

BREAST

MUSEUM CATALOGUE

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Department of Pathology, University of Adelaide, 2004

BREAST

INTRODUCTION

The pathology of the breast is of importance because of the prevalence of breast carcinoma in the Australian population. However, you not only need to understand breast carcinoma, but also the common benign conditions that may present as lumps in the breast, causing a considerable amount of understandable anxiety in affected women. As you progress in your learning, it is useful to get some idea of the more important subtypes of breast carcinoma with their associated prognostic implications.

The bulk of the breast is composed of adipose tissue. Within the adipose tissue are a number of essentially separate large branching glands, each draining into a lactiferous duct emerging independently at the nipple. The ducts branch successively and entering into the terminal ducts are a number of alveoli or acini, which develop into the secretory portions of the gland upon appropriate hormonal stimulation. The terminal duct and its acini comprise the terminal duct lobular unit. The acini and ducts are lined by two layers of cells. The outer flattened layer is myoepithelial in nature, these cells have a contractile function. The inner layer is epithelial. Surrounding the acini is a specialised loose connective tissue. During pregnancy and lactation, the histological appearance of the breast changes considerably, the acini proliferating such that most of the adipose tissue becomes replaced by glandular tissue.

Breast lesions may arise from the epithelial elements and/or the stromal (connective tissue) elements of the breast. Most epithelial pathologies are thought to arise from the epithelium of the terminal duct lobular unit.

Any comments on this catalogue are welcome. Please contact a member of the department.

HOW TO USE THIS CATALOGUE

This catalogue can be used as a tool to develop your knowledge, as well as provide an opportunity for revision.

It is divided into:

- Introduction and approach to specimens (pages 105-107).
- Index (page 108). Examples of specific diagnoses can be found via the index.
- Core and classic disease processes (pages 109-117). This gives examples and discussion of core and/or classic diseases of the breast. These are the specimens that students should focus on being able to identify initially. However, it depends to some extent on what you have covered in lectures and practical classes or resource sessions as to what you should know. Some of the specimens and discussion are directed more towards clinical medical students.
- Main catalogue (pages 118-126). This section covers the specimens in numerical order. Questions and/or comments accompany some of the specimens to help you expand your knowledge. In order to fit more specimens in the museum, not all of the pots are in numerical order on the shelves, and large specimens are often found on the bottom shelves.

You might find it useful to work quietly with a few friends and to have a few textbooks handy (e.g. pathology, medical, anatomy). As well as learning pathology, you will also find that you can learn and revise some anatomy and clinicopathological correlation from the specimens and information given.

You do not have to examine every specimen in the museum. However, just as in clinical practice, you will not become proficient in diagnosing a condition if you have only seen one case. Exposure to a variety of cases (specific diagnoses can be found via the index) to experience the variability in morphology will help your learning greatly. In general the red and blue dots on the pots indicate basic and straightforward pathology, whereas yellow dots tend to indicate less readily diagnosable conditions. This is not a hard and

fast rule, and you will find yellow dot specimens turning up in resource sessions/practical classes and even exams, if they represent classic pathology.

In general

- read the clinical information given
- look at the entire specimen, not just the front
- identify and orientate the organ or tissue (where possible)
- identify the abnormality and from your knowledge of pathology (which will come with time) look for relevant features to help you make the diagnosis. Of course to appreciate the abnormal you first need to have an appreciation of normal anatomy
- make a diagnosis or differential diagnosis using any clinical information given to you – it is often relevant – sometimes the diagnosis is only made with a knowledge of the clinical features. Even when you know the diagnosis, attempt to identify relevant features in the specimen and understand why this is the diagnosis.
- attempt to correlate the pathological features with the clinical features (clinico-pathological correlation) i.e. explain how the pathological features have caused the patients symptoms and signs (when relevant)
- try to answer any questions presented yourself before reading the answers.

You may prefer to look at the specimen 'blind', without reading the clinical information given first.

Limits to diagnosis on macroscopic examination

In all cases a diagnosis is given, but it is important to realise that sometimes the final diagnosis was only made based on the clinical history and histological examination. In some cases the macroscopic appearance is classic and even without the history and histology you should be able to make the diagnosis from the appearance, in others, it might only be possible to give a list of differential diagnoses or a more general diagnosis.

Remember that some of these specimens are very old, and some of the investigations and treatments mentioned may be out of date.

BASIC APPROACH TO THE INTERPRETATION AND DESCRIPTION OF BREAST PATHOLOGY SPECIMENS

Students are expected to be able to give a brief succinct description of relevant macroscopic features of a specimen using appropriate terminology and to arrive at a diagnosis or differential diagnosis. Specimen description is helpful in the diagnostic process as it prompts you to look for relevant diagnostic features.

Your descriptive skills will improve with practice. Some pathological abnormalities, whether macroscopic or microscopic, are easy to recognize, but even so, make sure you understand why this is the diagnosis and be able to recognize and describe the features, such that you can defend your diagnosis if necessary.

The basic approach is similar to that for all specimens and includes the famous rules:

- Always look at the front of the pot first (i.e. the one with the number and the dot)
- Having said that, always make sure to look at the back and sides as well
- If there is more than one tissue specimen in a pot it is there for a reason and that reason is to help you with the answer
- Describe the obvious

In breast pathology the specimen is always a breast or part thereof \pm overlying skin \pm nipple. There may also be some other related tissue in the pot. Once you have determined what tissues are present, the next decision to make is what abnormality is present and whether it is focal or diffuse/multifocal.

Focal lesion

These are probably the easiest and consist of single abnormalities that anyone can point to with confidence and say "This is the abnormality". Having identified the abnormality, you then have to describe it:

- Colour: What colour is it? Is it all one colour or is it many colours (variegated)? Does it look homogenous (all the same the whole way through)?
- Size: You can give a measurement but don't get too obsessive
- Shape: A term that can be useful in describing some breast lesions is stellate (star shaped). A stellate lesion is likely to be a carcinoma (though not all carcinomas are stellate), with numerous infiltrative arms extending into the normal breast tissue.
- Consistency: This is of course difficult to assess when the specimen is in a pot and you are unable to touch it, although it can be useful when assessing fresh specimens. But even just by looking you can get some idea. Many breast carcinomas are firm and fibrous, described as schirrous. The fibrosis results from the florid desmoplastic response that occurs in and around the lesion. Necrosis suggested by focal areas of friability or grey discoloration may be present.
- Margins: Margins can be helpful in deciding if a lesion is likely to be benign or malignant. The best way to think of them is as being either well defined or well demarcated – i.e. is there a clear line between the lesion and the adjacent normal tissue – or diffuse/irregular where the line between the lesion and the adjacent normal tissue is harder, perhaps impossible, to trace. Malignant lesions typically have diffuse/irregular or infiltrative margins. Benign tumours tend to have well defined or sometimes encapsulated (surrounded by a rim of fibrous tissue) margins. However, you won't be surprised to hear that there are exceptions to this rule: certain malignant tumours have deceptively well-defined margins and some benign lesions may have irregular poorly defined edges.

Multifocal

This means that there is more than one distinct lesion within the specimen. All the above comments regarding the description of focal lesions apply here as well. In addition, it may be important to note any differences between the lesions.

Diffuse

In the case of breast pathology this usually means that there is either a widespread disease process such as fibrocystic change or a focal lesion that involves a large portion of breast.

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CORE AND CLASSIC DISEASE PROCESSES

FIBROCYSTIC CHANGE

CASE 9292

Clinical information

The patient was a woman aged 48. For 20 years she had had "chronic interstitial mastitis" and on 4 occasions lumps had been removed for biopsy. Both breasts were involved and each was removed by simple mastectomy, leaving the nipple and a small amount of breast tissue.

Describe the specimen

The specimen shows the two breasts bisected. Each contains many simple cysts with smooth linings varying in size up to 4cm in diameter that are embedded in dense fibrous tissue. The upper specimen also shows two small areas of haemorrhagic fat necrosis, each about 5mm in diameter.

What is the diagnosis?

Fibrocystic change of the breast

Comment

Fibrocystic change is an extremely common condition in women, mainly occurring in the mid-late reproductive years. There is variable fibrosis, duct dilatation with cyst formation and variable epithelial hyperplasia. It may cause a generalised lumpiness to the breast, a single lump or a thickening that is poorly circumscribed. A single lump may be caused by a predominant cyst. Its significance is in the fact that it can cause lumps that need to be distinguished from malignant lumps. In general it is not a risk factor for developing carcinoma. However, sometimes the epithelial hyperplasia is severe or atypical in type (diagnosed histologically) and this signifies an increased risk of developing malignancy.

FAT NECROSIS

CASE 8628B

Clinical information

No clinical information is available.

Describe the specimen

The specimen consists of a slice of tissue from the breast that contains a rounded focally encapsulated nodule 2.5cm in diameter. The cut surface is granular with some haemorrhage and degeneration at the lower pole.

What is the diagnosis?

Fat necrosis

What causes fat necrosis of the breast?

The cause is often unknown but there may be a history of trauma, prior surgery or radiotherapy. Rupture of fat cells releases lipid into the tissues, triggering an inflammatory response followed by organization with repair.

What type of inflammatory response develops?

A granulomatous inflammatory response develops with multinucleate giant cells, macrophages, lymphocytes and fibrosis, often with cholesterol crystals, the latter formed following degeneration of cell membranes.

What is the significance of fat necrosis of the breast?

Its main significance is that it causes a mass that needs to be distinguished from a malignancy.

FIBROADENOMA

CASE 16882

Clinical information

The patient was a young woman aged 19 who developed a mobile lump in the left breast. The lesion was excised.

Describe the specimen

The specimen shows part of an oval tumour that measures 4.5cm in maximum diameter. The cut surface is pale, firm and somewhat lobulated. The reverse of the specimen shows it to have a smooth surface. There is little surrounding breast tissue.

What is the diagnosis?

Fibroadenoma

What age range does this typically affect?

Fibroadenomas tend to occur in young women (age generally 20-35).

What changes occur in this condition?

These are very well circumscribed benign lesions, usually less than 3cm in diameter, comprising both fibrous and glandular elements, demonstrating a loose fibrous stroma containing numerous benign breast ducts.

CARCINOMA OF THE BREAST

CASE 19578

Clinical information

The patient was a woman aged 65. Seven years previously she had been given radiotherapy for an adenocarcinoma of the cervix. A pelvic recurrence developed 5 years later, but hormone treatment produced some symptomatic improvement. A year later a tumour was noted in the right breast and lesions were also found in the cervical, lumbar and thoracic spine and the humerus. On her last admission there was a mass in the right iliac fossa, the liver was palpable 2 fingers below the costal margin and there was a vesico-vaginal fistula. She died a few days later from renal failure secondary to ureteric obstruction caused by recurrent adenocarcinoma of the cervix in the pelvis.

Describe the specimen

The specimen consists of a portion of breast tissue with overlying skin sectioned through the nipple. Within the normal fatty breast tissue is a pale stellate schirrous tumour measuring at least 60mm in maximum diameter. The nipple is markedly retracted by the tumour beneath it and there is thickening of the overlying skin.

What is the diagnosis?

Carcinoma of the breast with nipple retraction and possible skin invasion.

Comment

This tumour demonstrates the typical schirrous stellate appearance of primary ductal carcinoma of the breast. Many malignancies (not just breast) induce fibrosis around them (termed desmoplasia) from release of inflammatory mediators by the tumour itself or from surrounding inflammatory cells. The fibrosis gives the tumour a hard consistency, leading to the classic macroscopic descriptive term schirrous.

Note how difficult it is to assess the size of the tumour macroscopically. Small groups of tumour cells can infiltrate widely. Microscopic measurement is more accurate.

The breast is a very rare site of metastases.

CASE 13152

Clinical information

No clinical information is available.

Describe the specimen

The specimen consists of a slice of breast together with overlying skin and underlying pectoral muscle as well as a separate group of axillary lymph nodes. Within the breast is a large pale irregular infiltrating tumour mass approximately 6.5cm in maximum diameter. Nodules of tumour are also seen within the underlying muscle. The axillary nodes are enlarged and pale.

What is the diagnosis?

Carcinoma of the breast with involvement of the pectoral muscle and lymph node metastases

What are the predisposing factors for and pathogenesis of this disease?

Genetic factors: as with all neoplastic lesions, the tumour develops as a result of alterations in a variety of genes influencing cell proliferation

- sporadic cases: various alterations in tumour suppressor genes and proto-oncogenes are identified
- familial cases: approx. 13% of patients have one or more first degree relatives that have had the disease: generally unknown or multiple genes are involved

A few % of familial cases are transmitted in an autosomal dominant fashion from germline inheritance of certain altered tumour suppressor genes:

- BRCA-1, ovarian cancers also
- BRCA-2, increased risk of male breast cancer also
- p53 -> LiFraumini syndrome, patients may also get brain tumours
- others

One mutation is inherited, the other is acquired during the patient's lifetime, leading to loss of function.

The lifetime risk of developing breast cancer in women with germline mutations is 60-85%. Young women developing breast cancer are especially likely to have a germline mutation.

Oestrogen

- oestrogen metabolites may -> DNA alterations and many tumours are oestrogen driven (oestrogen receptors)
- increased lifetime oestrogen exposure predisposes: early age of menarche, late age of menopause, nulliparous or late age of first birth, use of HRT, postmenopausal obesity
- breast feeding appears to be protective

Previous breast pathology

- more severe degrees of epithelial hyperplasia, especially atypical epithelial hyperplasia
- lobular or ductal carcinoma in situ
- invasive breast cancer

Environmental, geographic, racial and dietary influences: greater incidence in developed countries

How may this disease present clinically?

As with any malignancy it may present with symptoms related to local disease e.g.

- breast lump (most common)
- nipple retraction, changes in overlying skin, nipple discharge

or to metastatic disease e.g.

- axillary lump
- bone pain
- breathlessness
- anorexia, lethargy

It may also be detected following mammographic screening.

What features influence the prognosis and treatment of this disease?

- the histologic type
- the histologic grade (generally determined using Elston's/Nottingham modification of the Bloom and Richardson system in which degree of tubule formation, nuclear pleomorphism and number of mitoses are assessed)
- the stage
 - TNM classification commonly used, it incorporates:
 - the size: several prognostic groups: <2cm, 2-5cm, >5cm, with direct extension to chest wall or skin

- lymph node spread: axillary or internal mammary. The number of lymph nodes involved and whether there is extracapsular spread is also important.
- the presence or absence of more distant spread
- the presence or absence of oestrogen and progesterone receptors
- age of the patient
- the presence or absence of c-erbB-2 (neu/HER-2) proto-oncogene amplification
- others, including
 - the extent of associated in situ carcinoma
 - the presence or absence of microscopic vascular invasion

What is c-erbB-2 (neu/HER-2) and what is its role in breast cancer?

This is a proto-oncogene that encodes an epidermal growth factor receptor. In approx. 25% of cases of breast carcinoma the gene is amplified resulting in excessive copies of the protein being made -> over stimulation of cell growth. Tumours demonstrating amplification of HER-2 appear to have a worse prognosis than others. The number of copies of the gene can be assessed by FISH (Fluorescence in situ hybridisation) and protein content by immunohistochemical techniques. Monoclonal antibodies have been developed that target the protein and prevent its function, a novel new therapy.

What histological types of this disease are there?

The vast majority of breast carcinomas are adenocarcinomas of which there are a variety of different types.

- Invasive ductal carcinoma (commonest). These may be subdivided further: most are of the usual, classic or not otherwise specified type, but other types include tubular, mucinous (e.g. specimen 11299), medullary and papillary. Tubular and mucinous breast carcinomas generally have a very good prognosis. Invasive ductal carcinomas are often stellate in appearance macroscopically and very fibrous or schirrous.
- Invasive lobular carcinoma (of which there are also various subtypes)

What is a phyllodes tumour?

Phyllodes tumours (specimen 16199) are typically well-circumscribed lesions comprising both stromal and glandular elements. It is primarily a neoplasm of the specialised breast stroma, the epithelial proliferation is probably not neoplastic, being induced by the stromal proliferation. The stromal element is more cellular than that of a fibroadenoma and the stromal cells can show varying degrees of atypia and mitotic activity, correspondingly, some (most) behave in a relatively 'benign' or low grade fashion, though local recurrence is not uncommon, others in a more aggressive malignant fashion.

PAGET'S DISEASE OF THE NIPPLE

CASE 22912

Clinical information

The patient was a woman aged 80 who died from congestive cardiac failure with terminal pulmonary embolism. On admission it was noted that her right nipple was reddened and eczematous, but she could not say for how long this condition had been present. No mass was felt in the breast on examination.

Describe the specimen

The specimen consists of a breast viewed from the front. The nipple is flattened, widened and darker than normal. The areola and surrounding skin are also discoloured and crusted.

What is the diagnosis?

Paget's disease of the nipple

What is this condition and how does it arise?

Paget's disease of the nipple is associated with underlying in situ ductal carcinoma, with or without stromal invasion. Malignant cells extend along the ducts up to the nipple where they infiltrate the epidermis, causing inflammation and oozing. In some cases, such as here, the cells invade beyond the nipple into the epidermis of the areola.

What is in situ carcinoma? Can it metastasise? If not, why not?

The term in situ carcinoma is generally equivalent to severe dysplasia and refers to a proliferation of abnormal epithelial cells which exhibit the cytological features of malignancy, marked architectural disorganisation and lack of maturation, but which have not invaded through the epithelial basement membrane. As a result the lesion cannot metastasize as the cells cannot reach lymphatic or blood vessels.

Comment

In situ carcinoma can also arise in other areas where dysplasia occurs e.g. the bronchi, epidermis, cervix and oesophagus. The malignant cells have acquired various mutations that allow them to proliferate but they have not yet acquired the ability to invade. However, if untreated, they may eventually do so.

GYNAECOMASTIA

CASE 18231

Clinical information

The patient was a man aged 76 who collapsed and died soon after the repair of a ruptured iliac aneurysm. He had been receiving stilboestrol (oestrogen) for carcinoma of the prostate.

Describe the specimen

The specimen shows a section of breast with overlying skin including the nipple. Beneath the nipple is a diffuse area of pale, firm, rubbery and slightly lobulated breast tissue.

What is the diagnosis?

Gynaecomastia

What is gynaecomastia and what are its causes?

Gynaecomastia refers to enlargement of the male breast resulting from a proliferation of both stromal and glandular tissue. It generally arises as a result of imbalances between oestrogenic and androgenic hormones, with relative oestrogen excess. This may occur at puberty, in cirrhosis, in Klinefelter's syndrome, with taking exogenous oestrogens or with oestrogen producing testicular or adrenal tumours. Other causes include prolactin excess from pituitary adenomas and certain drugs including spironolactone, chlorpromazine and digitalis. Many cases have no identifiable cause.

Does carcinoma of the breast occur in men?

Yes, but it is rare. Lesions tend to be more locally advanced at the time of diagnosis than in women, presumably related to the lesser amount of breast tissue and closeness of the lesion to chest wall and skin.