Breast audit – hormone receptor practice

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Introduction

"The steroid receptor status of a breast cancer is used to determine whether or not a patient will benefit from anti-oestrogen treatment either as adjuvant therapy or for metastatic disease."

-Royal College of Pathologists *Pathology reporting of breast disease* 2005

Hormone therapy

- Tamoxifen: competitively antagonises ER
- Reduced recurrence (13% at 15 years) cf. placebo and mortality (9% at 15 years)[1]
- Aromatase inhibitors: post-menopause only
  - Reduced recurrence cf. tamoxifen at 5 years.[1]
- Switching thought to produce good results

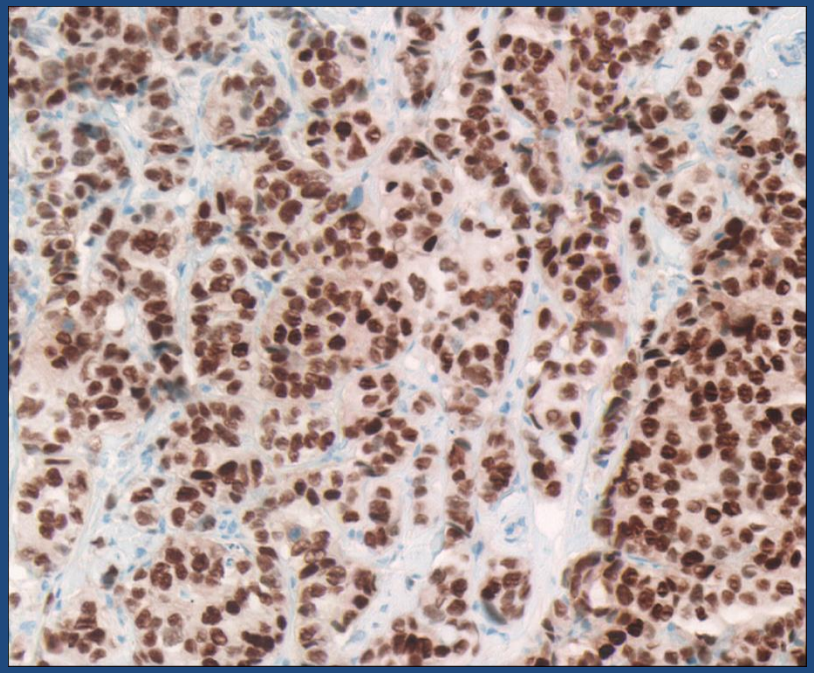
Steroid receptors

- ER and PR exist in the cytosol
- Migrate to the nucleus after binding agonist
- Subsequently result in DNA transcription

- Measurement of ER/PR over-expression thought to help identify good candidates for hormone therapy.

Steroid receptor testing

- Previously, homogenisation of tumour tissue with ligand/ab binding
- Now, IHC is method of choice
- Many variables
  - Tumour heterogeneity
  - Tissue fixation
  - Antigen retrieval
  - Antibody binding
  - Background noise
  - Interpretation of staining



Current issues

- Around 1/3 of ER+ tumours do not respond to hormone therapy.[2]
  - Reason for this is poorly understood
  - Hypothesis of receptor ratio (ER alpha v ER beta)
    - Testing for ER beta not recommended

- Use of -ve PR in ER+ tumours as a predictor of response to tamoxifen remains controversial[2]

Current practice (NICE CG80, 2009)

- 70% of tumours are ER+
- ER status forms part of the minimum dataset
- Prediction of response not straightforward
- PR does not yield useful information in ER+ cases
- <5% of cases are ER-/PR+
  - Value of PR in this situation regarding therapy is unclear

Current practice (CG81, Feb 2009)

“Current practice in some centres is to establish ER and PR and HER-2 status on all newly diagnosed breast cancers.

However there is no evidence that assessing PR status adds significant information to ER status in predicting response to hormone treatment.”

Contribution of PR

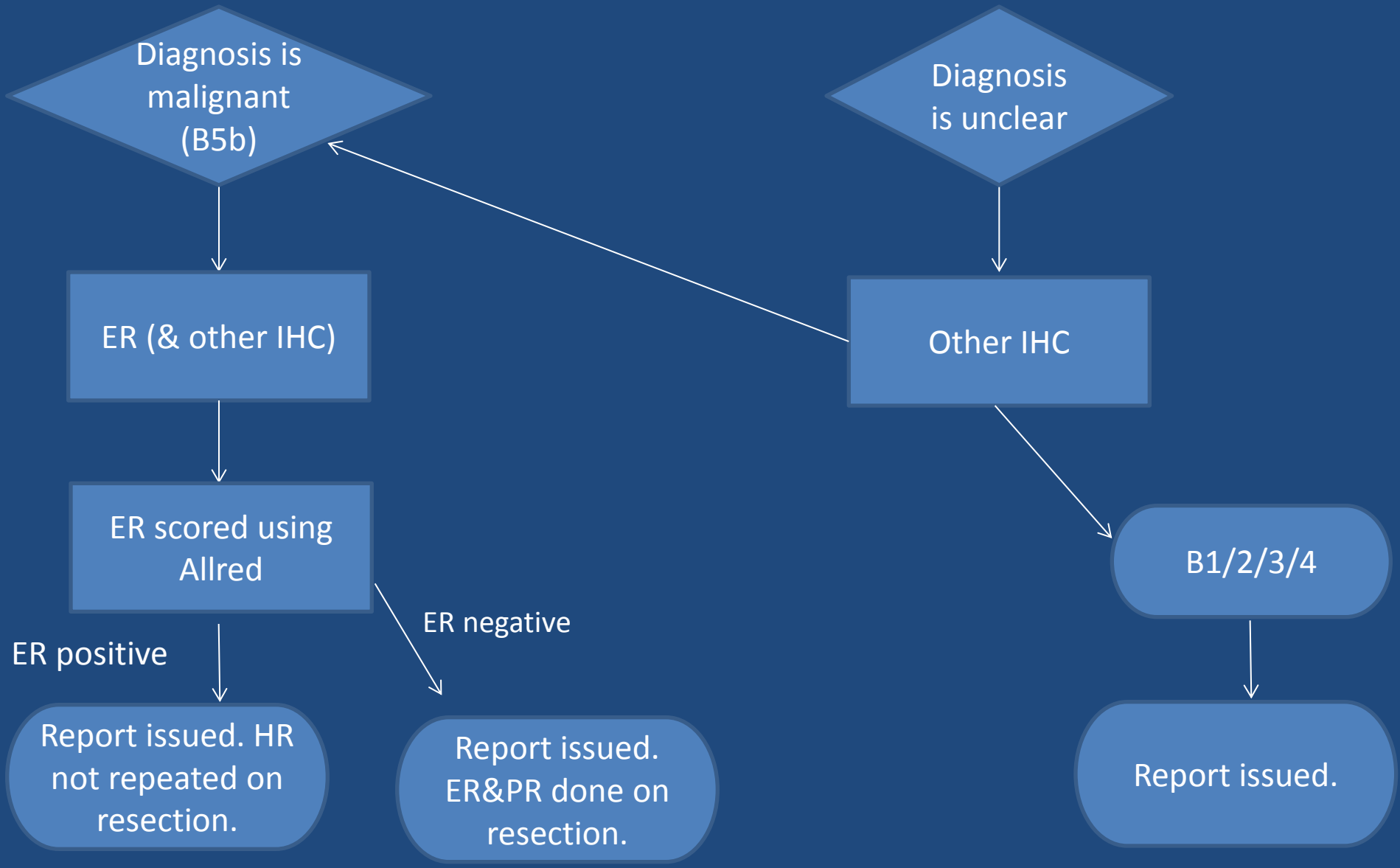
- Controversial
- Gene encoding for PR is oestrogen dependent
  - PR may indicate 'intact' oestrogen-ER-response pathway[3]
  - Some studies show predictive value for PR independent of ER, esp. premenopausal women[4]
- PR may therefore be useful in selecting patients with ER- tumours for endocrine Rx.[4]

Variation in practice

- USA: ER & PR routinely performed on all invasive breast cancers. (ASCO & CAP guidelines)

- ER and PR receptor overexpression routinely tested for with Oncotype DX

Local practice on receipt of biopsy



Local practice

- ER & Her-2 performed on all B5b breast biopsies
- ER positivity scored using Allred
- If ER negative biopsy with good tumour load, ER&PR performed on resection
- If ER negative biopsy with poor tumour load, ER only initially repeated on resection

Aims

- To evaluate the number of cases in which:
  - ER status changes from negative to positive from biopsy to resection & why
  - The tumour has an ER-/PR+ profile
- To ensure local protocols are followed with regards to appropriate request of PR.
- To establish a record of patients with ER-/PR+ tumours for follow-up of response to hormone treatment

Standards

- All cases (100%) with negative ER on core biopsy should have ER and PR performed on resection

- Less than 5% of tumours should be ER-/PR+

Methodology

- Reports searched using Pathosys
- 1 year of data from 1/7/12 to 31/6/13
- All ER- reports pulled
- Biopsies matched with resection specimens
- Cases going from ER- to ER+ pulled and slides reviewed by CH & KS
- ER-/PR+ cases pulled and slides reviewed by CH & KS

Results

- 231 biopsies had hormone IHC in 1 year
- 42 cases with an ER-ve tumour on biopsy
  - 7 biopsy cases lost to further follow up

- Of remaining 35:
  - 3 did not have a PR recorded (8.6% of all ER- cases)
  - 3 cases went from ER- to ER+ from biopsy to resection
  - 3 cases were ER-/PR+ (<1% of total)

3 cases without PR

- 1x not performed
  - went on to be ER-/PR+
  - ER 2/8 on biopsy, 0/8 on resection
  - PR 3/8, supplementary report issued
- 1x recurrence of medullary type cancer
  - originally ER & PR negative (2009)
  - recurrent biopsy only had ER.
  - PR was not repeated on the resection of recurrence.
- 1x PR done but not recorded, actual PR score 0/8
  - no change in management

3 cases from ER- to ER+

- 1x interpretation error on core:
  - small focus of strongly staining nuclei (<1%, strong) on biopsy, therefore 4/8, not 0/8.
  - Resection ER 4/8.

- 2x score initially 0/8 on biopsy then 4/8 on resection:
  - tumour volume and heterogeneity related change

ER-/PR+ Case 1 (13H15790)

- Biopsy: G3 Ductal NST, ER scored as 0/8

- Resection: Ductal NST, ER 0/8, PR 5/8
  - Strong internal control for ER
  - Positive for PR, moderate staining in about 20% of tumour cells

ER-/PR+ Case 2 (13H4107)

- Biopsy: G2 Ductal NST, ER2/8
- Resection: G3 Ductal NST, ER 0/8, PR not done
- PR performed retrospectively, scored as 3/8 (+)
- Supplementary report issued

ER- / PR+ Case 3 12H30462

- Biopsy

  Grade 3, ?Metaplastic carcinoma, ER 0/8

- Resection

  Ductal NST G3, ER 0/8, PR 4/8

Aims

- To evaluate the number of cases in which:
  - ER status changes from negative to positive from biopsy to resection & why
    - 3 cases in one year:
      - 1x interpretation error
      - 2x tumour volume/heterogeneity related change
  - The tumour has an ER-/PR+ profile
    - 3 cases in one year (less than 5%)

- To ensure local protocols are followed with regards to appropriate ordering of PR.
    - Protocols were followed in 41/42 cases requiring PR

- To establish a record of patients with ER-/PR+ tumours for follow-up of response to hormone treatment

Conclusions

- A proportion of tumours appear to have a definite ER-/PR+ phenotype
- Many centres would not pick these up under current UK practice
- Follow-up of patients with ER-/PR+ tumours could lead to a changes in NICE guidance
- High levels of consistency with respect to local protocol for hormone receptor status within the department

References

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4. Stendahl M, Ryden L, Nordenskjold B et al, High progesterone receptor expression correlates to the effect of adjuvant tamoxifen in premenopausal breast cancer patients. *Clin cancer res* 2006;12(15):4614-8


Thank you