Relapse of Invasive Lobular Carcinoma

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INTRODUCTION

The diagnosis of Invasive Lobular Carcinoma (ILC) in the relapse setting is as problematic and challenging as in the primary setting due to the enigmatic nature of this malignant process.

As discussed in previous chapters for early ILC, this special neoplastic process is often difficult to identify by clinical and imaging studies, which applies to the metastatic situation, too. These difficulties relate to a variety of factors, including the diffusely infiltrative nature of the malignant process, the spatial and site specific pattern of metastatic disease which is associated with ILC.

It is of the utmost importance that the past history of Invasive Lobular Carcinoma of breast is available to the entire clinical team involved in the management of the individual patient, even if this history is many (often 20 or 30) years prior to the current clinical episode.

Invasive Breast Carcinoma of any histological type may be associated with relapse which may be loco regional, involving the breast, chest wall or regional lymph nodes, or distant relapse at any anatomical site.

Due to the possibility of relapse and the increased risk of a second primary breast carcinoma, it is recommended that all individuals should be followed up. Follow up should include clinical and radiological options for assessment of the patient as a whole as well as both the treated and contra lateral breast.

The aim of the follow up is that the early detection of recurrence either local or distant will be more effective and be associated with a survival benefit however no robust evidence exists to support this belief. Through regular surveillance the clinician aims to identify recurrence or be informed of new symptoms affecting the patient at the earliest opportunity.

It is known that Invasive Lobular Carcinoma has an early advantage in disease free survival when compared to Invasive Ductal Carcinoma, but when compared at 6 & 10 years the invasive ductal carcinoma group has a late advantage. Invasive Lobular Carcinoma is associated with an increased incidence of bone metastases but a decrease in regional and lung relapses [1].

Thus, due to the nature of this process, the diagnosis of cancer relapse can be difficult.

FOLLOW UP OF INVASIVE BREAST CANCER

All individuals with the diagnosis of invasive breast carcinoma should be offered regular follow up for some time after the diagnosis of their primary disease. Follow up is advised to allow identification of recurrent disease which may be local or systemic, the supervision of adjuvant treatment & side effects. Follow up also permits the review of individuals involved in clinical trials. Careful follow up with accurate data collection is essential for the success of all clinical trials which are dependent on accurate information on individual patient outcome to assess the efficacy of the trial.

The American society of Clinical Oncology (ASCO) recommends that Breast Cancer survivors be followed up by regular history, physical examination and mammography. Examination should be performed at 3–6 months for the first 3 years 6–12 months for years 4–5 & annually thereafter. If the individual has had conservation surgery a post treatment mammogram should be obtained 1 year after the initial mammogram and at least 6 months after completion of radiotherapy. Thereafter a yearly mammographic examination should be performed unless otherwise indicated. Those at high
risk of familial breast cancer should be referred for genetic counselling [2].

ASCO guidelines do not recommend follow up with CBC, chemistry pane, bone scan, chest x-ray, CT scan, PET scan MRI or tumour markers in the otherwise asymptomatic patient with no specific clinical findings.

In the United Kingdom the National Institute for Clinical Excellence (N.I.C.E.) advises that all cases of invasive breast cancer should be followed up for these reasons. The exact schedule and length of time of follow varies from unit to unit. Visit schedules vary from 3, 6 or 12 months and the length of follow up varies from 2–10 years [3].

Follow up involves clinical examination and mammography in the first instance. Between one half and one third of local recurrence is detected by mammography alone. Mammography is not an effective method of detecting skin or chest wall recurrence. This is usually detected clinically or skin changes are noted by the patient. Breast ultrasound is not recommended as a follow up tool but it may be a useful adjunct in the dense breast or when the initial tumour is mammographically occult as is often the issue with Invasive Lobular Carcinoma. Magnetic Resonance Imaging is not currently recommended for routine surveillance but can be used for the further assessment of problem areas.

If at the clinic visit either local or systemic recurrence is suspected due to clinical findings or symptoms other imaging investigations may be appropriate [3].

LOCAL RELAPSE

As with all invasive breast carcinoma, Invasive Lobular Carcinoma is associated with a risk of local recurrence of 0.5–1% per annum. This risk is life long and includes new primary carcinoma in the ipsilateral breast. As highlighted in previous chapters Invasive Lobular Carcinoma is more often occult on imaging than other types of invasive breast carcinomas. This issue remains problematic in the relapse setting. This may be the result of Invasive Lobular Carcinoma being associated with the main glandular density of the breast [4] or due to the failure of the tumour cells to elicit a desmoplastic response resulting in false negative imaging [1].

The use of ultrasound and Magnetic Resonance Imaging as adjuncts to mammography improves the sensitivity of detection of Invasive Lobular Carcinoma. In the primary diagnostic setting a study involving 28 biopsy proven cases of invasive lobular carcinoma showed mammographic sensitivity of 79%, ultrasound sensitivity of 68% and MRI sensitivity of 83% in the detection of invasive lobular carcinoma [5]. It is likely that similar numbers would be achieved in the local relapse setting. Magnetic resonance imaging has increasingly become accepted as a management tool in breast disease. It has the greatest sensitivity of all imaging modalities but is hampered by its low specificity [6]. When dealing with Invasive Lobular Carcinoma MRI has the highest cancer detection rate when compared to other imaging modalities.

While MRI is superior in detection of ILC it is essential that all MRI detected suspicious lesions are confirmed histologically [7].

Local nodal recurrence is usually detected clinically either in the axilla or supraclavicular area but may also be detected by CT staging.

Thus detection of local recurrence is dependent on clinical examination and imaging. In general, all suspected local recurrence should be confirmed histologically.

DISTANT RELAPSE

The specific histological subgroups of invasive lobular carcinoma, discussed in this monograph in the chapter on histology, are associated with different patterns of prognosis with classical lobular carcinoma having a better outlook than the variant forms, the variant subsets showing more frequent recurrence and death from disease [8]. A study of 530 cases of invasive lobular carcinoma found that 57% of cases were of classical type, 19% alveolar, 11% solid and 13% pleomorphic subtype. The non classical types of ILC were associated with a higher risk of breast related events and a trend towards reduced disease free survival [9].

As detailed in the chapter on prognosis of this monograph, Invasive Lobular Carcinoma is associated with an increased incidence of bone events but a decreased incidence of regional and lung events when compared to invasive ductal carcinoma [1].

Another clinicopathological analysis of 975 cases of invasive lobular carcinoma studied 726 cases of pure invasive lobular carcinoma & 249 cases of mixed ductal/lobular carcinoma showed that bone involvement was more common in ILC and that metastatic spread to peritoneum, uterus, ovary, gastrointestinal tract and skin was more common in ILC compared to non ILC [10].
Contrast enhanced CT is the state of the art modality for restaging of oncological patients. A CT study of 56 patients with metastatic lobular carcinoma identified metastatic disease in common sites e.g. lymph node, lung and liver but also in peritoneum, colon, pleura, adnexa, stomach, retroperitoneum and small bowel. In this study 32% of patients had gastrointestinal tract involvement manifest as bowel thickening on CT scan & 11% of patients had hydronephrosis [11].

Carcinomatous meningitis is rare in breast carcinoma and it is usually associated with highly aggressive disease behaviour. Carcinomatous meningitis is said to occur in 1–3.5% of cases of metastatic breast carcinoma. In cases with brain metastases 6% display leptomeningeal involvement. The individual can present with cerebral, cranial nerve and spinal signs and symptoms or a mononeuritis multiplex presentation. The diagnosis may be made on CT scanning or with MRI as a useful aid to diagnosis. CSF examination confirms the diagnosis. In a study of 35 cases of leptomeningeal disease were identified. This affected 0.86% of all cases in the study population and 1.9% of those with recurrent disease 67% of these cases were of lobular or mixed histological subtype. 14% of the cases had no other metastatic disease at presentation. This is a highly aggressive form of relapse with median interval from primary treatment to relapse of 10.9 months and from recurrence to death of 15 months [12].

Bone marrow metastases are also observed in Invasive Lobular Carcinoma. In a study of 54 patients with ILC marrow involvement was suspected. The study concluded that examination of bone marrow specimens, in cases of known ILC, should utilise cytokeratin immunohistochemistry to ensure maximum detection of clinically relevant metastases [13].

The pattern of relapse in ILC can be confusing to the clinician. Metastases may present more than 30 years after the primary diagnosis. Local recurrence is always a possibility many years after primary diagnosis. A presenting symptom of haematemesis, dysphagia or haemoptysis may be due to recurrent lobular carcinoma initially diagnosed many years ago. Recurrent lobular carcinoma may present as an orbital or periadnexal swelling related to the eye, as described in several case reports.

A post-mortem study from 1991, examined 226 cases of metastatic breast carcinoma including 25 cases of invasive lobular carcinoma. The authors concluded that lobular subtype was more often associated with metastases to the peritoneum/retroperitoneum, hollow viscera, internal genital organs, leptomeninges and myocardium [14].

HISTOLOGICAL CONFIRMATION

In many cases of systemic relapse biopsy confirmation is not possible and imaging modalities are relied upon before instigating treatment.

If biopsy is possible, at any site or with any presenting symptom the reporting pathologist should be given the information that the patient has a history of invasive lobular carcinoma. This will prevent unnecessary diagnosis of second malignancies, in particular gastric carcinoma, which has morphological similarities to invasive lobular carcinoma on H and E examination.

If the morphology of the cancer infiltration is suspicious of an invasive lobular carcinoma, further immunohistochemistry for E-Cadherin, cytokeratin and hormone receptors can be carried out.

Comparing the morphology of the recurrent carcinoma with the primary tumour if available, can confirm the morphological similarity. If the recurrent tumour can be biopsied, this is advisable as it allows repeated assessment of the biomarker status. Several studies have shown variation in biomarker status between the original tumour and metastatic disease which may alter treatment strategy [15].

The morphological and immunohistochemical feature of invasive lobular carcinoma have been discussed in previous chapters. In the following chapter three case illustrations of distant/late relapses of ILC are presented.

There are also situations where carcinomas arising in other sites may show morphological similarities to Invasive Lobular Carcinoma. On rare occasions these tumours may metastasise to the breast and be mistaken for a primary breast carcinoma with lobular features. This error can be prevented if the presence of another primary carcinoma is known. On the other hand, performing further immunohistochemistry can lead to the proper diagnosis.

The correct diagnosis may prevent inappropriate breast surgery in an individual with breast metastases from a primary tumour elsewhere.

Case illustration 4 in the following chapter represents a lung cancer metastasising into the breast, mimicking pleomorphic lobular carcinoma.

The continued follow up and assessment of individuals with invasive lobular carcinoma has many problems affecting the surgeon, oncologist, radiologist and pathologist. It is essential that all members of the team are aware of the initial diagnosis and the problems involved in their specialty. They must also communicate the history to any members of the team who may
not be aware of the initial diagnosis. This will ensure the highest level of patient management and help avoid diagnostic error.

References