Previous irradiation to breast
  - Multifocal/diffuse disease (including carcinoma in situ)
  - Positive margins/residual disease after BCS
  - Tumours >5cm*
  - Very large or very small breasts*
Lymphoedema after axillary surgery
Treatment of breast carcinoma:

- Modern treatment based on multimodal approach combining surgery, chemo, RT and HT
- Chemotherapy (CMF) / Radiotherapy
- Tamoxifen (if ER +ve)
- Arimidex (if ER +ve, postmenopausal and contraindication to Tamoxifen)
- Herceptin (if HER2 positive)
ER immunohistochemistry
Herceptin
Spread of breast carcinoma

- **Direct**: skin, pec major, seratus anterior, chest wall
- **Lymphatic**: skin (Peau d’orange), axillary, internal thoracic. Later to supraclavicular, abdominal, mediastinal, groin, contralateral nodes.
- **Blood stream**: lungs, liver, bones (sites of red bone marrow) brain, ovaries, adrenal glands.
- **Trans-coelomic**: pleural (effusion) and peritoneal (ascites) in advanced disease.
Staging workup

• FBC, LFTs
• CXR
• CT scan
• Bone scan
• Liver USS
Staging breast carcinoma (TNM)

- **Stage 1** - Tumour less than 2cm in diameter with no LN involvement

- **Stage 2** - Tumour 2-5cm with or without LN involvement

- **Stage 3** - Tumour cells spread to axillary LN’s but not to other parts of the body

- **Stage 4** - The cancer cells spread to other parts of the body
What have we talked about?

- Anatomy of breast
- Types of lumps in breast
- Features of benign and malignant lumps
- Clinical assessment, symptoms and signs
- Genetic and hormonal factors including HER2
- Difference between DCIS and LCIS
- Mastectomy vs breast conservation
- Chemo, hormonal therapy and Herceptin
Questions?