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Original article

The presentation, management and outcome of inflammatory breast cancer cases in the UK: Data from a multi-centre retrospective review

E. Copson [a, *], A.M. Shaaban [b], T. Maishman [a], P.M. Moseley [c], H. McKenzie [a], J. Bradbury [d], A. Borley [e], M. Brzezinska [f], S.Y.T. Chan [c], J. Ching [g], R.I. Cutress [a], I. Danial [b], B. Dall [h], M. Kerin [i], A.J. Lowery [i], I.R. Macpherson [j], L. Romics [j], E. Sawyer [k], N. Sharmat [h], T. Sircar [l], R. Vidya [l], Y. Pan [m, n], D. Rea [o], L. Jones [p], D.M. Eccles [a], F. Berditchevski [o]

[a] Cancer Sciences Academic Unit and Southampton Clinical Trials Unit, University of Southampton, Southampton General Hospital, Tremona Road, Southampton, UK
[b] Department of Histopathology and University of Birmingham, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Edgbaston, Birmingham, B152GW, UK
[c] Clinical Oncology Department, Nottingham University Hospitals NHS Trust, Nottingham, NG5 1PB, UK
[d] Department of Oncology, Salisbury NHS Foundation Trust, Salisbury District Hospital, Odstock Road, Salisbury, Wiltshire, SP2 8BJ, UK
[e] Velindre Cancer Centre, Whitchurch, Cardiff, CF14 2TL, UK
[f] Edinburgh Breast Unit, Western General Hospital, Edinburgh, Crewe Road South Edinburgh, EH4 2XU, UK
[g] Poole Hospital NHS Foundation Trust, Longfleet Road, Poole, BH15 2JB, UK
[h] Breast Unit, Level 1 Chancellor Wing, St James Hospital, Leeds Teaching Hospitals NHS Trust, Becket Street, Leeds, LS9 7TF, UK
[i] The Lambe Institute for Translational Research, National University of Ireland & University Hospital Galway, Galway, Ireland
[j] Wolfson Wohl Cancer Research Centre, University of Glasgow, Glasgow, G61 1QH, UK
[k] Research Oncology, Division of Cancer Studies, Guy's Hospital, King's College London, London, SE1 9RT, UK
[l] Royal Wolverhampton NHS Trust, New Cross Hospital, Wolverhampton Road, Wolverhampton, WV10 0QP, UK
[m] Centre for Computational Biology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK
[n] Institute of Immunology and Immunotherapy, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK
[o] Institute of Cancer and Genomic Sciences, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK
[p] Barts NHS Trust and Barts Cancer Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, Charterhouse Square, London, EC1M 6BQ, UK

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ABSTRACT

Objectives: Inflammatory Breast cancer (IBC) is a rare but aggressive form of breast cancer. Its incidence and behaviour in the UK is poorly characterised. We collected retrospective data from hospitals in the UK and Ireland to describe the presentation, pathology, treatment and clinical course of IBC in the UK.
Materials and methods: Patients with IBC diagnosed between 1997–2014 at fourteen UK and Irish hospitals were identified from local breast unit databases. Patient characteristics, tumour pathology and stage, and details of surgical, systemic and radiotherapy treatment and follow-up data were collected from electronic patient records and medical notes.
Result: This retrospective review identified 445 patients with IBC accounting for 0.4–1.8% of invasive breast cancer cases. Median follow-up was 4.2 years. 53.2% of tumours were grade 3, 56.2% were oestrogen receptor positive, 31.3% were HER2 positive and 25.1% were triple negative. 20.7% of patients had distant metastases at presentation. Despite trimodality treatment in 86.4%, 40.1% of stage III patients developed distant metastases. Five-year overall survival (OS) was 61.0% for stage III and 21.4% for stage IV patients.
Conclusions: This is the largest series of UK IBC patients reported to date. It indicates a lower incidence than in American series, but confirms that IBC has a high risk of recurrence with poor survival despite contemporary multi-modality therapy. A national strategy is required to facilitate translational research into this aggressive disease.

* Corresponding author. Cancer Sciences Academic Unit, Faculty of Medicine, University of Southampton and University Hospital Southampton Foundation Trust, Tremona Road, Southampton, SO16 6YD, UK.
E-mail address: E.Copson@soton.ac.uk (E. Copson).

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1. Introduction

First described in 1924, inflammatory breast cancer (IBC) is a rare but aggressive form of invasive breast cancer [1]. US registry data indicate that IBC accounts for 2–4% of breast cancer cases but up to 10% of breast cancer deaths owing to the associated poor prognosis [2,3]. In other industrialised countries the incidence of IBC varies from 0.09 to 2.9% (Japan) to 0.6–2.0% (Italy) [4,5]. No comparable data are available for the UK, as IBC cases are not identified within National Cancer Intelligence reports [6].

The diagnosis of IBC is based on clinical features of erythema and skin oedema with prominent dermal hair follicles (peau d'orange) of less than 6 months duration [7,8], and no unique histological identifiers [9]. Dermal lymphatic invasion (DLI) with tumour emboli is considered a histological hallmark, being the primary cause of the breast lymphatic obstruction seen in IBC, but is identified in less than 75% of IBC cases [10].

Clinical guidelines recommend use of aggressive primary systemic therapies; however outcomes remain poor with series reporting high rates of systemic recurrence and poor overall survival [9,11,12]. A better understanding of the biology of IBC is clearly required [3], but clinical trial data for interventions in IBC are severely limited. A 2011 multidisciplinary meeting of UK specialists with an interest in IBC resulted in the establishment of the UK IBC consortium, [13]. Our aims are to establish a national mechanism for conducting research into IBC, through provision of practical guidelines to encourage: 1) consistent definition, 2) uniform collection of diagnostic information, and 3) standardisation of treatment approaches. To inform the design of future prospective and interventional studies, we have reviewed the incidence, pathology, treatment and outcomes of UK IBC patients with primary IBC (IBC in a previously normal breast) treated at thirteen UK and one Irish breast cancer units between 1997 and 2014.

2. Patients and methods

Breast unit databases at fourteen participating hospitals were reviewed to identify patients with primary invasive breast cancer documented as IBC and/or TNM stage T4d and diagnosed between 2014 and 1997 (or as far back as records were available). Participating centres were chosen to represent different geographical regions: 3 centres from central England; two from London; three from the South; one from North England; two from Scotland; one from Wales; one from Ireland. Medical records were interrogated to confirm that identified cases fulfilled clinical criteria for a diagnosis of IBC published at the time of presentation [7–9]. Patients received treatment and follow-up according to local protocols. The total number of breast cancer cases diagnosed at each unit during the record availability period was requested. Data were collected from hospital electronic patient records and patient case notes. Patient characteristics, imaging findings, tumour pathology, disease stage, treatment received, pathological response rate, time to locoregional and distant disease recurrence, site of metastases, and overall survival were recorded. Follow-up data were censored at last clinic attendance. Hormone receptor levels equivalent to an Allred score of >2 were categorised as positive [14]. A complete pathological response after primary chemotherapy was defined as no residual invasive carcinoma within the breast (DCIS permitted) following surgery and no evidence of metastatic disease within resected lymph nodes. A partial response was defined as showing residual disease following surgery with some features of response to therapy [15].

All data collections were registered and approved locally. Storage and transfer of anonymized data were performed according to institutional governance protocols.

2.1. Statistical analyses

Summary statistics were used to describe both cohorts. Analyses were performed in STATA v11.2. Overall survival (OS) and distant relapse free survival (DRFS) were assessed using Kaplan-Meier curves and their corresponding hazard rates were evaluated using Cox proportional hazards model. OS and DRFS were assessed as time from date of invasive breast cancer diagnosis to death from any cause (OS), and to date of distant relapse or death from breast cancer (DRFS). Patients who had not experienced an event at the time of analysis were censored at their date of last follow-up. Patients with Stages III and IV at presentation were analysed separately for OS.

3. Results

A total of 445 patients with IBC diagnosed between 1997-2014 were identified by the 14 participating hospitals. Ten breast cancer units provided numbers of total invasive breast cancer cases diagnosed during the search period; the incidence of IBC at these units ranged from 0.4% to 1.8%. Full details of the hospitals involved and number of cases submitted are provided in Supplementary Table 1.

3.1. Patient characteristics

Table 1 demonstrates patient demographics. Median age at diagnosis of IBC was 56 years, (range 26–92). Data on ethnicity were available for 248 patients: 88.7% of these were white/Caucasian.

Body mass index data were available for 160 patients (36%); median BMI at presentation was 28.72 kg/m^2 (range 18.2–48.9) with 26.3% within the World Health Organisation healthy weight category (BMI 18.5–24.9 kg/m^2), 31.9% being overweight (BMI 25.0–29.9 kg/m^2) and 41.3% being obese (BMI $\geq$ 30.0 kg/m^2).

3.2. Presentation and diagnostics

Patient presentation details were provided for 226 cases and 19% (43) of these were treated for presumed infection prior to diagnosis of IBC. Sonographic results were available for 314 cases (Table 1). Four patients had bilateral tumours. A measurable tumour mass was visible on initial imaging in 276 cases (87.9%) with a median size of 40 mm (range 5.4–145), whilst diffuse changes only were visible in 38 (12.1%). One hundred and forty-two tumours were multifocal (40.5%) and oedema was present in 250 (82.8%). All patients had a core biopsy. Skin punch biopsies were performed in 18 cases: 13 (72.2%) were positive for malignant cells. Abnormal axillary lymph nodes were seen on imaging in 301 cases (86.7%). Data on core biopsy and/or fine needle aspiration of axillary lymph nodes were available for 252 cases, and 214 of these (84.9%) were positive for malignant cells. Evidence of distant metastases at presentation was found in 20.7% of patients (90/434).

3.3. Tumour pathology

Tumour core pathology details are presented in Table 1. Grade 3 tumours represented 53.2% of all cases, 56.2% were oestrogen receptor (ER) positive, and 31.1% were HER2 positive, with 25.1% having triple negative phenotype (ER and HER2 negative, with PR negative or unknown). Vascular invasion was identified in 39.8% of tumours.