The UK Inflammatory Breast Cancer Research Programme

BSBR Research Afternoon November 2015

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Introduction

• Inflammatory breast cancer (IBC) is rare
• ≈ 2.5% all cases of breast cancer
• Stage T4d by definition
• Dire prognosis (median 5 y. survival ≈ 40%)
• Understanding of IBC hampered by lack of consistent, documented diagnostic criteria
• International panel released consensus statement on diagnosis & management in 2011

\(^1\text{Dawood et al. Ann Oncol 2011;22:515-23}\)
Aims of the UK Group

• To coordinate UK practice and research into IBC

• To develop a base for academic and translational research into IBC

• To optimise treatment of IBC through research-driven clinical medicine
Where do we start?

- Ensure we are talking about the same entity!
- Established diagnostic criteria
- Uniform investigation and description
- Uniform data collection
Recommended minimum criteria:

- Rapid and progressive onset of breast erythema (over >30% of breast) or peau d’orange +/- an underlying mass with a maximum symptomatic duration of 6 months
  - To aid differentiation from neglected LABC

- Histopathological confirmation of breast cancer on preoperative biopsy
  - No specific histological or molecular markers
Pathology

- Receptor status

- Ideally, skin biopsy of 1 or 2 representative areas of erythema/peau d’orange
Documentation of medical history and clinical findings

- Duration and nature of symptoms
- Description of breast appearance and examination including proportion of breast involved by erythema (*NB clinical photographs*)
- Degree of extension beyond the breast if present
- Size and location of any breast mass, presence of palpable axillary and supraclavicular fossa nodes
- Presence of any symptoms or signs of metastatic cancer
- A clear statement that the condition fulfills the diagnostic criteria for inflammatory breast cancer
Role of Imaging in IBC

• Diagnosis and characterisation
• Image guided biopsy
• Delineation of locoregional disease
• Identification of distant metastases
• Prognostication
• Prediction and evaluation of response to $R_x$
Local and whole body staging

- Mammography and US as normal
- Ultrasound SCF if axilla abnormal
- US guided biopsy: focal/diffuse US abnormality
- MRI:
  - recommended where no parenchymal lesion shown by XRM or US
  - recommended for monitoring of response to therapy
- Whole body staging: absolutely indicated
Mammography (XRM): Findings

- Frequently difficult (pain, breast enlargement)
- Key features:
  - skin and trabecular thickening (80%)
  - stromal thickening/distortion
  - diffuse increase in density
  - better depicted with digital mammography (FFDM)
- Masses: often absent
- Calcification rarer cf. locally advanced BC
- Axillary nodal enlargement; 30%
Mammography
Ultrasound

Advantages over mammography:

• Patient acceptability

• Better identification (& therefore biopsy) of focal lesions

• Diagnosis of multicentricity
Ultrasound: Findings

- Skin thickening
- Dilated lymphatics
- Generalised hyperechoic oedema
- Distortion, hypoechogenicity, acoustic attenuation
- Discrete focal abnormalities (90% cases)
- Multifocality/centricity
Ultrasound
‘Novel’ Imaging

NCCN guidelines v.2:

• Level 2A evidence for breast MRI

• Level 2B evidence for FDG-PET/CT
  - very helpful for equivocal diagnostic CT CAP
  - may obviate need for isotope bone scan
  - can identify unsuspected regional nodal disease as well as distant metastases
MRI

- **Diagnosis**
  - Most accurate test for identification of focal lesion
  - Can differentiate between IBC and LABC\(^1\)
- **Baseline overview of extent of local disease**
- **Most accurate test for interim and final response assessment\(^2\)**

\(^1\)Girardi et al. *Radiol Med (Torino)* 2012
\(^2\)Shin et al. *Br J Radiol* 2011
MRI: Key Findings

- Increased breast size, skin thickening (>90%)
- Diffuse oedema, skin and prepectoral oedema
- Focal parenchymal lesion: >95%
- Non-mass enhancement, linear/nodular
- Skin enhancement (intradermal foci): >30%
- Multifocal/multicentric disease: >70%
- Axillary adenopathy: >80%

Girardi et al. Radiol Med (Torino) 2011
MRI of IBC

T2 weighted imaging:
• prepectoral oedema suggests IBC$^1$

$^1$Uematsu et al. Breast Cancer 2012
$^2$Renz et al. Acad Radiol 2008
Multiparametric MRI
mpMRI
FDG-PET/CT

• One-stop shop
  • Regional lymph node involvement
  • Occult distant metastases eg. bone\textsuperscript{1}

• Prognostication??
  • Survival associated with fall in $SUV_{\text{max}}$ on MVA\textsuperscript{2}
    - resolution of tumour FDG uptake resulted in 80% lower probability of death

• Early response prediction\textsuperscript{3}

\textsuperscript{1}Groheux et al. J Nucl Med 2013
\textsuperscript{2}Carkaci et al. Eur J Nucl Med Mol Imaging 2013
\textsuperscript{3}Kolesnikov-Gauthier et al. Breast Ca Res Treat 2012
FDG-PET/CT of IBC

- Retrospective review, n=41\(^1\)
- Increased FDG uptake in skin (100%)
- Increased FDG uptake in breast (98%)
- Axillary lymph node uptake (90%), confirmed in 70%
- 1 FN axillary node, 0.7cm diameter
- Subpectoral LN in 44%, confirmed in 30%

\(^1\)Carkaci et al. J Nucl Med 2009
Identification of Distant Metastases

• 20-40% have distant metastases at presentation
• CT: identifies asymptomatic mets in ≈ 25-30%
• Pleural metastases more frequent cf. LABC\(^1\)
• PET/CT: 30-50% (mediastinal LN, bone, liver)\(^2,3\)
• ≈ 20% occult with conventional staging\(^2\)
• May improve prognosis (stage migration)

\(^1\)Mvere et al. Clin Oncol 2011
\(^3\)Alberini et al. Cancer 2009
PET/CT

From: Carkaci et al., J Nucl Med 2009
Yang et al., Breast Cancer Res Treat 2008
Identification of Distant Metastases

- Always check the MRI!
Response Assessment

- Local disease: MRI
  - Interval assessment post 1-2 # NAC
    - Prediction of response
  - Final response assessment
    - Overall accuracies \( \approx 70\%^{1,2} \)
    - High FN rate - caution needed in diagnosis of CR
    - ? Poorer for non-mass lesions
- Locoregional & distant disease: PET/CT

\(^1\)Shin et al. Br J Radiol 2011
MRI: Response Assessment
MRI: Response Assessment
Future Directions

• Further research needed on standardisation of functional techniques and response criteria

• Studies should explore role of mpMRI & PET/CT in
  • Prognostication
  • Early response prediction

• Future trials should include MRI and PET/CT wherever possible
How we can make progress in the UK

• Publicise guidelines/consensus manuscript\(^1\)

• Establish registry and database

• Establish Tissue bank (network)

\(^1\)Rea D et al. Br J Cancer. 2015 Apr 28;112(9):1613-5

UK Inflammatory Breast Cancer Working group
Diagnostic details: clinical, radiological, pathology

Treatment details: systemic therapy, surgery, RT

Imaging

Outcomes: locoregional, distant, breast cancer specific and overall survival
## Database

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## Database

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- 20.4% of patients receiving neo-adjuvant chemotherapy achieved a pathological complete response in the breast;

- The estimated 5-year overall survival was 60.2% for stage III patients.

- 131 patients (38.7%) developed distant metastases with the brain being the first site in 20.4% of cases.

- Median overall survival of stage 3 patients was 90 months whilst median overall survival of the 87 patients who were stage 4 at presentation was 21 months.
The next steps

• Establish working IBC team in collaborative centres – oncologist, radiologist, surgeon, pathologist

• Define research priorities, develop theme-focused research plan (e.g. the role of stroma in IBC)

• Develop well defined collaborative strategies
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**UK IBC CONSORTIUM**