

MALE BREAST DISEASE: INVESTIGATION AND MANAGEMENT

CLEMENT WONG

INTRODUCTION

- Breast develops from ectodermal mammary ridge
- Before puberty, breast development is identical in male and female
- At puberty in female, estrogen stimulates the development of lobular structure in the breast tissue
- In male, the relative hyperestrogenism around puberty can lead to the development of gynaecomastia in 50% of adolescent

History

- Age
- Pain
- Nipple discharge
- Change of libido or sexual function
- Family history of male breast cancer
- Medication (prescription drug, alcohol, marijuana, anabolic steroid)
- Medical history (e.g. Klinefelter syndrome, prostate cancer)

History

- Symptoms of pituitary, renal, thyroid, hepatic or adrenal disease
- Occupation (present/previous)
- Recent trauma

Physical Examination

- Location of mass (eccentric/concentric), unilateral or bilateral
- Nature of mass (size, shape, fixed/hard, rubbery)
- Ulceration
- Colour of discharge
- Axillary lymph nodes
- Chest, abdominal and testicular examination

DIFFERENTIAL DIAGNOSIS

- A) GYNECOMASTIA (80%)
- *Primary*
- 1) Infant (resolve by 4 months)
- 2) Pubertal (93% resolve by 3 yrs)
- 3) Senile (60% by the age of 70)

DIFFERENTIAL DIAGNOSIS

- *Secondary*

- 4) drug

Anabolic steroid, stilboestrol, digoxin,
rantidine, methyldopa, risperodone

hormone therapy (oestrogen, androgen)

- 5) hormonal disturbance

- (i) decrease androgen

Alcohol, Klinefelter syndrome (40%)

5 alpha reductase deficiency

Testicular failure (bilateral cryptorchidism)

DIFFERENTIAL DIAGNOSIS

- (ii) increase oestrogen
 - Testicular tumour (10% BhCG)
 - Adrenal tumour, pituitary tumour
- (iii) increase aromatisation
 - Hepatic failure, hyperthyroidism
 - renal failure on dialysis (30%)

DIFFERENTIAL DIAGNOSIS

- 6) Idiopathic

- (i) associated with chronic disease

- Chronic lung disease (T.B./tumour)

- R.A., U.C., paraplegia

- (ii) otherwise healthy adult

DIFFERENTIAL DIAGNOSIS

- B) Pseudogynecomastia
- Fatty hypertrophy
- C) Benign Lesion
- 1) adenoma, lipoma, fibroadenoma
- 2) cysts (retention, dermoid)
- 3) infection (specific and non-specific)
- 4) fat necrosis

DIFFERENTIAL DIAGNOSIS

- D) Malignant
- 1) carcinoma
- 2) sarcoma
- 3) metastatic disease

Investigation

- Options:
- 1) mammogram
- 2) USS breast+/-testis
- 3) FNA/core biopsy if suspicious of malignancy
- 4) blood test (LDH, BhCG, Alpha FP, ELFT, prolactin, testosterone)

Mammogram

- Typical features of gynaecomastia: triangular/round area of increased density with flame shaped margins that is position symmetrically in the retroaerolar region
- 3 mammographic patterns in gynaecomastia: an early nodular/florid pattern, dendritic pattern/fibrous phase and a diffuse glandular pattern (exogenous hormones)
- Male breast cancer: well-defined mass eccentric to nipple, spiculated margins with occasional microcalcifications

USS

- Able to differentiate solid from cystic lesions
- Combine with mammogram improve diagnostic accuracy (Jackson et al, 1983)
- Easy to use

FNA

- ? First line investigation for lesion in male
- Highly sensitive and specific
- Problem:
 - 1) unsatisfactory sample (15% fibrous tissue)
 - 2) uncomfortable
- Janes et al (2006) reported using needle core biopsy as a safe and effective method for assessment of unilateral male breast lump

Pseudogynaecomastia

- Pseudogynaecomastia is due to excess subcutaneous fat in the obese
- Characteristics features in mammogram (radiolucent fat)
- Cosmetic problem
- Liposuction may be an option

Gynaecomastia

FEATURES:

- may be unilateral/bilateral
- may be associated with pain or discharge
- Usually rubbery, round or oval directly behind areola with clear demarcation from the outer surrounding fat

Classification

Grade	
I	Small with no redundant skin
IIa	Moderate breast development with no redundant skin
IIb	Moderate breast development with redundant skin
III	Marked breast development with much redundant skin

Management

- Conservative
- -reassurance for primary cause
- -treat the underlying problem / withdrawal of drug for secondary cause
- Medical
- Surgical

Medical Treatment

- Danazol has been shown to reduce symptoms for idiopathic gynacomastia (Jones et al 1990)
- Ting et al (2000) compared Tamoxifen vs danazol for symptomatic relief. The effect of Tamoxifen was more pronounced (78%) than that of danazol (40%) with high relapse

Surgical

- Subareolar excision using circumareolar incision
- Mastopexy with repositioning of nipple on de-epithelialised pedicles in patients with redundant skin
- liposuction

MALE BREAST CANCER

- Accounts for 0.87% of all breast cancer
- Varies widely between countries (between 5% to 15% in Uganda and Zambia)
- Increase incidence in Jews
- Incidence increase with age with a peak of 71 yrs old (unimodal)
- Behaves in a similar way to postmenopausal breast cancer

Risk Factors

- GENETIC

- BRCA2, AR gene mutation, CYP 17 polymorphism, CHEK2 (Li-Fraumeni), PTEN (Cowden syndrome)

- Klinefelter's syndrome (XYY, XXY)

- LIFESTYLE

- Obesity, alcohol, estrogen intake

- WORK

- Exhaust emission, high ambient temperature

Risk Factor

- Disease
 - Testicular damage, liver damage, radiotherapy to chest
 - hyperprolactinaemia
 - no link between gynaecomastia and breast cancer

BRCA

- 15% of MBC is familiar
- Lifetime risk of MBC in BRCA2 carrier is 6.3% up to the age of 70
- 11% of all breast cancer in BRCA2 families were MBC
- The link to MBC in BRCA1 is less strong

Klinefelter Syndrome

- Typically with testicular dysgenesis, gynaecomastia and low testosterone level
- Risk of breast cancer is 20 to 50 times higher than normal

Features

- Eccentric/unilateral/hard lump
- Painless (75%)
- Nipple discharge (6%) and retraction (9%)
- Ulceration (6%)
- Palpable axillary nodes (40%)
- Mean age of 60 years old
- 33% of patients are in stage III when presented

Histology

- 90% are invasive ductal carcinoma
- ER +ve in 90% and PR +ve in 92-96%

Diagnosis

- Triple assessment
- Core biopsy is better (confirm invasion)
- Mammogram: 92% sensitive, 90% specific
- Microcalcification less common
- USS cystic vs solid/complex → biopsy

Management (Local Disease)

- Modified radical or simple mastectomy (vs radical mastectomy → no decline in survival Ribeiro et al 1996)
- WLE → ? Effective
- ? Sentinel Lymph node biopsy

Sentinel Lymph Nodes

- Boughey et al 2006 compared SLN biopsy in male and female with breast cancer
- Male tends to present older ($p=0.005$) with larger tumour ($p=0.04$)
- For those who have +ve SLN, 62.5% (male) vs 20.7% (female) have additional non-SLN positive ($p=0.01$)
- They concluded SLN is accurate and feasible

Sentinel Lymph node

- For node –ve: Sentinel node biopsy +/- complete axillary clearance (DeCicco et al 2004)
- For node +ve: complete axillary clearance
- May need reconstruction (33%)

Management (Local Control)

- Adjuvant radiotherapy to chest wall+/- supraclavicular fossa+/- internal mammary nodes is indicated for node +ve patient + risk factors
- Risk factors:
 - 1) large tumour; extension to skin/muscle
 - 2) high grade; high tumour proliferation rate
 - 3) vascular invasion
 - 4) unclear margin

Management (Local Control)

- The reported 5 year locoregional recurrence rates with XRT ranging from 5% to 20% [Chakravarthy et al 2002] (c.f. 2/3 reduction in female)

Management (Local Control)

- Tamoxifen improves survival rates in ER +ve women
- No randomised trial for male breast cancer
- Goss et al reported improved disease free and overall survival in men
- ? Role of aromatase inhibitor
- Recommend: tamoxifen for ER +ve male breast cancer

Management (local Control)

- Role of adjuvant chemotherapy
- Giordano et al 2005 and Bagley et al 1987 reported adjuvant chemotherapy improved overall survival (5 yr 80%)
- Regimen used included CMF (cyclophosphamide, methotrexate and 5- FU) and Anthracycline based regimen
- Recommend: intermediate and high risk patients especially in ER –ve
- ? Role of trastuzumab in HER 2 +ve male breast cancer

Management (metastatic)

- 4% to 7% presented with metastatic disease
- 18% to 54% treated for local disease will develop distant metastasis
- Tradition treatment:
 - 1) orchidectomy: RR 80%
 - 2) adrenalectomy: RR 80%
 - 3) hypophysectomy: RR 56%

Management (metastatic)

- Tamoxifen is the first line treatment with 80% response rate in ER +ve patients
- Aromatase inhibitor as a second line treatment
- For those who are ER–ve → combined chemotherapy (fluorouracil, doxorubicin and cyclophosphamide) → 35% response rate
- Palliative radiotherapy + supportive therapy if failed

Prognosis

- Stage and lymph node status are the most important factors
- Overall 5 yr survival 40 to 65%
- Stage I → 5 yr 75-100%
- Stage II → 5 yr 50-80%
- Stage III → 5 yr 30-60% (Ribeiro 1996)

Prognosis

- Some studies suggested male breast cancer has a worse prognosis than female breast cancer
- Willsher et al reported in their study that there is no difference in prognosis between male and female breast cancer when age and stage were matched

Conclusion

- The assessment of breast lump in male is the same as female (triple assessment)
- Most of the lumps are benign (gynaecomastia)
- Male breast cancer shares a lot of similarity to female breast cancer
- This uncommon disease preclude large randomised control trail
- The management may need to use the same guidelines as for women (adjuvant hormone/chemotherapy)

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