

CASE FIVE

Short case number: 3_11_5

Category: Endocrine and Reproductive

Discipline: Surgery

Setting: General Practice

Topic: Breast cancer – new diagnosis

Case

Rhonda Wong, aged 58 years, presents anxiously for the results of her mammogram. The results report an irregular spiculated mass with microcalcifications that are branching. A follow up ultrasound demonstrated poorly defined margins and heterogeneous internal echoes.

Questions

1. Outline your further assessment and management of Rhonda in terms of history, examinations and investigation.
2. Briefly describe ductal carcinoma in-situ; infiltrating ductal carcinoma; infiltrating lobular carcinoma; tubular carcinoma; medullary carcinoma; colloid carcinoma; papillary carcinoma; inflammatory carcinoma and Paget's Disease of the nipple.
3. Summarise the TNM Staging system for breast cancer
4. Outline the treatment of breast cancer in terms of surgery, chemotherapy, hormone therapy and radiation.
5. List the common complications of surgical, chemotherapy, hormonal and radiation therapy in breast cancer and their relative frequency.
6. List the key prognostic factors for breast cancer.

Suggested reading:

- Henry MM, Thompson JN, editors. Clinical Surgery. 3rd edition. Edinburgh: Saunders; 2012. Chapter 28.
- Garden OJ, Bradbury AW, Forsythe JLR, Parks RW, editors. Davidson's Principles and Practice of Surgery. 6th edition. Philadelphia: Churchill Livingstone Elsevier; 2012. Chapter 19.

ANSWERS

1. Outline your further assessment and management of Rhonda in terms of history, examinations, and investigation.

The most important part of the diagnostic process will be to gain a tissue diagnosis, using the most appropriate sampling technique. Factors that will influence this are:

- Risk factor assessment for breast cancer
- General medical history
- Presence /absence of a palpable lump
- Examination for evidence of metastasis

2. Briefly describe ductal carcinoma in-situ; infiltrating ductal carcinoma; infiltrating lobular carcinoma; tubular carcinoma; medullary carcinoma; colloid carcinoma; papillary carcinoma; inflammatory carcinoma and Paget's Disease of the nipple.

Carcinoma in situ

Carcinoma in situ (CIS) refers to the period during which normal epithelial cells undergo apparent malignant transformation but do not invade through the basement membrane. There are two forms:

- lobular (LCIS)
- ductal (DCIS), representing all types of CIS that are not identified as lobular. It can be further subdivided into:
 - comedo
 - solid
 - cribriform
 - micropapillary.

More recently, as for invasive cancers, a formal grading system has been introduced for in-situ disease. However, the distinction remains primarily between LCIS and DCIS, although comedo DCIS is a particularly menacing type of CIS. Necrosis and microcalcification are common and, because the second may be seen on mammography, the incidence may be increasing as earlier diagnosis becomes more widespread. By contrast, LCIS is not associated with any radiological markers and therefore may not be detected early.

The ratio of DCIS to LCIS is 3:1, and approximately 10-37% of those with LCIS and 30-50% of those with DCIS go on to develop invasive carcinoma.

With LCIS, future cancers may be in either breast regardless of the site of the in-situ changes. A further confounding statistic is that approximately 50-65% of future malignancies are of ductal origin, which indicates that LCIS is a marker of increased risk of diffuse bilateral disease as opposed to a true anatomic precursor of lobular cancer.

However, with DCIS, the subsequent malignancies are ductal in origin, arise in the ipsilateral breast and usually are confined to the same quadrant from which the biopsy which yielded the diagnosis was taken.

Infiltrating Ductal Carcinoma

This is the commonest form of cancer of the breast—approximately 80%. The most common form is of non-descript but highly variable histological type. Sheets, cords, nests and trabeculae of tumour cells may be present all in varying amounts. If the main bulk of tumour is of this type then the presence of more-specific histological features in small amounts does not appear to alter the prognosis.

Medullary

This form constitutes about 6% of the total. Histologically, it has completely circumscribed borders with a syncytial sheet-like growth pattern, a diffuse infiltrate of lymphocytes and a variable number of

plasma cells. Nearly 50% of these tumours are associated with intraductal carcinoma, usually at the periphery of the main tumour.

Colloid (mucinous)

Largely confined to the elderly population, this tumour accounts for approximately 2% of breast cancers. Histologically, large pools of mucin are surrounded by variable groups of tumour cells. The classical signet ring appearance of mucinous tumours in other sites is not seen in breast colloid carcinoma.

Tubular

Clinically, tubular carcinoma is found in younger than average patients, with the late 50s being the peak age, the diagnosis usually being made at mammography. In consequence, the lesion is still small (less than 1 cm), and up to a fifth of breast tumours identified at mammography may be of this type. Histologically they are well differentiated and have randomly arranged tubular elements in a loose stroma.

Papillary

This accounts for less than 2% of cases of breast carcinoma and usually presents in the seventh decade. Histologically, it is well circumscribed with marked papillary differentiation.

Inflammatory breast carcinoma

This tumour accounts for 1% or slightly more of breast carcinomas. It is rapidly progressive and is characterised by erythema, peau d'orange and skin ridging with or without a palpable mass. Unlike other breast cancers, the commonest presenting feature is pain. The characteristic appearance of a diffusely enlarged breast is consequent upon the dissemination of tumour cells through the lymphatics of the dermis. If the tumour cells remain within the superficial lymphatics and the blood vessels, then a condition known as telangiectatic carcinoma may arise with numerous purple papules and haemorrhagic, vesicle-like lesions covering the breast. Extensive involvement along tissue planes may produce a nodular pattern or, when associated with extensive fibrosis, a diffuse thickened lesion-a thoracic girdle (carcinoma en cuirasse).

Paget's disease

This condition presents clinically as a chronic, eczematoid eruption of the nipple. Indeed the diagnosis may be confused with eczema although there are distinct differences. It constitutes approximately 2% of histological types and is almost always associated with an underlying intraductal or invasive carcinoma.

3. Summarise the TNM Staging system for breast cancer

The international TNM classification allows grouping of the disease into clinical stages. Staging allows comparison between groups of patients and also defines those unsuitable for an attempt at surgical removal but who may be suitable for the other forms of adjuvant therapy.

TNM classification of breast cancer

TNM stage Pathological description

Tis	Carcinoma in situ (pre-invasive) Paget's disease (no palpable tumour)
T0	No clinical evidence of primary tumour
T1	Tumour less than 2 cm
T2	Tumour 2-5 cm
T3	Tumour greater than 5 cm
T4	Tumour of any size but with direct extension to chest wall or skin: (a) Fixation to chest wall (b) Oedema, lymphocytic infiltration, ulceration of skin or satellite nodes

	(c) Both (a) and (b)
N0	No palpable ipsilateral axillary lymph nodes
N1	Palpable nodes not fixed: (a) Inflammatory only (b) Containing tumour
N2	Fixed ipsilateral axillary nodes
N3	Ipsilateral supraclavicular or infraclavicular nodes or oedema of arm
M0	No evidence of distant metastasis
M1	Evidence of distant metastasis

Stage and prognosis according to TNM classification

UICC stage	TNM	Category	5-year survival
I	T1, N0, M0	Early cancer	84%
II	T1, N1, M0 T2, N0-1, M0	Early cancer	71%
III	Any T, N2-3, M0 T3, any N, M0	LABC	48%
IV	Any T, any N, M1	Metastatic	18%

4. Outline the treatment of breast cancer in terms of surgery, chemotherapy, hormone therapy and radiation.

Breast surgery

The principle of surgery in early breast cancer is to completely eradicate the primary tumour and any local extension.

2 Components – (1) Breast, (2) Staging of axilla, or if clinically positive, an axillary dissection

1. Breast

TOTAL MASTECTOMY

Involves complete excision of the breast and nipple with preservation of the underlying pectoral muscles. This used to be standard therapy, but it now reserved for:

- Large cancers relative to breast size
- Cancer that involves the nipple or overlying skin
- Multifocal disease
- Prior breast irradiation
- Women who chose not to have breast conservation or breast radiotherapy

RADICAL MASTECTOMY

Involves excision of the breast together with pectoralis minor and major. Used in

- Locally advanced disease that involves these muscles

BREAST CONSERVATION SURGERY

This involves complete local excision of the primary breast tumour with clear margins. Whole breast adjuvant radiotherapy must be given post-op.

2. Axilla

AXILLARY staging- Aims:

- Assess nodal status for prognosis
- Assess nodal status to determine adjuvant systemic therapy

- Axillary dissection for clinical positive axilla (palpable nodes or pre-op abnormal ultrasound/biopsy/metastases) OR finding of a positive sentinel LN biopsy

Radiotherapy

Is indicated following breast conservation surgery, and reduces the risk of local recurrence. The use of radiotherapy after mastectomy is more limited.

Adjuvant Systemic Therapy

The aim is to eradicate micrometastases. Adjuvant systemic therapy with tamoxifen, with combination chemotherapy (most commonly CMF) or, in premenopausal women, ovarian ablation, reduces the risk of recurrence and death after treatment for node positive and node negative breast cancer.

Ovarian Ablation (in some cases)

Ovarian ablation in premenopausal women is associated with an improvement in recurrence –free and overall survival. The benefits are greater in tumours which are oestrogen receptor positive.

Ovarian ablation is achieved by surgical oophorectomy, ovarian irradiation or by using luteinising hormone releasing hormone (LHRH) analogues e.g. goserelin

5. List the common complications of surgical, chemotherapy, hormonal and radiation therapy in breast cancer and their relative frequency.

COMPLICATIONS OF SURGERY

Mastectomy/breast conservation therapy

- Breast haematoma
- Wound infection
- Seroma
- Psychological effects on body image

Axillary dissection

- Seroma of the axilla
- Limited shoulder movement
- Pain and numbness from division of the intercosto-brachial nerve
- Lymphoedema of the arm

COMPLICATIONS OF RADIOTHERAPY

- Redness and soreness of the field of radiation
- Lymphoedema after treatment of the axilla
- Breast-feeding from the affected breast is unlikely
- Cardiac damage following left breast irradiation
- Brachial plexus palsy
- Osteitis of the ribs
- Shoulder stiffness
- Pulmonary fibrosis

COMPLICATIONS OF ADJUVANT SYSTEMIC THERAPY

Chemotherapy

- Nausea, vomiting, lethargy, alopecia, early menopause, anxiety
- Mucositis and diarrhoea
- Febrile neutropenia
- Cardiac toxicity

Tamoxifen

- Hot flushes, vaginal discharge

- Increased incidence of endometrial cancer in post-menopausal women (protective effect greatly outweighs risk)
- Increased risk of coronary artery disease, stroke, TIA

6. List the key prognostic factors for breast cancer.

Prognostic variables other than TNM in breast cancer

Biological factors	Favourable	Unfavourable
Histological type	Tubular, colloid, papillary	Scirrhou
Size	Small	Large
Grade	Low (I)	High (III)
Necrosis	Absent	Present
Lymphocytic infiltration	Present	Absent
Oestrogen status	Positive	Negative
involved lymph nodes	absent	present
Proliferative rate	Low S phase	Aneuploid
Chromosomal defect		Deletion/alteration 1, 3, 6, 7, 9
		Shortening of allele on chromosome 11
Proto-oncogenes		c-erbB/c-H-ras
Growth factors (GF)		Epidermal GF
		Transforming GF
		Platelet-derived GF
		Fibroblast GF
		Insulin-like GF