CASE THREE

Short case number: 3.11.3
Category: Endocrine and Reproductive
Discipline: Surgery
Setting: General Practice
Topic: Breast cancer – Clinical presentation and assessment of breast cancer risk. [SDL]

Case

Michelle Feeney, aged 35 years, presents requesting testing for the BRCA–1 or BRCA-2 gene. Her sister aged 38 years, has been diagnosed with breast cancer and has refused genetic cancer testing, but Michelle is concerned. Her mother and father both died from non-cancer disease.

Questions

1. In a table list the common hormonal and genetic breast cancer risk factors and their relative risk.
2. What further history, examination and investigation would you undertake for Michelle?
3. What are the current recommendations for breast cancer screening in asymptomatic women in Australia?
4. How would you evaluate a 38 year old woman who presents with a "breast mass"?
5. Summarise the vascular supply, neural supply, and lymphatic drainage of the breast.
6. What is the rationale for sentinel lymph node biopsy in the surgical treatment of early breast cancer?

Suggested reading:

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

Further Reading

- National Breast and Ovarian Cancer Centre. Breast cancer risk factors: a review of the evidence. National Breast and Ovarian Cancer Centre, Surry Hills, NSW, 2009. https://canceraustralia.gov.au/sites/default/files/publications/breast-cancer-risk-factors-review-evidence/pdf/rfrw-breast-cancer-risk-factors-a-review-of-the-evidence_1.15.pdf
- Early detection of breast cancer – Cancer Australia Position Statement http://canceraustralia.gov.au/about-us/position-statements/early-detection-breast-cancer

ANSWERS

1. In a table list the common hormonal and genetic breast cancer risk factors and their relative risk. (NB for tutors far right column RR<0.8 – protective factors)

(Protective factors)

Table 1 Summary of risk factors for invasive breast cancer

	RR >4 +++	RR 2–3.99 ++	RR 1.25–1.99 +	RR <0.8 –
Sex, age and residence	Female, increasing age (50+ years vs <50 years) Affluent country of residence (NAm/Aus/ NZ/Eur vs Africa/Asia)			
Family history and genetics	BRCA1, BRCA2, ATM or TP53 gene (p53) mutation carrier	Two or more first-degree relatives with breast cancer CHEK2 mutation carriers	One first-degree relative or multiple second-degree relatives with breast cancer	
Breast conditions	DCIS in same breast **Previous invasive cancer**	Atypical ductal hyperplasia	DCIS in opposite breast Proliferate BBD without atypia	
Reproductive and menstrual history			Age at first period younger than 12 years (vs >12 years) Age at menopause older than 55 years (vs < 55 years)	Parity (vs nulliparity) Four births or more (compared with one) Age at first birth younger than 25 years (vs older than 29 years) Breastfeeding at least 12 months total duration (vs no breastfeeding)
Endogenous and exogenous hormones		High circulating levels of oestrogen (top 20% vs bottom 20%, in postmenopausal women only)	Use of oral contraceptives within past 10 years (vs never) Use of combined hormone replacement therapy (current users vs never) High circulating levels of androgens (top 20% of levels vs bottom 20%) high circulating levels of IGF-1 and IGFBP-3 (top 25% of levels vs bottom 25%, possibly only for postmenopausal women)	Use of tamoxifen for more than 5 years Use of raloxifene
Body size and lifestyle behaviours			Height >175 cm (vs < 160 cm) BMI >25 kg/m² (vs <21 kg/m²), for postmenopausal breast cancer Daily intake of three or more standard alcoholic drinks (vs none)	Obesity for premenopausal breast cancer (BMI ≥31 kg/m² vs BMI <21 kg/m²) Physical activity - two or more hours of brisk walking or equivalent per week (vs no activity)
Medical history	Radiation treatment for Hodgkin's disease before age 30 years History of breast cancer in opposite breast		History of cancer in other organs (including ovary, thyroid, endometrium, colon, melanoma) Treatment with high-dose ionising radiation, especially before age 20 In utero exposure to diethylstilbestrol , **Mantle radiotherapy**	
Environmental exposures			High-dose ionising radiation, especially before age 20	

2. What further history, examination and investigation would you undertake for Michelle?

- History of symptoms or previous breast changes
- Assessment of risk: further family history, medical history, hormone exposure
- At 38yo is not recommended for mammogram in asymptomatic woman, unless history reveals a higher risk assessment.

3. What are the current recommendations for breast cancer screening in asymptomatic women in Australia?

This position statement applies to screening methods for the early detection of breast cancer in asymptomatic women, it does not apply to diagnostic tests used to assess women presenting with breast changes.

Detection of breast cancer while it is still small and confined to the breast provides the best chance of effective treatment for women with the disease. Benefits of early detection include increased survival, increased treatment options and improved quality of life. For women, age remains the biggest risk factor in the development of breast cancer with over 70% of cases found in women aged 50 years and older. However, in younger women, tumours are likely to be larger and more aggressive and overall survival is lower than for older women with the disease. It is therefore important that women of all ages understand the importance of finding and treating breast cancer early.

The early detection methods are:

- breast awareness – awareness by a woman of the normal look and feel of her breasts
- clinical breast examination – physical examination of an asymptomatic woman's breasts by a medical professional
- Screening mammography – use of mammography in asymptomatic women to detect breast cancer at an early stage (BreastScreen Australia is the national mammographic screening program).

Recommendations

<u>Women at population risk</u> (the level of risk of developing breast cancer for women in the general population –*currently estimated 1/11*)

- Breast awareness - recommended that women of all ages, and regardless of whether they attend for mammographic screening, are aware of how their breasts normally look and feel and report any new or unusual changes promptly to their general practitioner. No one method for women to use when checking their breasts is recommended over another.

- Clinical breast examination - A firm recommendation regarding clinical breast examination is not possible as there is no evidence to either encourage or discourage the use of clinical breast examination as a screening method for women of any age. Women who are eligible and are attending for regular mammographic screening should be aware that there is no evidence that clinical breast examination will provide additional benefit. Women who are not attending regular mammographic screening may gain some benefit from regular clinical breast examination.

- Mammographic screening:
  - Women younger than 40 years
    Mammographic screening is not recommended for women younger than 40 years of age.
  - Women aged 40–49 years
    Eligible for free two-yearly screening mammograms through the BreastScreen Australia

Program (although they are not targeted by the Program). In deciding whether to attend for screening mammography, women in this age group should balance the potential benefits and downsides for them, considering the evidence that screening mammography is less effective for women in this age group than for older women.

- Women aged 50–69 years
  It is recommended that women aged 50–69 years attend the BreastScreen Australia Program for free two-yearly screening mammograms.
- Women aged 70 years and older
- eligible for free two-yearly screening mammograms through the BreastScreen Australia Program (Women at increased risk of developing breast cancer (strong family history of breast or ovarian cancer (two or more family members have had breast or ovarian cancer, especially if they are close relatives – mother, sister or daughter – and/or if they were younger than 50 when their cancer was diagnosed), are a carrier of a gene mutation, ductal carcinoma in situ or other high-risk pre-invasive breast disease)

- Individualised surveillance program be developed in consultation with the woman's general practitioner and/or specialist. This might include regular clinical breast examination and breast imaging with mammography and/or ultrasound. Women should also be aware of the normal look and feel of their breasts and report any changes promptly to their general practitioner or specialist irrespective of whether they are having regular follow-up tests/examinations.

4. How would you evaluate a 38 year old woman who presents with a "breast mass"?

Any palpable breast abnormality should be assessed by the process of triple assessment:

- clinical evaluation
- radiological evaluation
- Cytological/histological evaluation.

History

- nature of the breast mass
- Risk factors mentioned above: family, menstrual and reproductive history, the use of hormones and a personal history of breast cancer or breast disease.

Physical examination

- Inspection and palpation of the entire breast and lymph node-bearing areas
- Features of mass: position, size, consistency and any fixation to surrounding deep or superficial structures.
- Should the patient complain of discharge, then an attempt to reproduce this should be made. Any discharge that is obtained should be tested for blood using a reagent stick and be sent for cytological examination.

Investigation

Mammography
Generally, mammography in women under 35 years is often not helpful because they have particularly dense breasts at this age which can mask any underlying tumours and also make interpretation very difficult. However, it should be done if there is clinical suspicion of malignancy.
Mammographic abnormalities that warrant further investigation include:

- radiological masses undetected on clinical examination
- microcalcifications
- stellate densities
- architectural distortion
- Change from a previous mammogram.

Ultrasound
Useful in discriminating solid from cystic masses and especially in the evaluation of the dense breast. Other uses include ultrasound-guided biopsy or needle localisation. In younger women, ultrasound may reveal more information than mammography, and most surgeons would perform this test first in women less than 35. Masses smaller than 5-10 mm may not be visualised, and masses in fatty breasts are also difficult to assess.

MRI
Further research is being done to evaluate the role of breast MRI in the clinical setting.
Needle aspiration and cytology
For impalpable lesions, stereotactic techniques can be used to localise the lesion for needle aspiration.
core needle biopsy
The method provides a sample of tissue for histological rather than cytological examination. The pathological diagnosis which results should be more certain because cellular architecture can be assessed.
Excision biopsy- This refers to the removal of all gross evidence of disease with a small rim of normal breast tissue. If the tumour is small enough, all macroscopic disease is removed, but the primary objective is for diagnostic purposes.

Incision biopsy
This is similar to excision biopsy except that only a part of the lump is removed. It is generally felt that this is not good surgical practice. The use of incision biopsy is therefore restricted to larger tumours. Screening mammography (above) demonstrates many clinically impalpable lesions. To localise these, a marking wire is placed under mammographic guidance before surgical excision. The tissue around the wire is then excised and further imaging done to ensure that the indicated lesion has in fact been removed.

Ultrasound-guided biopsy
Both the technique of needle-guided biopsy and real-time cyst aspiration can be used. Techniques of one or the other are dependent on the expertise available.

5. Summarise the vascular supply, neural supply, and lymphatic drainage of the breast.

Arterial supply
The breast is related to the thoracic wall and to structures associated with the upper limb; therefore, vascular supply and drainage can occur by multiple routes:

- laterally, vessels from the axillary artery-superior thoracic, thoraco-acromial, lateral thoracic, and subscapular arteries;
- medially, branches from the internal thoracic artery;
- The second to fourth intercostal arteries via branches that perforate the thoracic wall and overlying muscle.

Venous drainage
Veins draining the breast parallel the arteries and ultimately drain into the axillary, internal thoracic, and intercostal veins.

Innervation
Innervation of the breast is via anterior and lateral cutaneous branches of the second to sixth intercostal nerves. The nipple is innervated by the fourth intercostal nerve.

Lymphatic drainage
Lymphatic drainage of the breast is as follows:

- approximately 75% is via lymphatic vessels that drain laterally and superiorly into axillary nodes;

- most of the remaining drainage is into parasternal nodes deep to the anterior thoracic wall and associated with the internal thoracic artery; and
- Some drainage may occur via lymphatic vessels that follow the lateral branches of posterior intercostal arteries and connect with intercostal nodes situated near the heads and necks of ribs.

Axillary nodes drain into the subclavian trunks, parasternal nodes drain into the bronchomediastinal trunks, and intercostal nodes drain either into the thoracic duct or into the bronchomediastinal trunks.

6. What is the rationale for sentinel lymph node biopsy in the surgical treatment of early breast cancer?

It has been demonstrated that there are usually one or two nodes that are the first nodes draining the breast. It appears that, if these nodes are identified and removed, they are predictive for the rest of the axilla. They are identified preoperatively by using a special blue dye and/or radioactive technetium sulphur colloid and a modified directional Geiger counter.

If lymph node involvement is demonstrated following sentinel node biopsy, axillary radiotherapy is given to help control axillary nodal metastasis, or an axillary clearance is performed. Both axillary radiotherapy and axillary lymph node clearance have lymphoedema as a potential side effect.