58 T_h e breast

- Mastitis of infants
- Metastatic carcinoma of the breast (stage IV)
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- Treatment of breast cancer
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Acute inflammation of the breast

Acute inflammation of the breast

Mastitis refers to inflammation of the breast tissue that may or may not be accompanied by infection. Acute mastitis can occur in lactating as well as non-lactating women, with the former being more common. Lactational (puerperal) mastitis The incidence of acute mastitis in lactating mothers varies from 3% to 20%. Most cases are caused by S. aureus and, if hospital acquired, may be to be due to methicillin-resistant S. aureus Aetiology Mastitis may be bacterial or non-bacterial. Bacteria may enter the nipple through a cracked or retracted nipple. In many cases the lactiferous ducts get blocked by epithelial debris, leading to stasis, which is followed by infection. Once within the ampulla of the duct, staphylococci cause clotting of the milk and then multiply within the clot. Abscess formation is most commonly seen at two stages during lactation: in the first month after the first childbirth owing to inexperience or inappropriate and inadequate breastfeeding; and at weaning owing to engorge ment and trauma to the nipple by the baby’s teeth. Clinical features Initially there is generalised cellulitis, which if left untreated progresses to suppuration and abscess formation. An abscess presents as a fluctuant lump (in a deep-seated abscess fluctu ation may be absent) with pain, signs of inflammation, fever, malaise and di ffi culty in feeding. It may also be associated with enlarged tender axillary nodes. Ultrasonography reveals cellu litis (seen as an area of incr eased echogenicity) and liquefaction necrosis (pus is seen as a hypoechoic collection with floating debris that changes with posture). Management During the cellulitic stage, the patient should be treated with anti-staphylococcal antibiotics such as cloxacillin, flucloxa cillin or erythromycin. Breastfeeding from both the breasts should be encouraged 2-hourly , followed by emptying the breast. A breast support garment, cold compression on the breast and analgesia aid in symptomatic relief. Any pus seen on ultrasonography should be aspirated and sent for culture and sensitivity . Contrary to the practice of incision and drainage, in a breast abscess ultrasound-guided drainage gives an excellent cosmetic result, does not hamper breastfeeding and can be done as a day-care procedure with a high rate of non-healing milk fistula. In abscesses >3 /uni00A0 cm in diameter or those containing more than 30 /uni00A0 mL of pus (assessed on ultrasonography), a vacuum suction catheter is inserted under ultrasound guidance to drain 58.5). The patient should be the pus (Figure 58.24 and reviewed on alternate days by clinical examination and ultra - sonography . Any residual collection should be aspirated. The antibiotics are modified according to the microbiological cul - ture report. In patients with a suction drain, the catheter is irrigated with cold normal saline (cold to reduce pain) on each visit until complete resolution. Antibiotics should be continued f or 14 days.

BENIGN BREAST DISEASE Nomenclature

BENIGN BREAST DISEASE Nomenclature

The nomenclature of benign breast disease in the past has been confusing owing to the use of a variety of terms – namely , fibrosis, adenosis, epitheliosis, fibroadenosis and fibrocystic disease – for clinical patterns of pain, nodularity , benign lumps and nipple discharge. However, such terms do not relate to clinical or histological features. Most benign disorders are derived from minor aberrations of the normal process of development, cyclical hormone-related change and involu - tion. To address this confusion, the concept of Aberrations of Normal Development and Involution (ANDI), developed and described by the Cardi ff Breast Clinic in the UK, helps in better understanding and treatment of benign breast disease.

Figure 58.10 Positron emission tomography showing hot spots in the left breast and in axillary lymph nodes in (a) transverse and (b) /uni00A0 coronal view.

The breast is a dynamic structure that undergoes alterations due to the cyclical changes in oestrogen and progesterone in every menstrual cycle. These hormones act as growth factors on the epithelial and stromal cells of the TDLU (The pathogenesis of ANDI involves disturbances in the breast physiology extending from a perturbation of normality to well-defined disease processes.

Breast cancer in pregnancy

Breast cancer in pregnancy

Pregnancy is associated with aggressive tumour biology such as TNBC. Ultrasonography of the breast, mammogram and chest radiograph with abdominal shielding of the fetus may be considered. In cases where bone or brain metastasis is suspected or other investigations are inconclusive, MRI - without gadolinium contrast should be used. CT and PET-CT - should be avoided (high radiation dose). Genetic counselling should be o ff ered. Surgery can be performed in any trimester. Joseph F Fraumeni Jr , b. 1933, National Institutes of Health, Indications for genetic risk evaluation /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Mastectomy is preferred during the first and second trimester as the delay in administering radiotherapy until delivery may be associated with a higher risk of recurrence in the breast. SLNB with low-dose technetium-tagged sulphur colloid is considered safe for the fetus. Chemotherapy should not be administered during the first trimester (period of organo genesis) but can be safely administered during the second and third trimesters (until 34 weeks to allow haematological recovery at the time of delivery). Anthracyclines and taxanes remain the preferred agents. 5-Fluorouracil should be avoided. Anti-HER2/neu and endocrine therapy should be given after delivery , as indicated.

An individual at any age with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene within the family Breast cancer diagnosed age ≤ 50 years TNBC diagnosed age ≤ 60 years Two breast cancer primaries Breast cancer at any age with one or more relative with breast cancer diagnosed ≤ 50 years, invasive ovarian cancer, male breast cancer, pancreatic cancer, high-grade or metastatic prostate cancer Breast cancer at any age with two or more affected relatives Male breast cancer An individual with a personal or family history of three or more of the following: Breast cancer, sarcoma, adrenocortical carcinoma, brain tumour, leukaemia Colon cancer, endometrial cancer, thyroid cancer, kidney cancer, dermatological manifestations, macrocephaly or hamartomatous polyps of the gastrointestinal tract Lobular breast cancer, diffuse gastric cancer Breast cancer, gastrointestinal cancer or hamartomatous polyps, ovarian sex chord tumours, pancreatic cancer, testicular Sertoli cell tumours or childhood skin pigmentation

CARCINOMA OF THE BREAST

CARCINOMA OF THE BREAST

Breast cancer is the most frequent cancer among women, with an estimated 2.3 million new cases diagnosed worldwide in 2020, representing about 25% of all cancers in women. Inci dence rates vary widely across the world, from 27 per 100 /uni00A0 000 in Middle Africa and East Asia to 92 per 100 /uni00A0 000 in North America. In western Europe approximately one in nine women will develop breast cancer, accounting for 3–5% of all deaths in women. In resour ce-poor countries 1 in 28 women will develop breast cancer in her lifetime and for every 2 women diagnosed with breast cancer 1 dies of cancer. Henri Mondor , 1885–1962, Professor of Surgery , Paris, France.

(b) (c) (b) Bluish

COMPARATIVE AND SURGICAL ANATOMY

COMPARATIVE AND SURGICAL ANATOMY

The breast in adult females overlies the pectoral region, extend ing from the second rib above to the sixth rib or inframammary crease below . Medially it extends to the lateral border of the sternum and laterally it reaches the anterior axillary line or the mid-axillary line. In adult males the breast tissue is rudimen tary and about 2 /uni00A0 cm in diameter; it lies deep to the areola and extends up to the areolar edge. The anatomy of the breast is illustrated in Figure 58.1 and 58.1 . The axillary tail of the breast is palpable in some w and can be seen in the premenstrual period or during lactation. A well-developed axillary tail is sometimes mistaken for a mass of enlarged lymph nodes, a breast mass or a lipoma. The breast parenchyma consists of ductolobular and supportive tissue. The terminal ductule together with the lobule constitute the t erminal d uctal l obular u nit, which is referred to by the acronym TDLU. The TDLU is the most active part of the breast tissue and responds to a number of hormones: - namely , oestrogen, progesterone, prolactin and growth hor - mone. There are five to nine major lactiferous (milk) ducts carrying milk from the lobes. Approximately 10–100 lobules empty via ductules into a lactiferous duct. Each lactiferous duct - is lined with a spiral arrangement of contractile myoepithelial cells. Most diseases of the breast arise from the TDLU. About 50% of the ductolobular tissue is located in the upper outer omen quadrant and about 20% in the central region. Hence, during breast examination particular attention must be paid to the upper outer quadrant, r etroareolar region and the nipple– areola complex. The supportive tissue of the breast comprises fibrous tissue in the form of suspensory ligaments of Cooper, adipose

Clavicle Second rib Pectoralis major muscle Intercostal muscle Intercostal vessels and nerves Lung Retromammary fat Sixth rib Figure 58.1 Cross-sectional anatomy of the breast. Types and management of mastitis • Modern management of breast cancer • Pectoral fascia Premammary fascia Suspensory ligament of Cooper Ampulla Nipple and areola Lactiferous duct Mammary lobules Subcutaneous fat

of Cooper are attached to the undersurface of the dermis superficially and to the pectoral fascia deeply . The areola and nipple contain involuntary muscle arranged in concentric rings as well as radially in the subcu taneous tissue. The circular muscle fibres constitute Sappey’s muscle (causes erection of the nipple), whereas longitudinal fibres form the Myerholtz muscle (causes retraction of the nipple). The areolar epithelium contains n umerous sweat glands and sebaceous glands; the latter enlarge during preg nancy and serve to lubricate the nipple during lactation (Mont gomery’s tubercles). The nipple is covered by thick skin with corrugations. Near its apex lie the orifices of the lactiferous ducts. The lymphatics of the breast drain predominantly into the axillary and internal mammary lymph nodes. The axillary nodes receive appro ximately 85% of the lymph from the

breast and are arranged in the following g roups: /uni25CF lateral nodes along the lower border of the axillary vein lying lateral to the thoracodorsal vascular pedicle; /uni25CF anterior or pectoral nodes between the lateral borders of pectoralis major and pectoralis minor and the lateral tho racic vessels; these are the sentinel lymph nodes in most patients; /uni25CF posterior along the subscapular and thoracodorsal vessels just anterior to the latissimus dorsi muscle; /uni25CF a central or medial group of nodes embedded in fat in the centre of the axilla; /uni25CF interpectoral or Rotter's nodes – a few nodes lying between the pectoralis major and minor muscles; /uni25CF apical nodes that lie above and medial to the pectoralis minor tendon and lateral to the first rib; the apical nodes receive the e ff erent lymphatic channels from all the axillary nodes. The apical nodes are in continuity with the supraclavicular nodes and drain into the subclavian lymph trunk, which enters Sir Astley Paston Cooper , 1768–1841, surgeon, Guy's Hospital, London, UK, described these ligaments in 1845. Marie Philibert Constant Sappey , 1810–1896, French anatomist who published his comprehensive atlas in 1874. William Fetherston Montgomery , 1797–1859, obstetrician, Dublin, Ireland, described these tubercles in 1837. Josef Rotter , 1857–1924, German surgeon, described these nodes in the early nineteenth century . Surgically the axillary lymph nodes are classified into three levels: /uni25CF level I , below and lateral to the lateral border of the - pectoralis minor muscle (the majority); /uni25CF level II , in front of and behind the pectoralis minor muscle (including Rotter's nodes); /uni25CF level III , above and medial to the medial border of pectoralis minor. - - The internal mammary nodes lie along the internal mam - mary vessels deep to the plane of the costal cartilages and just superficial to the parietal pleura. These drain the medial half of the breast.

Triple assessment Imaging Pathology Clinical History Ultrasonography Core biopsy Examination Mammography Con /f_i dent diagnosis in 99.9% of cases Figure 58.2 Triple assessment.

Carcinoma of the male breast

Carcinoma of the male breast

Carcinoma of the male breast (Figure 58.39) accounts for less than 0.5% of cases of breast cancer. The most common symp tom at presentation is a painless subareolar lump. Involvement of the nipple–areolar complex and underlying pectoral muscles occurs early . Treatment comprises mastectomy with a 2-cm margin along with a portion of underlying pectoralis major muscle follow ed by radiotherapy . SLNB should be performed in node-negative patients. Tamoxifen 20 /uni00A0 mg daily for 5 years is recommended for those with ER-positive tumours.

Clinical features

Clinical features

The most common manifestations of ANDI are breast pain and benign nodularity . The breast pain usually follows the menstrual cycle, appearing around day 14 and increasing in severity until day 28, when it becomes severe (cyclical pronounced mastalgia with premenstrual exacerbation). Nodularity or lumpiness may be either localised or spread Alexander Tietze , 1864–1927, Professor of Surgery , Breslau, Germany (now Wroc ł aw , Poland), described this condition in 1921. conspicuous in the upper outer quadrant. The nodularity may be cyclical, appearing 1–2 weeks prior to menstruation and regressing with the onset of the menses. A discrete lump in the breast is commonly a fibroadenoma in the young and a cyst in 58.1). the middle-aged.

Clinical presentation

Clinical presentation

A discrete lump in the breast is the most common presentation, and the most common tumour site is the upper outer quadrant of the breast (50% of TDLUs lie there). Other symptoms include nipple retraction, nipple discharge (blood or serous), skin changes such as ulceration, peau d’orange (Figure 58.28), satellite nodules or dimpling/tethering. Peau d’orange is a sign of locally advanced disease due to obstruction of cutaneous lymphatic drainage of the breast, by infiltration of either subdermal lymphatics or axillary lymph nodes by tumour /uni2192 cells. Cancer en cuirasse (Figure 58.29) is due to extensive tumour infiltration of the skin of the breast, chest (in cases of postmastectomy recurrence), upper limb and abdomen. Few breast cancers in high-income countries present with either locally advanced disease or symptoms of metastatic disease; however, the incidence is much greater in resource- poor countries, where up to 60% of women still present late. Enquiry should be made for the presence of any swelling in the neck or armpit and for the presence of any symptoms due to distant metastasis (bony pain, cough, breathlessness, haemop tysis, headache, visual disturbances, neurological deficit, epi leptic fits, abdominal distension, jaundice, anorexia, weakness, weight loss, hypercalcaemia, etc).

Figure 58.29 Cancer en cuirasse: advanced breast cancer with extensive tumour in /f_i ltration of the skin of the breast, upper limb and abdomen.

Congenital abnormalities

Congenital abnormalities

Amazia Congenital absence of the breast may occur on one or both sides. It is sometimes associated with Poland’s syndrome, which is characterised by the absence of the sternal portion of the pectoralis major and short webbed fingers (symbrachydactyly) on the side of the involved breast (Figure 58.21). The breast may be reconstructed with a latissimus dorsi muscle flap and a silicone breast implant.

Figure 58.21 Poland’s syndrome with congenital absence of the left breast and pectoralis major muscle ipsilateral hand (b) . Figure 58.22 Polymazia left side.

Cracked nipple

Cracked nipple

This is observed in about 10% of nursing mothers and is thought to arise from the strong negative force created by suckling. It initiates as a small blister on the nipple that soon ruptures to give rise to a small ulcer. The crack thus formed is often colonised by bacteria or fungi. The microbes from the crack may enter the milk ducts and may progress to lactational mastitis. If the nipple becomes cracked during lactation, it should be rested for 48 hours and the breast should be emptied with a breast pump. The sore nipple should be gently washed with warm water and moisturising soap followed by application of an antimicrobial cream (m upirocin).

Discharges from the nipple

Discharges from the nipple

Most nipple discharges are caused by physiological aberrations as part of ANDI, may emanate from a single or many milk - ducts and may involve one or both sides. The presence of a s ingle, s erous, s anguineous and s pontaneous discharge (‘ four S ’) should be considered pathological and triple assessment should be carried out. Both serous and sanguineous discharges are caused by excessive proliferation of the ductal epithelium, which can be either di ff use or localised or may result from a ductal carcinoma. During pregnancy , the increase in blood flow to the ductolobular tissue may lead to serous or bloody nipple discharge. Hence, a bloody discharge during pregnancy is considered physiological and usually abates spontaneously after childbirth; however, ultrasonography should be performed to rule out malignancy . The clinical significance of the specific colour of the nipple discharge is as follows: /uni25CF A clear, serous discharge is commonly caused by duc - tal papilloma. It is potentially serious and should not be ignored. Multiduct, multicoloured discharge is physio - logical and the patient may be reassured (Figure 58.20). /uni25CF A bloodstained discharge may be caused by a duct papil - loma, carcinoma or duct ectasia. A duct papilloma is usu - ally single and situated in a major milk duct usually within 5 /uni00A0 cm from the nipple. /uni25CF A black, green or muddy-coloured discharge is usually the result of duct ectasia. Galactorrhoea is defined as spontaneous milk discharge from several ducts of both nipples unassociated with childbirth or breastfeeding. It may be associated with a prolactin-secreting adenoma of the pituitary gland. Many drugs can also lead to increased prolactin secretion and galactorrhoea, including haloperidol, chlorpromazine, amitriptyline, metoclopramide receptor antagonists (cimetidine). and H 2 Summary box 58.2 Discharges from the nipple /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF in situ /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Management Triple assessment to exclude carcinoma should be carried out. Ultrasonography may reveal dilated subareolar ducts and a Geo ff rey John Hadfield , 1923–2006, surgeon, Stoke Mandeville Hospital, Aylesbury , UK. Alfred Poland , 1822–1872, surgeon, Guy’s Hospital, London, UK, described this condition in 1841. filling defect indicating a duct papilloma with a diagnostic accuracy of 85%. Ductoscopy (inspection of the internal structure of the duct system) using microendoscopes is technically feasible. Ductog - raphy is currently not practised in most centres because of the poor diagnostic yield. Most breast clinics hav e abandoned the cytological examination of nipple discharge as it has a poor yield for cancer. Non-bloody discharge Simple reassurance may be su ffi cient. However, if the discharge is profuse (wetting of the clothes causing social embarrassment) an operation to remove a 1.5- to 2-cm length of the a ff ected major milk duct (microdochectomy) or ducts (major duct excision) can be performed. Blood or serous discharge The risk of cancer is related to the patient’s age. Patients below 40 years with a bloody discharge and normal triple assessment may be reassured and followed up with annual imaging. Patients over the age of 40 years should be o ff ered microdochectomy for single-duct discharge or Hadfield’s major mammary duct excision for multiduct discharge. A segment of major milk ducts 5 /uni00A0 cm in length from the nipple is usually removed as most duct papillomas are located up

to a distance of 5 /uni00A0 cm from the nipple (58.4).

(d) Figure 58.20 Different types of nipple discharge. (a) serous; (b) pus; (c) bloody; (d) cheesy; (e) greenish; (f) watery. Discharge from a single duct Bloodstained Intraduct papilloma Intraduct carcinoma Duct ectasia Serous (sticky translucent /f_l uid) Duct papilloma Ductal hyperplasia Duct ectasia Ductal carcinoma (and invasive) Discharge from more than one duct Bloodstained Carcinoma Duct ectasia Black, green or muddy Duct ectasia Purulent Periductal mastitis Milk Lactation Galactorrhoea Rare causes: hypothyroidism, pituitary tumour Discharge from the surface (not from within nipple) Paget’s disease Skin diseases (eczema, psoriasis) Rare causes (e.g. chancre) (e) (f)

Discrete lumps in the breast

Discrete lumps in the breast

The main causes of discrete lumps in the breast are listed in Summary box 58.1 . Sometimes a lump appears in the breast evanescent lump . It is caused by an inflammatory mass of periductal mastitis; the lump, pain and tenderness all disappear together. Sometimes, a cyst or a galactocele may rupture; the lump disappears but pain and tenderness appear. The cyst fluid or milk leaking in the stroma may induce inflammation, causing pain and tenderness. Summary box 58.1 Causes of discrete breast lumps /uni25CF - /uni25CF - /uni25CF). - - Breast cysts Breast cysts are common in the 35- to 55-year-old age group and usually present as a painless lump. Several causative factors contribute as part of ANDI, including lobular involu - tion, increased secretion, ductile obstruction, loss of stroma, hyperoestrogenaemia and hormone replacement therapy . Cysts are often multiple, may be bilateral and can mimic malignancy . They typically present suddenly and cause grea t alarm; prompt diagnosis by ultrasonography and aspiration under ultrasound guidance provides immediate relief. A smooth-walled cyst without any solid component in its wall is classified as BI-RADS 2 and requires only observation without biopsy . The presence of a solid component in the cyst wall is classified as a complex cyst and necessitates a core biopsy to rule out cystadenocarcinoma. This should be distinguished from a complicated cyst , which is defined as a cyst contain - ing intracystic floating debris that moves within the cyst with change of posture.

Nodularity 0 1 3 4 Figure 58.13 The Lucknow–Cardiff breast nodularity scale. A visual analogue scale for nodularity: an ordinal scale. 0, normal or non- nodular; 1, minimal; 2, mild; 3, moderate; 4, severe. Benign Malignant Non- Fibroadenoma Carcinoma in /f_l ammatory of the breast (invasive, DCIS) Ductal papilloma Malignant phyllodes Phyllodes Hamartoma Galactocele Breast cyst Haematoma Traumatic fat necrosis In /f_l ammatory Breast abscess (acute in /f_l ammatory, tubercular) Antibioma Periductal mastitis (evanescent mass) Granulomatous mastitis Parasitic: hydatid, /f_i lariasis Fungal: aspergillosis, blastomycosis, Cryptococcus , Histoplasma 2

Treatment A solitary cyst or small collection of cysts may be aspirated if associated with pain or inflammation. If the cyst(s) resolve(s) completely , and if the fluid is not bloodstained, no further treatment is required. Cytological examination of cyst fluid is not useful. If there is a residual lump or if the aspirate is blood stained, a core biopsy or excision for histological diagnosis is advisable. A complicated cyst with associated infection may be treated with a short course of antibiotics. Galactocele Galactocele is rare and usually presents as a solitary subareolar milk-filled cyst seen during or just after lactation. It disappears completely and is usually cured by a single aspiration. If it recurs, it may be reaspirated or a nylon strand (2/0) may be passed to clear the blocked duct. Complications of galactocele are non-resolution because of inspissated material and calcifi cation. Surgical excision is rarely indicated. Lactating mothers should be encouraged to continue breastfeeding. Fibroadenoma A fibroadenoma is the most common cause of a breast lump in women aged 15–25 years. It arises from hyperplasia of a lobule and usually grows to 2–3 /uni00A0 cm in size. It is surrounded by a well-defined capsule. A clinically typical fibroadenoma, confirmed

on ultrasonography , may be observed without a biopsy . A biopsy should be obtained if the patient is over 25 or if there are atypical features on ultrasonography . Regression with antioestrogen drugs has been observed with tamoxifen and ormeloxifene (58.3). Giant fibroadenomas occasionally occur during puberty . They are over 5 /uni00A0 cm in diameter, often rapidly growing and can be enucleated through a submammary incision (Figure 58.14 The RR of cancer with fibroadenoma ranges from 1.5–1.7 if simple to 3.4–3.7 in the presence of epithelial hyperplasia. Complex fibroadenoma with a family history has an RR for cancer of 3.0–4.0, particular ly lobular carcinoma. Indications for surgical excision are: age over 30 years; sus picious features on imaging, such as microlobulation; atypia on histology; size >5 /uni00A0 cm; family history of breast cancer; and the patient's preference. Excision of fibroadenoma in the elderly should include a rim of normal tissue as it may contain malig nancy or a phyllodes tumour. Theodore Gaillard Thomas , 1831–1903, American gynaecologist, Columbia University College of Physicians and Surgeons, New Y ork, NY , USA. - - Phyllodes tumour Previously known as cystosarcoma phyllodes, these benign tumours usually occur in women over the age of 30 years but can appear in younger women and present as a large, some - times massive, tumour with an unevenly bosselated surface (Figure 58.15). Occasionally , the overlying skin is ulcerated owing to pressure necrosis. Despite their size, phyllodes tumours hest wall and rarely infiltrate the skin remain mobile on the c until late. It is a true mixed neoplasm comprising both epithelial and mesenchymal elements and resembling a fibroadenoma. Some have a higher mitotic index with infiltrating borders and). may rarely metastasise via the bloodstream. Phyllodes tumours are classified according to histological behaviour into benign (mitotic rate <4 per 10 high-power fields [HPF]), borderline (mitotic rate 4–9 per 10 /uni00A0 HPF) and malignant (mitotic rate >10 per 10 /uni00A0 HPF) tumours. - Treatment Treatment is by wide local excision (WLE) with a 2-cm margin along with the overlying skin and underlying pectoralis major - muscle because of a high incidence of local recurrence.

Figure 58.14 Giant /f_i broadenoma. (a) Clinical picture; (b) excised specimen; (c) submammary (Gaillard Thomas) incision. Figure 58.15 Phyllodes tumour of the left breast.

Massive tumours, recurrent tumours and those of the malig nant type require mastectomy . Postoperative radiotherapy may be o ff ered to women with recurrent or malignant phyllodes tumours. Systemic chemotherapy may be o ff ered f or malig nant phyllodes.

Figure 58.16 Accessory nipple with congenital inversion of the normal nipple.

Eczema

Eczema

Eczema of the nipple and areola is a rare condition and is often bilateral; it is usually associated with eczema elsewhere on the body . It is treated with 0.1% betamethasone skin cream by local application and by using moisturising soaps. If the nipple fails to heal, Paget’s disease must be excluded by taking a wedge biopsy of the lesion.

FURTHER READING

FURTHER READING

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Follow-up of operable breast cancer

Follow-up of operable breast cancer

Follow-up after initial therapy routinely includes clinical exam ination every 3 months for 2 years, followed by every 6 months for the next 3 years. Thereafter the follow-up is scheduled yearly . A mammogram is also scheduled yearly . Patients with an implant and those with BRCA or other genetic mutations need contrast breast MRI annually . Development of any new symptom or sign during follow-up merits detailed clinical evaluation and relevant investigation. Patients presenting with metastatic disease and those with a local/systemic recurrence are seen more frequently depending on the clinical condition.

Haematogenous spread

Haematogenous spread

5 At a tumour size of 1–2 /uni00A0 mm (10 cells) neoangiogenesis occurs. The onset of angiogenesis ushers in rapid growth, invasion and metastatic potential. Haematogenous metastasis occurs to the skeletal system (in order of frequency: lumbar vertebrae, neck of femur, thoracic vertebrae, rib and skull). The bony metastasis is generally osteolytic, although osteosclerotic and mixed types may be seen. Haematogenous metastasis may) and also occur to the liver, lungs and brain and, occasionally , the adrenal glands and ovaries. In limbs these deposits occur above the elbow and above the knee (haematopoietic vascular bone marrow is confined to the axial skeleton and in limbs above the elbows and the knees). Extensive bone marrow replacement by tumour cells may result in release of immature blast cells in the peripheral blood, giving rise to ‘leukoerythroblastic anaemia’. Peripheral blood samples for circulating cell-free tumour deoxyribonucleic acid (cf-DNA) and circulating tumour cells are being studied as potential prognostic markers to predict disease recurrence.

Hereditary and familial breast cancer

Hereditary and familial breast cancer

- Hereditary breast cancer (HBC) runs in families, a ff ect - ing several close relatives, and is associated with an identifiable genetic mutation. Familial breast cancer (FBC) a ff ects several members of a family but is not attributable to any known genetic mutation. HBC accounts for 5–10% and FBC for 20–30% of all breast cancers. HBCs are more aggressive, present at an earlier age and are more often multicentric and bilateral. High-penetrance mutations are found in BRCA1 , - BRCA2 , Li–Fraumeni syndrome, Cowden syndrome, Peutz– Jeghers syndrome and hereditary gastric cancer syndrome. BRCA1 (17q21) is associated with a 50–85% lifetime risk of developing breast cancer and up to a 40% risk of ovar - ian cancer. The breast cancers in BRCA1 are mostly TNBC. BRCA2 (13q12.3) is associated with an up to 50–60% lifetime risk of breast cancer and a 20% risk of ovarian cancer. It is also associated with cancer of the prostate, colon, gallbladder, bile duct, stomach and pancreas. BRCA mutation is more common in males with breast cancer. Genetic risk evaluation should be considered in high-risk individuals (Summary box 58.5). Women with a BRCA mutation may be o ff ered a bilateral risk-reducing mastectomy with immediate breast reconstruc - tion. This reduces the risk of breast cancer by 90%. Chemo - prophylaxis with tamoxifen or anastrozole may reduce the - risk to 50%. Premenopausal women may be o ff ered bilateral salpingo-oophorectomy after they hav e completed their family at around 35–40 years of age.

INVESTIGATIONS FOR BREAST SYMPTOMS

INVESTIGATIONS FOR BREAST SYMPTOMS

The assessment of women presenting with symptomatic breast disease is carried out in a systematic manner. -

Injuries of the breast Haematoma

Injuries of the breast Haematoma

Haematoma, particularly a resolving haematoma, gives rise to a lump that, in the absence of overlying bruising, is di ffi cult to diagnose correctly unless it is biopsied. Traumatic fat necrosis may be acute or chronic and usually occurs in stout, middle-aged women. Following a blow , a lump, which is often painless, appears. This may mimic a carcinoma, even displaying skin tethering and nipple retraction; biopsy is required for diagnosis. A history of trauma is not diagnostic as this may merely have drawn the patient’s attention to a pre-existing lump. In a road tra ffi c accident, a seatbelt may transect or avulse the breast o ff the underlying pectoral muscles owing to a sudden deceleration injury .

Introduction

Introduction

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Learning objectives

Learning objectives

To understand: Appropriate investigation of breast disease • Aberrations of Normal Development and Involution (ANDI) • concept and management of benign breast disease

Lymphatic metastasis

Lymphatic metastasis

This occurs mainly to axillary lymph nodes. Tumours from the inner half of the breast may also spread to the internal mammary nodes. Involvement of the contralateral lymph nodes in the absence of a contralateral primary represents metastatic disease (Table 58.5). /uni25CF /uni25CF /uni25CF /uni2192 /uni2192 /uni2192 /uni25CF /uni25CF Alfred Armand Velpeau , 1795–1867, anatomist and surgeon, Tours, France, described cancer en cuirasse in 1838.

TABLE 58.5 Causes of contralateral axillary lymph node involvement in breast cancer. Haematogenous spread from the contralateral primary Spread of cancer from one breast to another via subdermal lymphatics in front of the sternum Spread of cancer from one breast to the other via the ipsilateral internal mammary nodes interconnecting lymphatics behind the sternum the contralateral internal mammary nodes the other breast the opposite axillary nodes Tumour developing in an epithelial embryonic cell rest trapped in a lymph node during embryonic development of a node (rare) Primary tumour of the opposite breast breast and is a sign of locally advanced the

Macromastia

Macromastia

Macromastia is a benign disorder characterised by massive enlargement of one or both breasts disproportionate to the body habitus. The aetiology of this condition is multifactorial: it is usually idiopathic or associated with obesity , the presence of excessive endogenous or exogenous hormones or increased sensitivity of the breast tissues to the hormones. The treatment is reduction mammoplasty (Figure 58.23) or a subcutaneous mastectomy along with breast reconstruction. -

(a) and symbrachydactyly of the (a) (b) Figure 58.23 Patient with macromastia (a) who underwent inferior pedicle reduction mammoplasty (b) with removal of 1600 g of tissue from the right breast and 1800 g from the left.

Magnetic resonance imaging

Magnetic resonance imaging

MRI of the breast (Figure 58.9) is useful in a number of settings: - /uni25CF women with dense breasts or discordant or equivocal find - ings on mammogram/ultrasonography; /uni25CF to distinguish scar from recurrence in women who have had previous breast conservation therapy for cancer; /uni25CF to assess multifocality and multicentricity and, in lobular cancer, high-grade ductal carcinoma in situ (DCIS); /uni25CF women with breast cancer (BRCA) gene or other genetic Otto Heinrich Warburg , 1883–1970, German physiologist, awarded a Nobel prize in 1931 for describing the metabolic dependence of tumour cells on glucose (the Warburg e ff ect). Most primary tumours and metastatic deposits exhibit high uptake of a radiopharmaceutical (detected by positron emission tomography . mutations or a strong family history; /uni25CF women with breast implants. MRI-guided biopsy may be performed for lesions not visi - ble on ultrasonography or mammogram.

Category Assessment Probability of malignancy Follow-up recommendation 0 Assessment is incomplete Not applicable 1 Negative Essentially 0% 2 Benign /f_i nding(s) Essentially 0% 3 Probably benign /f_i nding

> 0% but ≤ 2% 4 Suspicious abnormality: 4a: Findings needing intervention with a 2 to ≤ 10% low suspicion for malignancy 4b: Intermediate suspicion of malignancy 10% to ≤ 50% 4c: Findings of moderate concern, with 50% to <95% high suspicion for malignancy 5 Highly suggestive of malignancy ≥ 95% 6 Known biopsy-proven malignancy Not applicable (a) (b) Figure 58.7 Features of a normal mammogram. (a) Mediolateral oblique view; (b) craniocaudal view. (a) Figure 58.8 Imaging features of breast cancer on mammography (Category BI-RADS 5). (a) Irregular, spiculated mass; (b) /f_i ne pleomorphic microcalci /f_i cations; (c) /uni00A0 architectural distortion. Need for additional imaging evaluation and/or prior mammograms for comparison Routine annual screening mammography (for women over age 40) Routine annual screening mammography (for women over age 40) Initial short-term follow-up (usually 6 months) examination Biopsy should be considered Requires biopsy or surgical treatment Category reserved for lesions identi /f_i ed on imaging study with biopsy proof of malignancy prior to de /f_i nitive therapy

Mammography

Mammography

Mammography in two planes and ultrasonography are the first line investigations for imaging the breast. Magnetic resonance imaging (MRI) is a valuable adjunctive diagnostic tool because of its high sensitivity for breast pathology . Mammography is also used as an initial screening tool f or asymptomatic women in population-based programmes. Radiographs are taken by placing the breast in direct contact with ultrasensitive film and exposing it to low-voltage, high-amperage x-rays. The dose of radiation is approximately 1 /uni00A0 mGy per film (Figure 58.7 Mammography should be the first investigation in older women who present with breast symptoms. Mammographic features of cancer are shown in Figure 58.8 . Ancillary signs of malignancy such as lymphadenopathy , breast oedema and skin or areolar thickening or retraction may be seen in advanced cases. The mammographic and ultrasonographic features are not diagnostic of cancer; biopsy is required for definitive diagnosis in lesions with a Breast Imaging Reporting and Data System (BI-RADS) score of 4 or 5 (Table 58.1). Mammography reporting The American College of Radiology has developed guide lines – BI-RADS – to achieve uniformity and objectivity in the interpretation and reporting of mammograms and ultrasound. The mammographic assessments are ca tegorised from BI-RADS 0 to BI-RADS 6 (Table 58.1). Gy is short for Gray , the SI unit for the absorbed dose of ionising radiation. Louis Harold Gray , 1905–1965, Director, British Empire Cancer Campaign Research Unit in Radiobiology , Mount V ernon Hospital, Northwood, UK. -).

(b) Use the pad of three /f_i ngers and (c) the dial of a clock method Figure 58.5 Fibroadenoma. Ultrasonography shows a well-circum

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scribed, solid mass suggestive of /f_i broadenoma in a young woman. Breast Imaging Reporting and Data System (BI-RADS) score 3 (Table 58.1). Figure 58.6 Imaging features of breast carcinoma on ultrasonogra

phy. This shows a solid, irregular-shaped mass, taller than wider, with angular irregular margins. Breast Imaging Reporting and Data System (BI-RADS) score 5 (Table 58.1).

Management of local recurrence

Management of local recurrence

- The local recurrence should be biopsied as a change in receptor status may occur and influence further therapy . Whole-body MRI or PET-CT scan should be performed to detect metas - tasis. Systemic chemotherapy should be followed by surgical excision. Most surgeons perform a mastectomy for recurrence; how ever, second BCS and re-radiotherapy may be considered. -

Mastalgia

Mastalgia

Approximately 50–70% of women attending any breast clinic present with mastalgia (synonym: mastodynia or mazodynia). True mastalgia (arising from breast tissue) is classified into cyclical and non-cyclical types. Cyclical mastalgia The pain usually starts around the middle of the cycle on day 14 and gradually increases in severity (measured on a visual analogue scale [V AS] as 0–10) until day 27 or 28. Usually both breasts are involved. The pain is usually relieved with the onset of menses. Severe forms may lead to loss of sleep and impaired sexual and other activities of daily life. The pain may radiate to the upper arm and may be mistaken for angina pectoris. The cause is unclear and considerations of hormone imbalance, high ca ff eine intake, low dietary essential fatty acids, water retention or psychoneurosis are not supported by research. In most patients the basal lev els of oestrogen, pro - in gesterone and prolactin are in the normal range. However, most patients do respond to treatment with antioestrogen - drugs, such as tamoxifen, ormeloxifene, luteinising hormone analogues or danazol, suggesting excessive responsiv eness of breast tissue to circulating oestrogen. Non-cyclical mastalgia The pain presents at any time of the menstrual cycle, at any location of the breast and may occur both before and after menopause. It is often well localised. Some patients may have duct ectasia or periductal mastitis. Breast palpation may reveal a very tender spot confined to a point called the trigger spot or trigger point. Other causes are musculoskeletal, in the form of Tietze’s syndrome: a painful costochondral junction with no radiological anomaly and lateral chest wall pain in the anterior axillary line and over serratus anterior. Trauma, cancer or sclerosing adenosis may also result in breast pain. True breast pain must be distinguished from angina, biliary colic, reflex oesophagitis and cervical spondylosis. In low-/middle-income countries, vitamin D and calcium deficiencies are rampant, - leading to bony aches and pains that may present as non- - cyclical mastalgia. About 5% of breast cancers exhibit pain at presentation, but this is rarely the sole presenting feature. Treatment Treatment begins with assessment, including breast examina - tion and imaging. If normal, reassurance that the symptoms are not due to cancer helps the majority of women. The type of pain, cyclical or non-cyclical, should be identified by record - ing a pain chart for 1 month (Figure 58.12). The principles of trea tment are outlined in Table 58.2 and 58.1 . In patients /uni092E/uni093E/uni0939 /uni092E/uni093E/uni0939 /uni092E/uni093E/uni0939 with non-cyclical pain, musculoskeletal pain and other referred causes should be excluded. Trigger point pain may be relieved by local injection of a long-acting corticosteroid such as triamcinolone in combination with lidocaine at the point of maximum tenderness. This may be repeated at intervals until the pain is controlled.

Patient name: Age: Date: Month of visit: 0/1/2/3/4/5/6: Duration of complaint (/f_i rst visit only): Right Breast_____ Left Breast_____ Out of ten what was the maximum breast pain score in the last month? Please encircle the number. (Note: 10 is the maximum pain you ever experienced and 0 is no pain) On monthly period chart, insert the letter M below the date on days you have menses. 0 1 2 3 4 How many days in the last month were painful? Right breast pain score Month 1 2 3 4 5 6 7 8 9 10 11 12 13 1 2 3 4 5 6 7 8 9 10 11 12 13 Left breast pain score Month 1 2

3 4 5 6 7 8 9 10 11 12 13 1 2 3 4 5 6 7 8 9 10 11 12 13 Monthly period 3 4 5 6 7 8 9 10 11 12 13 1 2 Month 1 2 3 4 5 6 7 8 9 10 11 12 13 Note: Please bring this card with you on each visit Figure 58.12 Breast pain chart. All India Institute of Medical Sciences modi /f_i cation of the Cardiff Breast Pain Chart. Reg. number: 5 6 7 8 9 10 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

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Exclude cancer Reassure Use a VAS breast pain chart to record severity Adequate support Tight sports brassiere during the day Consider medication Flax seed 30 /uni00A0 g daily or oil Rich sources of omega 3 fatty acids of evening primrose and -linolenic acid, respectively Useful in mild to moderate mastalgia Topical non-steroidal anti-in /f_l ammatory cream (diclofenac or piroxicam) four times a day Consider systemic medication if pain score >3 on a VAS of 0-10 Tamoxifen 10 /uni00A0 mg daily For 3–6 months Danazol 50–300 /uni00A0 mg daily For 3–6 months Ormeloxifene 30 /uni00A0 mg twice For 3–6 months used in both cyclical a week and non-cyclical mastalgia and for treating nodularity Short duration: use for 3 months for LHRH agonist alone recalcitrant pain not relieved by the or with antioestrogen: above medications tamoxifen or ormeloxifene LHRH, luteinising hormone-releasing hormone; VAS, visual analogue scale.

Mastitis of infants

Mastitis of infants

Mastitis of infants may occur in both boys and girls. It is uncommon and is predominantly caused by Staphylococcus aureus .

Metastatic carcinoma of the breast (stage IV)

Metastatic carcinoma of the breast (stage IV)

Treatment of metastatic cancer is aimed at palliating symp toms, improving quality of life, preventing potential disabling complications and attempting to prolong life. Endocrine therapy for hormone receptor-positive disease is preferred for patients with bony metastasis and limited visceral metastasis . Systemic chemotherapy is preferred for patients with hormone receptor-negative cancers, hormone-refractory metastases and patients with visceral crisis. Oral low-dose metronomic chemotherapy has cytostatic and antiangiogenic e ff ects and may help in improving quality of life. Patients with bony metastasis should receive palliative radiotherapy to lesions in weight-bearing areas (e.g. vertebra, femur) and to painful bony deposits, along with bisphospho nates . Symptomatic pleural e ff usions are palliated by inter costal chest drainage and pleurodesis. Surgical resection of Frederick Pei Li , 1940–2015, Dana–Farber Cancer Institute, Boston, MA, USA, and Washington, DC, USA, in 1969 identified four families with increased susceptibility to cancer. This led to the discovery of mutation in the tumour suppressor gene p53 . Cowden syndrome was named after Rachel Cowden, in whom the features were first recognised. Jan Peutz , 1886–1957, Dutch physician, documented the eponymous condition. Harold Joseph Jeghers , 1904–1990, Boston, MA, USA, recognised the eponymous syndrome. - tasis in patients with good performance status and favourable tumour biology .

Needle biopsy

Needle biopsy

Tissue for histological examination can be obtained under local anaesthesia using a large-diameter core needle biopsy device (14G for breast tissue and 18G for axillary nodes) (Figure 58.11). The core needle biopsy should always be taken under image guidance. The passage of the biopsy needle can be guided by ultrasonography , mammogram or sometimes MRI; the needle tip should be used to take a sample from only the solid part of the mass, avoiding areas of cystic degeneration and blood vessels in and around the lesion.

(a) (b) Figure 58.11 Large-diameter core needle biopsy of the breast.

Nipple inversion and retraction

Nipple inversion and retraction

At birth the mammary glands in boys and girls are similar. At around 11–12 years of age, in girls the breast begins to grow . The onset of its growth is called ‘the telarche’ (1 year before menarche). Initially uniform growth of cells leads to a rounded breast mound. Later elongation of the major milk ducts at age 14–16 years leads to projection of the nipple. Lack of elonga tion of the major milk ducts leads to failure of the nipple to protrude, called nipple inversion (Figure 58.17). An inverted nipple interferes with feeding and may become a source of infection by deposition of debris. It does not pr edispose to breast cancer. Nipple retraction is an acquired phenomenon owing to fibrosis in and around the major milk ducts. Retraction of recent onset is always worrisome and may point towards an underlying carcinoma; howev er, the most common cause of longstanding retraction is periductal mastitis (Figure 58.18 Both nipple inversion and retraction may cause prob lems with breastfeeding and infection can occur because of retention of secretions. A transverse slit-like or fish mouth-like retraction of the nipple is classically seen in periductal mastitis (Figure 58.18a), but circumferential retraction may indicate a car cinoma (Figure 58.18b) . - - - -). -

Figure 58.17 Congenital nipple inversion. (a) (b) Figure 58.18 Two common causes of retraction of the nipple. (a) Slit- like retraction due to periductal mastitis. (b) Breast cancer with /f_i brosis around the major milk ducts.

Minor degrees of inversion can be corrected by gently pulling the nipple forward. Surgical correction is fraught with division of milk ducts and loss of nipple sensation and the patient should be fully informed of this risk. Mechanical suction devices have been used to evert the nipple, with some benefit.

Nodular or lumpy breasts

Nodular or lumpy breasts

Patients who present with painful tender nodularity with mastalgia should be treated for breast pain, as outlined in Table 58.2 . Patients with breast nodularity without pain should undergo triple assessment (Figure 58.2). The Cardi ff –Lucknow nodu larity scale – a five-point ordinal scale that grades the nodular ity on a scale of 0 to 4, providing an objective measur ement of nodularity – has been developed and validated (Figure 58.13 In the absence of a discrete lesion on breast imaging, reassur ance may be given. If necessar y , treatment with an antioestro gen such as tamoxifen or ormeloxifene (Centchroman) has been found to control nodularity within a few weeks.

Paget’s disease

Paget’s disease

Paget’s disease is a unique type of DCIS arising in the nipple. It presents as erosion of the nipple that slowly destroys the nipple and encroaches on the areola (Figure 58.19). It may become invasive with metastasis to the axillary lymph nodes. Triple assessment is needed to exclude underlying malignancy . Paget’s disease without associated underlying malignancy is treated by central core excision, removing a cone of major milk ducts along with the nipple and areola down to the pectoralis major muscle, followed by radiotherapy . Paget’s disease with Sir James Paget , 1814–1899, surgeon, St Bartholomew’s Hospital, London, UK, described this disease of the nipple in 1874. underlying malignancy is treated by mastectomy and evalua - tion of the axillary nodal status.

Figure 58.19 Nipple erosion in early Paget’s disease.

Papilloma of the nipple

Papilloma of the nipple

Papilloma of the nipple has the same features as any cutaneous papilloma and should be excised with a tiny disc of skin. Alter natively , the base may be tied with a ligature and the papilloma will spontaneously fall o ff .

Pathology

Pathology

This can be considered in three phases: lobule development at 15–25 years, cyclical changes at 15–50 years and involution at 35–55 years of age. It is believed that lobular proliferation leads to the formation of fibroadenoma and involution leads to cyst formation. Aberration in the above phases may lead to a number of benign conditions. /uni25CF Hyperplasia of the epithelium is defined as the presence of more than two layers of cells in the lining of the ducts and acini. It may occur with or without atypia. If atypia of epithelial cells is seen, the terms atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH) are used. If features of ADH are seen to involve more than two ducts or lesions measure >2 /uni00A0 mm in diameter, the term ductal carcinoma situ (DCIS) is used. /uni25CF Papilloma . Localised hyperplasia of the ductal epi thelium may produce a papilloma within the ducts. It is composed of a central fibrovascular core and papillary projections of the epithelium and myoepithelial cells. The papillary lesions in a duct are of three types: /uni25CF solitary papilloma (relative risk [RR] for cancer 1.5–2); /uni25CF papillomatosis: five or more papillomas in many ducts with peripheral and often bilateral distribution (RR for cancer 3); /uni25CF juvenile papillomatosis, also called Swiss cheese disease , a ff ects young women, who present with multiple firm palpable nodules; microscopically , there are multiple papillomas with/without atypia, apocrine cysts, ductal hyperplasia and sclerosing adenosis. A positive family history of breast cancer increases the lifetime cancer risk. /uni25CF Cyst formation . Kinking or narrowing of ductules is usually due to involution of the stroma and may result in accumulation of secretions in the lobules, forming a micro cyst. Many microcysts may join together to form a macro cyst.

Polymazia

Polymazia

Accessory breasts (Figure 58.22) have been recorded in the axilla (the most frequent site), groin, buttock and thigh. They have been known to fluctuate in response to hormones in a physiological manner, such as pubertal enlargement and lactation. They may also show the same spectrum of patho logical diseases observed in normal breasts. Polymazia may be associated with other congenital diseases, such as vertebral anomalies, cardiac arrhythmias or renal anomalies.

Positron emission tomography

Positron emission tomography

Positron emission tomography (PET) scans are used as a staging investigation in patients with T3, T4, N2, N3 breast cancer and in patients with T1, T2, N0, N1 breast cancer in the presence of symptoms/signs suggestive of metastasis (Figure 58.10). Inflammatory lesions (namely , mediastinal lymphadenopathy and pleuropulmonary lesions due to pulmonary tuberculosis [TB]) may give false-positive results, especially in Asian patients. Moreover, PET is very expensive and insurance policies may not cover its cost. 18 18 F-fluorodeoxyglucose [F-FDG]) that may be

(b) (c)

(b) (c) Figure 58.9 Magnetic resonance imaging showing carcinoma of the left breast (arrows). (a) Precontrast; (b) post gadolinium contrast; (c) /uni00A0 subtraction image.

Retention cyst of a gland of Montgomery

Retention cyst of a gland of Montgomery

These glands, situated in the areola, secrete sebum. If they become blocked a sebaceous cyst forms. Rarely they may become infected and need excision.

Risk factors

Risk factors

There are several factors known to increase the RR for developing breast cancer. These are called the risk factors and can be divided into modifiable (those that can be modified by adopting a healthy diet and lifestyle) and non-modifiable risk factors. The events increasing the oestrogenic exposure of the - breast are said to be risk factors for breast cancer, such as early menarche, late menopause, nulliparity , late first pregnancy and hormone replacement with high oestrogen therapy . These are listed in Table 58.3 . - - - -

Figure 58.27 Mondor’s disease in the lateral aspect of the right breast.

Harris JG Bloom , 1923–1988, radiation oncologist, Royal Marsden Hospital, London, UK. William W Richardson , 1915–2005, pathologist, Middlesex Hospital, London, UK, published a paper with Bloom on the na Breast carcinoma arises from the milk ducts in 90% (ductal carcinoma) or from the lobule in 10% (lobular carcinoma) of patients. The disease may remain confined to the epithelium of the duct or lobule with no breach in the basement membrane; this is called in situ disease . Infiltration of the surrounding tissue through a breach in the basement membrane leads to ‘invasive or infiltrative’ ductal or lobular carcinoma. The tumour may be well di ff erentiated, moderately di ff erentiated or poorly di ff erentiated. The modified Bloom–Richardson scoring system for tumour grade includes the sum of indi - vidual scores for three variables (percentage of tumour cells with tubule formation, nuclear pleomorphism and the size and number of mitoses/HPF), each of which is assigned from 1 /uni00A0 to /uni00A0 3 points according to the deg ree of deviation from normal breast epithelium. A total score of 3–5 defines grade I; 6 or 7 grade II; and 8 or 9 grade III. Invasive carcinoma is usually of no special type (NST), which represents the most common variety of breast cancer. Rare histological variants, usually carrying a better prognosis, include colloid or mucinous carcinoma, whose cells produce abundant mucin; medullary carcinoma, with solid sheets of large cells often associated with a marked lymphocytic reac - tion; and tubular carcinoma. The papillary type of carci - noma (both in situ and invasive) is a rare type of breast cancer accounting for 0.5–1% of all neoplasms. The lesion is char - acterised by papillomas with a fibrovascular core and surface covered by epithelial and myoepithelial cells. It usually carries a better prognosis and rarely spreads to lymph nodes and the bloodstream. The tumour cells may o verexpress oestrogen receptors (ER positive), progesterone receptors (PR positive), human epidermal growth factor receptor 2/neu (HER2/neu positive) and androgen receptors (AR positive). The degree of mitosis can be detected by the Ki-67 mitotic index. Gene array analysis has identified five major subtypes: luminal A, luminal B, basal, HER2/neu receptor enriched and a normal-like group (Table 58.4). In the absence of gene array testing such as prediction analysis of microarray-50 (PAM-50), immune histochemical receptor staining serves as a surrogate marker of molecular subtypes. tural history of breast cancer in 1957.

Remarks Modi /f_i able risk factors Obesity: BMI >30 Increased risk in postmenopausal women: RR = 1.29 Parity Increased risk in nulliparous women or /f_i rst pregnancy after 35 years of age Breastfeeding It is protective for breast cancer and >12 months of breastfeeding by women has a greater protective effect than shorter duration Age at /f_i rst childbirth Early: less risk, <20 years Late: high risk, >35 years Use of HRT Use for >10 years increased risk: RR = 1.2 Tobacco use RR = 1.14 for smoking 25 or more cigarettes/day; RR = 1.07 for smoking for 20 years or more Alcohol consumption RR = 1.05 for light drinking (<1 drink/day); RR = 1.32 for moderate drinking (3 or 4 drinks/day); RR = 1.46 for heavy drinking (>4 drinks/day) Radiation exposure RR = 6 Non-modi /f_i able risk factors Age Increasing age is a risk factor. While the median age at presentation is around 60 years in the West (UK, USA), it is around 48 years in low-/middle-income nations such as India Sex Female sex is a risk factor as only 0.5–1% of all breast cancers occur in males Ethnicity American white, African American (age <45 years), Ashkenazi Jew, Parsi in India Family history of One /f_i rst-degree relative (mother, sister or breast cancer daughter) with breast cancer: RR = 2; two /f_i rst-degree relatives with breast cancer: RR = 3 Genetic 5–10% of all breast cancers are hereditary; predisposition BRCA1 and BRCA2 mutations account for up to 70% of hereditary breast cancers Early menarche (<12 Breast cancer risk increases by around 5% years) for each year earlier menstruation begins: RR = 1.19 for age <11 years Late menopause Breast cancer risk increases by about 3% (>55 years) for each year later menopause begins: RR = 1.12 for menopause at 55 years versus menopause at 45 years High-risk breast Proliferative conditions without atypia: RR lesions = 1.8–2 Complex /f_i broadenoma: RR = 3 Papillomatosis: RR = 3 Proliferative diseases with atypia: atypical ductal and lobular hyperplasia: RR = 4–5 Lobular carcinoma in situ : RR = 8–10 BMI, body mass index; BRCA , breast cancer; HRT, hormone replacement therapy; RR, relative risk. TABLE 58.4 Molecular classi /f_i cation of breast cancer. Classi /f_i cation Hormone HER2/ Others receptor neu Luminal A Positive (either or Negative Ki-67 low both ER/PR) Luminal B Positive (either or Negative Ki-67 high both ER/PR) Basal type (triple Negative Negative Ki-67 usually negative) high HER2/neu Negative Positive Ki-67 high enriched Claudin low Negative Negative Claudin low ER, oestrogen receptor; HER2/neu, human epidermal growth factor receptor 2/neu; PR, progesterone receptor.

Figure 58.28 (a) Diffuse redness (erythema) and skin oedema involving more than one-third of the breast, with an enlarged left breast – features of in /f_l ammatory carcinoma. (b) Peau d’orange refers to the orange peel appearance of the skin of disease. Note that in people with darker skins the erythema takes on a brownish hue.

Sarcoma

Sarcoma

Sarcomas, most commonly fibrosarcoma and angiosarcoma, may arise de novo from the mesenchymal tissues of the breast. Enrico Sertoli , 1842–1910, Italian physiologist, discovered the Sertoli cells of the testis in 1865. Thomas Hodgkin , 1798–1866, lecturer in morbid anatomy and curator of the museum, Guy’s Hospital, London, UK, described Hodgkin’s lymphoma in 1832. Summary box 58.6 Prognosis /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF Some genetic conditions (Li–Fraumeni, neurofibromatosis type 1), exposure to alkylating agents, vinyl chloride or arsenic, - prior radiotherapy (e.g. for Hodgkin’s lymphoma) and chronic lymphoedema are associated with the development of sarcoma. Angiosarcoma (Figure 58.40) is the most aggressive of all breast tumours and arises from the endothelial cell lining of vascular or lymphatic channels. Angiosarcoma is associated with prior radiotherapy and carries a very poor prognosis.

Figure 58.39 Carcinoma of the male left breast (courtesy of Professor Mike Dixon). Disease factors Patient factors a Size of tumour Younger age Stage of disease Premenopausal a women Axillary lymph node involvement a BRCA -associated Grade of tumour tumour Histopathological variant Family history of (metaplastic carcinoma is breast cancer aggressive): Prior history of Her2/neu positive and triple breast cancer negative Obesity, sedentary Presence of lymphovascular lifestyle invasion Failure to complete Extensive DCIS component intended treatment High Ki-67 index DCIS, ductal carcinoma in situ . a The Nottingham prognostic index (NPI) is used to determine prognosis following surgery. It is calculated using tumour size /uni00A0 (S), number of involved lymph nodes (N) and tumour grade (G). NPI = (0.2 /uni00A0×/uni00A0 S) /uni00A0 + /uni00A0 N /uni00A0 + /uni00A0 G. Patients are grouped into four categories according to the NPI score: I (excellent) ≤ 2.4; II (good) >2.4 but ≤ 3.4; III (moderate) >3.4 but ≤ 5.4; and IV (poor) >5.4.

Screening for breast cancer

Screening for breast cancer

Screening for breast cancer involves a highly sensitive diagnostic test to detect the disease in either the preclinical detectable phase or a high-risk precancerous lesion. In most high-income countries population-based mammographic screening achieves very high (90–95%) long-term survival in patients with screen-detected tumours. In the UK, all women aged between 50 and 70 years are invited for mammographic screening every 3 /uni00A0 years. In low- and middle-income countries, population-based mammographic screening is not available. In some Asian countries clinical breast examination by a trained healthcare professional along with increasing breast health awareness by breast self-examination is being encouraged as a mode of screening. In India, national screening involves multidisease screening for cancer of the mouth, breast and cervix for all women aged 30–65 years. Clinical breast examination can detect the disease in the early stages while breast self-examination can help women become aware of breast health, detect breast changes and report to the healthcare facility early . Patients with a suspicious lesion on mammogram are invited for biopsy under image guidance. In small or impalpa ble lesions a metal clip may be inserted at the site of the lesion. If a carcinoma is found on histology , the metal clip facilitates insertion of a hook wire with its tip near the centre of the lesion to facilitate wire-guided excision. Further therapy is based on histolog y of the excised specimen after discussion in the MDT . The authors are grateful to Professors Smriti Hari and Maneesh Singhal from the All India Institute of Medical Sciences (AIIMS), New Delhi, India, for their assistance in providing illustrations used in the chapter, and to Dr Shivangi Saha of AIIMS, New Delhi, for her contribution to the breast reconstruction section and illustrations. Professor V Seenu of AIIMS critically reappraised the section on sentinel node biopsy . Professor Sandeep Kumar provided insight and critical reappraisal of the section on ANDI and benign breast disease. Dr Deepti Singh helped in the section on mastitis. Professor Manoj Kumar Singh and the team of artists at Virtual Skills Laboratory , AIIMS, designed most of the illustrations and videos for this chapter.

Figure 58.40 Angiosarcoma of the breast in a young woman.

Spread of cancer Local spread

Spread of cancer Local spread

The tumour increases in size and invades adjacent breast parenchyma. It may involve the skin, leading to ulceration and satellite nodules, and/or involve pectoralis major, serratus anterior and even the chest wall. The tumour cells release a number of growth factors; namely , fibroblast growth factor (FGF), transforming growth factor (TGF α and TGF β vascular endothelial growth factor (VEGF). FGF induces mitosis of adjacent fibrocytes, which convert to fibroblasts and lay down collagen (desmoplastic reaction). Contraction of collagen leads to shortening of Cooper’s ligament, pulling the skin inwards and giving rise to the telltale signs of dimpling (shortened single Cooper’s ligament), puckering or tethering (many Cooper’s ligaments shrunken) or nipple retraction.

Staging of breast cancer

Staging of breast cancer

Staging refers to the process of finding out the extent of tumour. The eighth edition of the Union for International Cancer Control (UICC)–American Joint Committee on Cancer (AJCC) TNM staging system is currently used (Table 58.6 In addition to anatomical staging, the eighth edition of the AJCC TNM staging system includes the histological grade, the ER, PR, HER2/neu and Ki-67 assessment, multigene testing ® with Oncotype DX and the response to neoadjuvant chemo therapy to refine the prognostic information. The key points in the eighth edition of the AJCC TNM staging system are listed in Summary box 58.3 .

Subacute and chronic inflammation of the breast

Subacute and chronic inflammation of the breast

Non-lactational mastitis Non-lactational mastitis may be defined as inflammation of the breast tissue in a nulliparous woman or occurring after a minimum of 6 months after cessation of lactation. Various forms of non-lactational mastitis include periductal mastitis, . idiopathic granulomatous mastitis (IGM) and tubercular mastitis. Periductal mastitis This is a chronic non-lactational inflammation around the major milk ducts. The pathogenesis is obscure and thought to be autoimmune in nature. The condition is much more common in smokers. It may progress to a subareolar inflammatory mass that may suppurate, forming a subareolar abscess. Thick areolar muscles do not allow the abscess to perf orate through the are - - ola so the pus follows the path of least resistance, rupturing the skin at the areolar edge and forming a mammary or milk duct fistula (Figure 58.25). In some cases, a chronic indurated mass forms beneath the areola, which mimics a car cinoma. Fibrosis in and around major milk ducts causes nipple retraction. The patient presents with central non-cyclical pain, pus - discharge from the nipple and a subareolar tender mass/ abscess or mammary duct fistula. The examination rev eals a tender, firm subareolar lump or abscess, purulent nipple - discharge, thickened tender major milk ducts and a transverse slit-like nipple retraction looking like a fish’s mouth (58.6). Ultrasonography shows thickened major milk ducts with surrounding inflammation or abscess. A lump should be biopsied under ultrasound guidance to confirm the diagnosis. Any pus discharge should be sent for culture sensitivity and ® GeneXpert Mycobacterium tuberculosis complex and resistance - to rifampicin (MTB/RIF) testing to rule out TB. The most common organisms isolated are staphylococci, enterococci, anaerobic streptococci and sometimes Bacteroides and mycobacteria. Many cases of periductal mastitis resolve with a course of antibiotics, combined with needle aspiration of an abscess. However, surgical treatment by major milk duct ex cision is needed in patients with a subareolar abscess or sepsis and a mammary duct fistula. A 1.5- to 2-cm length of the ductal cone should be excised. Smoking cessation must be encouraged to prevent recurrence. Idiopathic granulomatous mastitis This is a benign, self-limiting, inflammatory breast disease of unknown aetiology . It occurs most commonly in young parous women within the first few years after pregnancy . An association between IGM and Corynebacterium kroppenstedtii infection has been postulated. IGM may present as single or multiple central or peripheral inflammatory breast masses, with or without abscess formation. IGM may be associated with skin ulceration, nipple retraction, sinus formation, peau d’orange and axillary lymphadenopathy . These findings may mimic cancer. A needle biopsy of a solid mass establishes the diagnosis of IGM. The tissue/aspirate should also be sent for Gram stain and culture, acid-fast bacilli (AFB) stain and culture and fungal Hans Christian Joachim Gram , 1853–1938, Professor of Pharmacology (1891–1900) and of Medicine (1900–1923), Copenhagen, Denmark, described this method of staining bacteria in 1884. stain and culture. Histologically IGM shows a non-caseating granuloma with chronic inflammation. The di ff er ential diag - noses include

TB, foreign body reaction and sarcoidosis. eat - In symptomatic patients and in those with infection, tr ment with non-steroidal anti-inflammatory drugs and anti - biotics with or without drainage is indicated. In countries where TB is endemic, care should be taken to avoid admin - istering anti-tuberculous therapy as a blanket treatment to all patients with granulomatous mastitis. Anti-tuberculous tr eat - ment should only be given to patients with evidence of TB on imaging, histopathology or microbiological analysis and ® GeneXpert MTB/RIF . In cases of persistent symptoms or progression, treatment with prednisolone (oral or topical) with or without methotrexate has helped in regression of IGM. A major milk duct excision is indicated in patients with a mam - mary duct fistula. Excision of chronic abscess cavities is per - formed in patients with recurrence.

(c) Figure 58.24 (a) Breast abscess; (b) diagrammatic representation; in place. Pectoral fascia Second rib Premammary fascia Pectoralis major muscle Suspensory ligament of Cooper Intercostal muscle Ampulla Intercostal vessels and nerves Lactiferous duct Sixth rib Mammary lobules Intramammary breast abscess (d) (c) closed suction drainage; (d) breastfeeding while a drainage catheter is

Tuberculosis of the breast TB of the breast is uncommon. It is caused by spread from the axillary or internal mammary lymph nodes or osteitis of the rib or sternum. Sometimes infection may reach the breast from the pleural cavity . Uncommon sources of infection can be entry from a cracked nipple or a haematogenous route. It presents with multiple chronic abscesses and sinuses with a typical bluish discoloration of the surrounding skin. The diagnosis rests on bacteriological and histological examination. Tubercular mastitis results in epithelioid cell granuloma with caseating necrosis. AFB can be seen occasionally in the pus/ aspirate from caseation necrosis. Any pus or tissue should be ® sent for Ziehl–Neelsen staining, GeneXpert MTB/RIF test ing and mycobacterial culture. A computed tomography (CT) scan of the chest and abdomen aids in diagnosis by detecting other foci of present or past TB. A Mantoux test may be done; however, it is of little value in countries where TB is endemic. T reatment consists of anti-tuberculous chemotherapy for Franz Ziehl , 1859–1926, German bacteriologist and a professor in Lubeck, Germany . Friedrich Carl Adolf Neelsen , 1854–1898, German pathologist and professor at the Institute of Pathology , University of Rostock, Germany . Charles Mantoux , 1877–1947, physician, Le Cannet, Alpes Maritimes, France, described the intradermal tuberculin skin test in 1908. 6–9 months. Healing is usual, although often delayed with puckered scars (Figure 58.26). Duct ectasia Duct ectasia is defined as dilated major milk ducts. It is consid - ered a disorder of involution as part of ANDI. Abnormally dilated ducts are filled with debris. This acts as an irritant and can lead to periductal inflammation and subsequent fibrosis, leading to nipple retraction. Patients usually present with toothpaste-like or coloured (such as brown, gr een or mud coloured) nipple discharge. The clinical findings of duct ectasia can mimic malignancy as well as benign conditions such as mastitis. Ultrasonography reveals dilated major milk ducts - >3 /uni00A0 mm in diameter. Treatment Triple assessment should be followed by antibiotic therapy if inflammation/infection is present. Co-amoxiclav , flucloxacillin,

Second rib Pectoralis major muscle Subareolar abscess in periductal Intercostal muscle mastitis Intercostal vessels and nerves Lung Lactiferous duct Sixth rib (c) Clavicle Pectoral fascia Premammary fascia Second rib Suspensory Pectoralis ligament of major muscle Cooper Milk duct Intercostal muscle /f_i stula Intercostal vessels Ampulla and nerves Lung Lactiferous duct Sixth rib Figure 58.25 Periductal mastitis. (a) Subareoalar abscess due to blockage of a milk duct. areola. (c)

Diagrammatic representation of a milk (mammary) duct /f_i stula connecting the mammary duct epithelium (d) /uni00A0 Clinical photograph showing a retracted nipple and a milk duct /f_i stula at the areolar edge discharging pus. Clavicle Second rib Pectoralis Subareolar major muscle abscess rupturing Intercostal muscle at edge of areola Intercostal vessels and nerves Lung Lactiferous duct Sixth rib (d) (b) Subareolar abscess ruptured at the edge of the to the skin epithelium.

ciprofloxacin or cefixime along with anti-anaerobic cover with metronidazole or tinidazole for 2–3 weeks is recommended. In patients with profuse nipple discharge or subareolar abscess, major mammary duct excision is performed. Actinomycosis Actinomycosis of the breast is very rare. It is caused by anaer obic Actinomyces bacteria. The lesions present with multiple chronic, pus-discharging, non-healing sinuses over the breast. The pus demonstrates typical black granules and the specific pathogen on microbiology . The condition requires long-term penicillin injections along with curettage of necrotic granulo mas and sinuses. Mondor’s disease Mondor’s disease is thrombophlebitis of the superficial veins of the breast and anterior chest wall. In the absence of injury or infection, the cause of thrombo phlebitis is obscure. The pathognomonic feature is a tender thrombosed subcutaneous cord, usually attached to the skin. When the skin over the breast is stretched b y raising the arm, a narrow , shallow , subcutaneous groove alongside the cord becomes apparent (Figure 58.27). The di ff erential diagnosis is lymphatic permeation from an occult carcinoma of the breast. The only treatment required is to restrict arm movements. The condition usually subsides within a few months without recur rence, complications or deformity .

(a) Figure 58.26 Tuberculosis of the breast. (a) Multiple pus-discharging sinuses from the lower part of the breast and lower chest wall. discoloration of the skin around the tubercular sinus. (c) Undermined edge of a tubercular ulcer.

THE NIPPLE

THE NIPPLE

Absence of the nipple is rare and is usually associated with amazia (congenital absence of the breast). Supernumerary nipples are not uncommon and occur along a line extend ing from the anterior fold of the axilla to the upper chest (Figure 58.16). In the human embryo the milk ridge extends from the axilla to the upper chest only and not to the groin. Rarely , there is duplication of the nipple on a normal areola.

Treatment of breast cancer

Treatment of breast cancer

The treatment of breast cancer is multimodal (includes surgery , systemic treatment [chemotherapy , targeted therapy , hormonal therapy] and radiotherapy); hence, specialist breast Key points of the eighth edition of the AJCC TNM stag - ing system /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF - centres employ a multidisciplinary team (MDT) that - should include the surgeon, radiologist, pathologist, radiation oncologist, medical oncologist, plastic surgeon and allied health professionals, such as a breast care nurse, psychological counsellor and preferably a genetic counsellor (58.7). While some patients with low disease burden and low bio - logical aggressiveness can be treated with surgery followed by adjuvant therapy , others require downsizing of disease with neoadjuvant systemic therapy or primary systemic therapy . Neoadjuvant systemic therapy (NAST) consists of). neoadjuvant chemotherapy (NACT), targeted therapy or hormonal therapy prior to surgery . It aims to downsize the disease and enable clinicians to know the in vivo response of the tumour to therapy . The indications for NACT are as follows: - 1 Locally advanced breast cancer T3, T4/N2, N3 disease: to downsize the tumour. 2 Select cases of early breast cancer: a to downsize the tumour to facilitate breast conservation surgery (BCS); b HER2/neu-positive tumours; c triple-negative breast cancer (TNBC); d premenopausal women (age <50 years); e patients with axillary node metastasis. /uni25CF Neoadjuvant targeted therapy (trastuzumab, per - tuzumab) is administered for HER2/neu-positive tumours >5 /uni00A0 mm in diameter. - /uni25CF Neoadjuvant hormonal therapy is o ff ered to elderly or frail women (with ER and/or -, PR-positive advanced tumours) who are deemed unfit to receive systemic che - motherapy . Neoadjuvant hormonal treatment takes longer (around 3–6 months) for the response to become clinically evident. /uni25CF Response assessment and timing of surgery : the patient is examined 3 weeks after administration of

Lobular carcinoma in situ (LCIS) is a high-risk benign lesion not a cancer The T categorisation of multiple synchronous tumours is documented using the (m) modi /f_i er The pre /f_i x (y) is used to denote the post-neoadjuvant therapy status Satellite nodules in the skin must be separate from the primary tumour for it to be categorised as T4b Pathological complete response (pCR) denotes the absence of tumour cells in the breast and axillary nodes in surgical specimens In /f_l ammatory carcinoma remains classi /f_i ed as in /f_l ammatory carcinoma after NACT, even after complete remission Microinvasive (T1mi) carcinomas are de /f_i ned as invasive tumour foci ≤ 1.0 /uni00A0 mm Tumours >1 /uni00A0 mm and <2 /uni00A0 mm should be reported as rounded to 2 /uni00A0 mm Tumour size should be measured to the nearest millimetre

edition) for breast cancer. T category T criteria Tx Primary tumour cannot be assessed T0 No evidence of primary tumour Tis(DCIS) Ductal carcinoma in situ (DCIS) Tis(Paget’s) Paget’s disease of the nipple not associated with (Paget’s) invasive carcinoma and/or carcinoma in the underlying breast parenchyma. Carcinomas in the breast

parenchyma associated with Paget’s disease are categorised based on the size and characteristics of the parenchymal disease, although the presence of Paget’s disease should still be noted T1 Tumour ≤ 20 /uni00A0 mm in greatest dimension T1mi Tumour ≤ 1 /uni00A0 mm in greatest dimension T1a Tumour >1 /uni00A0 mm but ≤ 5

/uni00A0 mm in greatest dimension (round any measur T1b Tumour >5 /uni00A0 mm but ≤ 10 /uni00A0 mm in greatest dimension T1c Tumour >10 /uni00A0 mm but ≤ 20 /uni00A0 mm in greatest dimension T2 Tumour >20 /uni00A0 mm but ≤ 50 /uni00A0 mm in greatest dimension T3 Tumour >50 /uni00A0 mm in greatest

dimension T4 Tumour of any size with direct extension to the chest wall and/or to the skin (ulceration or macroscopic nodules); invasion of the dermis alone does not qualify as T4 T4a Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4a T4b Ulceration

and/or ipsilateral macroscopic satellite nodules and/or oedema (including peau d’orange) of the skin that does not meet the criteria for in /f_l ammatory carcinoma T4c Both T4a and T4b are present T4a /uni00A0 + /uni00A0 T4b /uni00A0

/uni00A0 T4c T4d In /f_l ammatory carcinoma; peau d’orange and redness involving >1/3rd of the surface of the breast with or without a breast lump cN category cN criteria cNx Regional lymph nodes cannot be assessed (e.g. previously removed) cN0 No regional lymph node metastases (by imaging or clinical examination) cN1 Metastases to movable ipsilateral level I, II axillary lymph node(s) cN1mi Micrometastases (approximately 200 cells, >0.2 /uni00A0 mm, but none >2.0 /uni00A0 mm) cN2 Metastases in ipsilateral level I, II axillary lymph nodes that are clinically /f_i xed or matted; mammary nodes in the absence of axillary lymph node metastases cN2a Metastases in ipsilateral level I, II axillary lymph nodes /f_i xed to one another (matted) or to other structures cN2b Metastases only in ipsilateral inter nal mammary nodes in the absence of axillary lymph node metastases cN3 Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or

without level I, II axillary lymph node involvement; or in ipsilateral internal mammary lymph node(s) with level I, II axillary lymph node metastases; metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement cN3a Metastases in ipsilateral infraclavicular lymph node(s) cN3b Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s) cN3c Metastases in ipsilateral supraclavicular lymph node(s) M category M criteria M0 No clinical or radiographic evidence of distant metastases cM0(i+) No clinical or radiographic evidence of distant metastases in the presence of tumour cells or deposits <0.2 /uni00A0 mm detected micr oscopically or by molecular techniques in circulating blood, bone marrow or other non-regional nodal tissue in a patient without symptoms or signs of metastases cM1 Distant metastases detected by clinical and radiographic means c, clinical. in situ (DCIS) ement >1.0–1.9 /uni00A0 mm to 2 /uni00A0 mm) or in ipsilateral inter nal or

in solid tumours (RECIST) are used for reporting the response to NAST . The four RECIST categories are: /uni25CF complete response (CR) (lesion not detectable on clini cal palpation and imaging); /uni25CF partial response (PR) (≥ 30% reduction in the maximal diameter); /uni25CF stable disease (SD) (<30% reduction in maximal diam eter); /uni25CF progressive disease (PD) (≥ 20% increase in the maxi mal diameter). For patients with CR and PR, the entire chemotherapy reg imen may be delivered prior to surgery . If the patient is being planned for BCS, a radio-opaque clip or magnetic marker such ® as Magseed is placed under image guidance in the epicentre of the tumour to allow identification at the time of surgery should there be a complete response to NACT . If the facility for clip placement is unavailable, in place of the metal clip a 0.5-cm piece of silicone or a polyvinylchloride (PVC) catheter tip may be inserted through a small skin incision just anterior to the tumour. This catheter tip remains palpable even after complete regression of the tumour and helps the surgeon in performing removal of the index area for BCS, excising 2 /uni00A0 cm of tissue all around this catheter. For patients showing stable or progressive disease, after the initial two cycles of chemotherapy , the patient should undergo surgery and be given second-line chemotherapy after surgery . Surgical management Surgery plays a central role in the management of breast cancer. There has been a general de-escalation towards more conservative techniques, backed up by clinical trials and meta-analyses showing equal e ffi cacy in locoregional cancer control and survival between mastectomy and WLE/BCS followed by radiotherapy . The aim of surgery is to remove all disease in the breast and axilla with negative margins. The pathologist reports the distance of the tumour to the nearest excision margin in the breast specimen. Indelible India ink is applied on the specimen surfaces. T here should be no tumour cells on the cut edge or ‘inked margins’ of the tumour for invasive cancer. However, in patients with DCIS a minimum of 2 /uni00A0 mm is considered a safe margin. Early breast cancer (stages 0, I ,II) The surgical options for the primary tumour include mastec tomy or BCS. Mastectomy is indicated for large tumours (in relation to the size of the breast), multicentric disease, di ff use microcalcification on a mammogram indicative of DCIS, BRCA -positive cancers, local recurrence following BCS or the patient’s preference. It entails removal of the entire breast tissue, including the skin over the tumour, the nipple–areola complex and the axillary tail. The breast tissue usually extends to a point where the anterior premammary fascia fuses with the William Stewart Halsted , 1852–1922, Professor of Surgery , Johns Hopkins Medical School, Baltimore, MD, USA the breast to the point of fusion between these two fasciae, which usually extends to the level of the second rib above, to - the parasternal edge medially , to the inframammary crease below and to the anterior border of latissimus dorsi laterally . This is di ff erent from the traditional view of raising flaps up to the inferior border of the clavicle superiorly and 2–3 /uni00A0 cm - below the inframammary crease (or

up to the upper fibres of the external oblique muscle/rectus abdominis) inferiorly . - The radical mastectomy (Halsted) included excision of the breast, all the axillary lymph nodes and both the pectoralis major and minor muscles. It is rarely indicated as it causes - excessive morbidity owing to the limitation in movement at the shoulder joint, extensive upper limb lymphoedema, pain and chest wall deformity with no survival benefit compared with less radical surgery . The modified radical mastectomy (MRM) entails mastectomy along with removal of the level I, II and III axillary lymph nodes. Skin- and nipple-sparing mastectomy is an option in DCIS and early breast cancers where a mastectomy is indicated and the tumour is >1 /uni00A0 cm away from the skin and >2 /uni00A0 cm away from the nipple. The breast may then be reconstructed using autologous tissue flaps/fat or a silicone breast implant. Breast conservation surgery (BCS) is aimed at removing the tumour along with a 1-cm margin of normal breast tissue. It is important to orient the surgical specimen with sutures: long lateral (‘L’ for ‘lateral’) and short superior (‘S’ for ‘superior’). This is important if one or more margins is pos - itive on histological examination. Patients with involved mar - gins should have a revision of margins called a ‘cavity shave’. All patients with BCS receive radiotherapy . BCS together with radiotherapy is called breast conservation therapy (BCT): BCS /uni00A0 + /uni00A0 RT /uni00A0 = /uni00A0 BCT . BCS is, however, best avoided in patients with a multicentric tumour, di ff use microcalcifications on a mammogram, a large tumour-to-breast ratio, two times positive surgical margins after re-excision, a history of previous breast or chest wall radiation, systemic lupus erythematosus or other collagen vascular disease (these patients have a high risk of a radiation reaction), or ankylosing spondylitis; it is also best avoided in those with severe orthopnoea (as the patient cannot lie on the radiation table). Wide local excision (WLE) of up to 20% of the breast volume can be achieved by excision of the tumour with ade - quate margins and closure of the defect by approximation of the breast tissue with absorbable sutures. V olume loss greater than 20% or an unfavourable breast-to-tumour ratio requires - an oncoplastic procedure to fill the defect so created by mobilising the breast tissue. Oncoplasty is defined as tumour excision with wide mar - gins followed by repair of the defect by local rearrangement/ replacement of the breast tissue and the nipple–areola com - plex to maintain shape and symmetry . This may be achieved by volume displacement (level 1) (Figures 58.30 and 58.31) or by volume replacement using a distant or local flap (level 2) (Figure 58.32) (Summary box 58.4). Surgery for the axilla The role of axillary surgery is to stage the patient (sentinel lymph node biopsy [SLNB]) and to treat disease by axillary lymph node dissection (ALND) for patients with positive axil 58.8) . lary nodes (Sentinel means ‘a guard’. Like a guard, the first echelon/level of axillary lymph nodes is located at the gateway of the axilla and provides information about the status of axillary node metastasis. The sentinel lymph node refers to the first echelon lymph node in the axilla draining the breast. The sentinel lymph node is identified by the injection of a blue dye (patent blue or methylene blue) and radioisotope technetium-99m-labelled albumin/ sulphur colloid/antimony in the breast. The fluorescent dyes fluorescein or indocyanine green can be used if radioisotope is not available. The combination of fluorescein and methylene blue can detect sentinel nodes with >90% identification. - Indocyanine green can detect sentinel nodes with 95–100% identification. The dye may be injected into the peritumoral tissue or the periareolar, subareolar or intradermal plane. The tracer(s) passes through lymphatics to the sentinel node and is detected visually as a blue-coloured node and/or a hot node (radioactive) with a handheld gamma ray detection probe or as a fluorescent node with blue light (480 /uni00A0 nm for fluorescein) or infrared light (780 /uni00A0 nm for indocyanine green) (Figure 58.33) . ex vivo count of the hot lymph node(s) is noted. All lymph The ex vivo count of the hottest node nodes with >10% of the and blue lymph nodes are removed and sent for histological confirmation of nodal metastasis. This may be done with

(d) Figure 58.30 Volume displacement oncoplasty for an upper outer quadrant tumour the lateral mammary crease (b) . Full-thickness excision of the tumour with 1-cm margins outer quadrant of the breast to /f_i ll the defect cavity (d) . Final sutured wound Figure 58.31 A patient with volume displacement with round-block oncoplasty for a right breast tumour. Sentinel lymph node biopsy. (e) (a) . Skin incision markings extending to the periareolar and (c) . Dermoglandular pillar mobilisation from the lower (e) . Figure 58.32 A patient with volume replacement oncoplasty with a muscle-sparing latissimus dorsi muscle /f_l ap reconstruction for a left breast tumour.

Surgical techniques used to treat breast cancer David Howard Patey , 1899–1976, surgeon, Middlesex Hospital, London, UK. John L Madden , 1913–1999, surgeon, St Claire Hospital, New Y ork, NY Hugh Auchincloss , 1915–1998, surgeon, Columbia College of Physicians and Surgeons, New Y ork, NY , USA. Edward F Scanlon , 1919–2008, surgeon, Evanston, IL USA. methods (GeneSearch Breast Lymph Node Assay™). These methods involve homogenising the node and detecting a gene expression of cytokeratin 19 or mammaglobin by RT-PCR. Frozen-section evaluation of sentinel nodes has a false- negative rate of 10–12%. Wherever the facility for frozen section is not available, the sentinel node should be sent for for malin- preserved para ffi n section processing and haematoxylin and eosin staining. SLNB is contraindicated in patients with inflammatory breast cancer and in those with T4 disease or a history of pre - vious breast or chest wall surgery , breast scar ring (burns) or radiotherapy . This is indicated for stag - ing and local disease control in patients with axillary lymph node-positiv e tumours that are clinically and/or biopsy-proven non-palpable nodes and those with three or more sentinel lymph nodes that are positive for macrometastasis. ALND requires car eful anatomical dissection to protect the axillary vein, thoracodorsal vessels, medial and lateral pecto - ral nerves, intercostobrachial nerves and the long thoracic and thoracodorsal nerves. The intercostobrachial nerv e may be divided in the presence of heavy nodal burden to achieve onco - logical clearance. Le vel I and II nodes are routinely removed (Figure 58.34). Level III axillary dissection is reserved for patients w ho have enlarged level I and II lymph nodes. Breast reconstruction Immediate breast reconstruction o ff ers the advantage of women waking up after surgery with a breast mound. Some women may prefer to undergo delayed reconstruction 6–12 months after completion of their adjuvant treatment. Immediate reconstruction can be performed using silicone gel breast implants or autologous tissue. Silicone gel implants can be placed superficial to (prepectoral) or underneath , USA.

Modi /f_i ed radical Mastectomy mastectomy

- level I, II, III axillary lymph node dissection: pectoralis minor muscle is removed in Patey/Madden, retracted in Auchincloss and is divided but not removed in Scanlon modi /f_i cations Simple or total Mastectomy including axillary tail mastectomy without axillary surgery Skin-sparing Mastectomy: breast skin envelope mastectomy is preserved, nipple–areola complex removed Mastectomy: breast skin envelope and Skin + nipple/ areola-sparing nipple–areola complex are preserved mastectomy Removal of tumour with a three- WLE (synonyms lumpectomy; dimensional clearance of a 1-cm margin breast of normal tissue conservation surgery, BCS) Quadrantectomy Removal of the tumour-containing quadrant of the br east Level I oncoplasty Volume displacement technique involves dual-plane mobilisation of the breast par enchyma (i.e. the dermoglandular plane and the plane between breast par enchyma and pectoralis muscle) to close the defect created after WLE Level II More complex pr ocedures that involve oncoplasty skin excision

and glandular mobilisation to allow major volume r esection, usually more than 20% of breast volume (a) (b) Figure 58.33 Sentinel lymph node biopsy done using (a) (b) indocyanine green – the /f_l uorescent sentinel lymph node is seen using infrared imaging with a ‘spy camera’; blue sentinel lymph nodes and lymphatics are seen in the axilla. Sentinel lymph nodes are marked with an arrow. Axillary lymph node dissection. (c) /f_l uorescein dye – the /f_l uorescent sentinel lymph node is seen with blue light; (c) blue dye (methylene blue) –

(subpectoral) the pectoralis major muscle. The tissue fl aps commonly used include the latissimus dorsi (Figure 58.35 the transverse rectus abdominis myocutaneous (TRAM) (Figure 58.36), the anterolateral thigh and the deep inferior epigastric perforator (DIEP) free tissue transfers (Figure 58.37 The DIEP fl ap is commonly used in the UK. It requires microvascular surgical skills and an operative time of about Paolo Mascagni , 1755–1815, Italian physician and anatomist, published the fi rst complete description of the lymphatic system. 4 /uni00A0 hours. The treatment algorithm for breast reconstruction is), set out in Figure 58.38 . Radiotherapy after insertion of a silicone prosthesis often leads to a high incidence of capsular contracture and unac -). ceptable results. To achieve symmetry after breast r econstruction or BCS, the opposite breast may require a cosmetic procedure such as

Thoracic duct Jugular lymph trunk Right lymphatic duct Bronchomediastinal lymph trunk Subclavian lymph trunk Interpectoral nodes Lateral thoracic vein Internal mammary lymph nodes (b) Biceps and coracobrachalis muscles Pectoralis major Pectoralis Subscapular minor nerves Axillary artery Axillary vein Latissimus dorsi muscle Subscapularis muscle Thoracodorsal nerve Long thoracic nerve Supraclavicular nodes Apical nodes Cephalic vein Cephalic Mascagni lymphatic pathway Level Level II III Lateral nodes Level I Central nodes Pectoral lymph nodes Sappey’s subareolar plexus Figure 58.34 (a, b) Lymphatic drainage of the breast depicting level I, II and III lymph nodes.

reduction or augmentation mammoplasty or mastopexy . The patient needs to be informed that she may require more than one procedure for symmetrisation . Surgical options for locally advanced breast cancers (stages IIIA, IIIB) Following NACT patients should be o ff ered the option of mastectomy or BCS, if suitable (Figure 58.38). Patients with initial skin or chest wall involvement and those with inflamma tory carcinoma should undergo MRM (58.9). The role of SLNB in patients with cT3N0 disease and those who become N0 after NACT is currently being studied in a number of trials. A high false-negative rate (>10%) has been reported; this can be reduced if at least three sentinel nodes are removed using dual tracers or using ‘targeted SLNB’. In the targeted technique, a metal clip or permanent India ink is applied to a positive node prior to NAST . During surgery after NAST , the node containing the clip or India ink is removed along with SLNB. Adjuvant treatment Radiotherapy Radiotherapy is shown to decrease the risk of locoregional and systemic recurrence and improve survival. The indications include the following: /uni25CF patients with locally advanced breast cancers T3, T4, N1, N2, N3 disease; /uni25CF following BCS; /uni25CF after mastectomy if: /uni25CF tumour size ≥ 5 /uni00A0 cm; skin or chest wall involvement; lymphovascular invasion (LVI), grade 3; /uni25CF axillary lymph node positive for metastasis. In pathologically lymph node-negative tumours, radio - therapy after BCS is given to the breast only as a dose of 45–50.4 /uni00A0 Gy (with or without a boost) delivered in 25 fractions or of 40–42.5 /uni00A0 Gy delivered in 15 or 16 fractions (hypofrac - tionation). In patients after mastectomy (T3N0M0), chest wall

radiotherapy is given if the sentinel lymph nodes are nega - tive. In patients with lymph node-positive disease locoregional radiotherapy is given covering the chest wall, supraclavicular - region, inter nal mammary nodes and the axilla. The axilla should not be irradiated after axillary node dissection as this increases the risk of lymphoedema. Accelerated partial breast irradia tion (APBI) is a modality of radiotherapy for selected patients meeting the following

Figure 58.35 Reconstruction with latissimus dorsi /f_l ap. Figure 58.36 Transversus abdominus muscle /f_l ap. Latissimus dorsi myocutaneous /f_l ap Deep inferior Superior gluteal epigastric artery perforator perforator /f_l ap /f_l ap Anterolateral Inferior gluteal thigh /f_l ap artery perforator /f_l ap Profunda artery Transverse upper perforator /f_l ap gracilis myocutaneous /f_l ap Figure 58.37 Autologous tissue options for breast reconstruction.

criteria (American Society for Radiation Oncology ABPI guidelines, 2016): /uni25CF women 50 years or older with T1 disease and negative resected margins with a margin width of ≥ 2 /uni00A0 mm, invasive ductal carcinoma, no LVI, ER positive, BRCA negative and sentinel node negative; /uni25CF women 50 years or older with low-risk DCIS (screen detected, low/intermediate nuclear grade, tumour size ≤ 2.5 /uni00A0 cm, negative resected margin widths ≥ 3 /uni00A0 mm). The tumour bed is irradiated along with a narrow rim of surrounding tissue so as to avoid the potentially harmful e ff ects of irradiation on healthy tissue . It is delivered twice daily for 5 days. Adjuvant systemic therapy The purpose of adjuvant systemic therapy is to control puta tive micrometastases, delay relapse and prolong survival. The results of many international clinical trials, including National Surgical Adjuvant Breast and Bowel Project (NSABP) trials and the Oxford overview meta-analyses b y the Early Breast Cancer Trialist Collaborative Group (EBCTCG), demonstrate the benefit of chemotherapy in improving relapse-free survival by approximately 30% and overall survival by 10% at 15 years. This is the most common systemic treatment for breast cancer. The following regimens are used: /uni25CF cyclophosphamide (C), methotrexate (M) and 5-fluorouracil (F) (CMF); /uni25CF anthracycline-based regimens: CAF (A, Adriamycin [doxo rubicin]), CEF (E, epirubicin); /uni25CF taxane (docetaxel, paclitaxel)-based regimens. Adjuvant chemotherapy is indicated for all invasive car cinomas >1 /uni00A0 cm in diameter, tumours >0.5 /uni00A0 cm with poor prognostic factors (presence of LVI, high grade, HER2/neu positive, TNBC) and node-positive tumours. Currently , deci - sions to administer chemotherapy as well as to choose a par - ticular regimen are based on tumour stage, tumour biology and discussion with the patient and/or care giver in an MDT . Gene signature panels help in assessing the benefit of chemotherapy in low-risk tumours , i.e. ER-positive, HER2/ neu-negative and node-negative tumours. The risk of recur - ® rence (ROR) scores include Oncotype Dx (21-gene recur - ® rence score), Prosigna PAM-50 (breast cancer prognostic gene ® signature) and MammaPrint (70-gene breast cancer recur - ® rence assay). Oncotype Dx is the most widely used ROR score and measures the expression of 16 cancer-related genes and five reference genes on para ffi n-embedded tumour tissue. The assay classifies the ROR score as low (<18), moderate (19–30) or high (>30). In patients with a low ROR score, chemotherapy can be avoided. - In patients with endocrine-responsive breast cancer, those with luminal A tumours may avoid chemotherapy if they ® have a low-risk score on Oncotype Dx and/or clinical risk assessment online tools (e.g. https://breast.predict.nhs.uk/ tool); however, patients with a high clinical and genomic risk should be considered for chemotherapy with an anthracycline (epirubicin) or taxane-based therapy . Patients with lumi - nal B tumours should receive an anthracycline and/or taxane-based therapy because of the greater risk of relapse. Those with HER2/neu-positive tumours should receive

trastuzumab+pertuzumab along with chemotherapy (taxane /uni00A0 + /uni00A0 anthracycline), while those with triple negative tumours should receive chemotherapy (taxane /uni00A0 + /uni00A0 anthra - cycline). Carboplatin-based regimens may be beneficial for - tumours with aggressive biology . The monoclonal antibody trastuzumab ® - (Herceptin) is e ff ective against the HER2/neu receptor. It is used along with pertuzumab to treat HER2/neu-positive

Candidate for breast conservation therapy Volume displacement Volume oncoplasty replacement (breast tissue oncoplasty rearrangement) Skin/muscle/ fascia or Autologous combined fat grafting /f_l aps Figure 58.38 Surgical options in women undergoing breast-conservating surgery and reconstructive options for women requiring mastectomy. DIEP , deep inferior epigastric perforator; TRAM, transverse rectus abdominis myocutaneous. Chemotherapy. Requires mastectomy Combined Expander/ Autologous autologous + implant-based reconstruction implant reconstruction Abdomen- Latissimus Other tissue based /f_l aps dorsi /f_l ap sources (DIEP , TRAM) Targeted therapy.

T-DM1 is used in HER2/neu-positive disease: a chemother apy agent, emtansine, is conjugated to trastuzumab to allow targeted delivery of the chemotherapy to HER2-positive cells. The selective oestrogen receptor modula tor tamoxifen and ar omatase inhibitors (anastrozole, letrozole, exemestane) are used for hormonal therapy in breast cancer. In premenopausal patients only tamoxifen is used for 5 years in low-risk patients and for 10 years in patients with a high risk of relapse (node positive, tumour >5 /uni00A0 cm, LVI). Aromatase inhibitors are used in postmenopausal women; in an adjuvant setting they have shown beneficial e ff ect com pared with tamoxifen in terms of relapse-free survival and overall survival. The y are more expensive than tamoxifen and their use is associated with bone density loss and risk of frac ture. A bone density scan is advised prior to commencement of trea tment with aromatase inhibitors. Bisphosphonates with vitamin D and calcium are used to restore bone loss and may also reduce the risk of recurrence .

Hormone therapy.

Triple assessment

Triple assessment

Patients presenting with a breast lump, nipple discharge or other symptoms are assessed by a combination of clinical examina - tion, radiological imaging and tissue sampling taken for either cytological or histological analysis. This combined approach is called ‘triple assessment’ (Figure 58.2). The positive predictive value and diagnostic accuracy of this combination approach 100%. The clinical assessment should inv olve a thorough history and clinical breast examination that includes inspection and palpation (Figure 58.3 and 58.2).

Ultrasonography

Ultrasonography

Ultrasonography is the primary imaging modality in young women with dense breast tissue in whom mammograms are di ffi cult to interpret. Ultrasonography can distinguish cystic from solid lesions. Simple cysts do not require further work-up and follow-up can be avoided. Therapeutic aspiration may be performed for cysts causing pain (Figure 58.4). A well-circumscribed, mobile, solid mass in a young woman is suggestive of a fibroadenoma and has an extremely low likelihood of malignancy . Such a finding requires reassurance and imaging follow-up (Figure 58.5). Solid masses with an irregular shape and ill-defined margins (indistinct, angular or spiculated) are suspicious for malignancy and require biopsy (Figure 58.6). Ultrasonography of the axilla is performed when cancer is diagnosed, with guided percutaneous biopsy of any suspicious lymph glands.

Figure 58.3 Clinical breast examination. (a) Patient lying supine for palpation. for a comprehensive examination. Figure 58.4 Therapeutic aspiration of a complicated cyst. Ultraso nography shows needle aspiration of a sharply de /f_i ned, anechoic cyst with internal echoes – the /f_l oating debris. Breast Imaging Reporting and Data System (BI-RADS) score 2 (Table 58.1).

Vacuum-assisted biopsy

Vacuum-assisted biopsy

The sampling error decreases as the biopsy volume increases and using 8G or 11G needles allows more extensive biopsies to be taken. This is useful in the management of microcalcifi - cations and removal of benign lumps such as fibroadenoma.

Work-up for metastatic breast cancer

Work-up for metastatic breast cancer

Contrast-enhanced CT of the chest, abdomen and pelvis and an isotope bone scan are needed for patients with locally advanced breast cancer (T3, T4 or N2, N3 disease). Patients with early breast carcinoma (T1, T2 and N0, N1 disease) need metastatic evaluation only if they present with symptoms to suggest metastatic disease or raised serum alkaline phospha 18 18 tase. A PET-CT scan with F-fluorodeoxyglucose (F-FDG) tracer may be used for metastatic work-up.