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### Original article

# When pathological and radiological correlation is achieved, excision of fibroadenoma with lobular neoplasia on core biopsy is not warranted



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#### ABSTRACT

Background: The diagnosis and management of lobular neoplasia (LN) including lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH) remains controversial. Current management options after a core needle biopsy (CNB) with lobular neoplasia (LN) incorporating both ALH and LCIS include excision biopsy or careful clinical and radiologic follow up.

Methods: A retrospective analysis of the surgical database at Cork University Hospital was performed to identify all core needle biopsies from January 1st 2010 to 31st December 2013 with a diagnosis of FA who subsequently underwent surgical excision biopsy. All cases with associated LN including ALH and classical LCIS were selected. We excluded cases with coexistent ductal carcinoma in situ (DCIS), invasive carcinoma, LN associated with necrosis, pleomorphic lobular carcinoma in situ (PLCIS) or lesions which would require excision in their own right (papilloma, radial scar, atypical ductal hyperplasia (ADH) or flat epithelial atypia (FEA)). Cases in which the radiologic targeted mass was discordant with a diagnosis of FA were also excluded.

Results: 2878 consecutive CNB with a diagnosis of FA were identified. 25 cases had a diagnosis of concomitant ALH or classical LCIS. Our study cohort consisted of 21 women with a mean age 53 years (age range 41–70 years). The core biopsy diagnosis was of LCIS and FA in 16 cases and ALH and FA in 5 cases. On excision biopsy, a FA was confirmed in all 21 cases. In addition to the FA, residual LCIS was present in 14 cases with residual ALH in 2 cases. One of the twenty-one cases (4.8%) was upgraded to invasive ductal carcinoma on excision.

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#### Introduction

Over seventy years on from the initial description by Foote and Stewart [1], the diagnosis and management of lobular neoplasia (LN) including lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH) remains controversial. Current management options after a core needle biopsy (CNB) with lobular neoplasia (LN) incorporating both ALH and LCIS, include excision biopsy or careful clinical and radiologic follow up. In addition some clinicians advocate endocrine chemoprophylaxis in such patients due to the increased risk of developing breast cancer in the future. One area in particular which lacks agreement is the optimum management of classical LCIS and ALH as the highest risk lesion diagnosed on CNB. At present there are

divided between excision and surveillance. The findings of numerous groups suggest that with robust clinico-radiological concordance excision may not be necessary in all cases [2-6]. Some authors however propose that excision is warranted in cases where LN is associated with a synchronous mass [7]. Since many of these studies include both calcifications and mass lesions as the radiologic target one question that arises is how best to proceed when the target is a mass lesion radiologically concordant with a fibroadenoma (FA) and the CNB shows LN associated with a FA. Interestingly over the last fourteen years there has been a significant reduction in excisional biopsy rates from a reported 37.8%-1.4% [8]. The aim of our study was to ascertain specifically whether subsequent excision is necessary in cases of LN associated with FA on core needle biopsy where the imaging target is a mass and radiological imaging is consistent with a typical FA.

no consensus guidelines and evidence in the literature is

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#### Methods

Cork University Hospital is a single large academic centre with a combined screening and symptomatic sub-specialty breast service and approximately 600 breast cancers diagnosed per year. A retrospective analysis of the surgical database at Cork University Hospital was performed to identify all core needle biopsies from January 1st 2010 to 31st December 2013 with a diagnosis of FA.

All cases with associated LN including ALH and classical LCIS were selected. To isolate cases with LN as the highest risk lesion we excluded cases with coexistent ductal carcinoma in situ (DCIS), invasive carcinoma, LN associated with necrosis, pleomorphic lobular carcinoma in situ (PLCIS) or lesions which would require excision in their own right [papilloma, radial scar, atypical ductal hyperplasia (ADH) or flat epithelial atypia (FEA)]. Cases in which the radiologic targeted mass was discordant with a diagnosis of FA were also excluded.

Patient demographics and radiologic data including indication for biopsy (mammographic screening vs radiologic evaluation of a clinical finding), radiologic target and the number of cores submitted recorded. All targeted lesions were classified using the breast imaging reporting and data system (BIRADS) to stratify the cases according to varying levels of suspicion for carcinoma [10]. All radiology was reviewed by a breast radiologist prior to inclusion in the study and there was histologic radiologic concordance with a diagnosis of a FA in all cases (RM).

All haemotoxylin and eosin (H&E) slides and associated immunohistochemcial studies from both the core needle biopsy specimens and the corresponding diagnostic excision specimens were reviewed by two subspeciality breast pathologists to confirm the diagnosis (FO'C, TJB).

All core biopsy tissue specimens were fixed with 10% formalin embedded in paraffin and stained with H&E. CNB tissue was sectioned at 4  $\mu$  intervals and three levels were examined on each block. The presence of LN and FA were confirmed on each case. For the purpose of this study LN included LCIS which was defined as monotonous dis-cohesive proliferation of small round cells that will distend >50% of the acini of the involved lobular units and ALH which was defined as the same cell population with <50% of the acini filled and distended.

All our CNB specimens are discussed at a weekly breast multidisciplinary meeting and as per our institutional practice excision biopsy was recommended in all cases with a diagnosis of LN associated with FA on CNB. Therefore each core biopsy had a corresponding excision biopsy specimen available for review.

All surgical excision specimens were macroscopically evaluated with sections submitted as per departmental protocols and published recommendations [9]. Excision diagnosis including the presence of LCIS, ALH and FA were recorded as well as the relationship of the LN to the FA, the FA size, the presence of calcifications and any other associated pathology.

#### Results

2878 consecutive CNB with a diagnosis of FA were identified. 25 cases had a diagnosis of concomitant ALH or classical LCIS. One case was excluded as it had coexisting DCIS, two cases were excluded because the radiologic target was not consistent with a FA and a third case was excluded as there had been a prior excision for invasive lobular carcinoma close to the targeted lesion. The remaining cases were included in the study and all of these had a subsequent excision biopsy at our institution available for review.

Our study cohort consisted of 21 women with a mean age 53 years (age range 41–70 years). Twelve cases were from the right breast and nine were from the left breast. The core biopsy target in

all cases was a radiologically confirmed circumscribed lobulated mass consistent with a FA. All cases underwent ultrasound guided vacuum assisted CNB using a 14 gauge needle. All of the cases were classified as BIRADS category 4 at the time of diagnosis and confirmed as same on review at the time of the study by a breast radiologist (RM) [10].

This cohort consisted of 17 cases from the symptomatic service presenting as a clinical finding with four cases from the breast screening service. The mean number of tissue cores per case was 3 (range 2–5 cores).

The core biopsy diagnosis was of LCIS and FA in 16 cases and ALH and FA in 5 cases. The LCIS or ALH was confined to the FA in 15 cases, involved the FA and adjacent breast parenchyma in 3 cases and was present only in breast tissue adjacent to the FA in the 3 remaining cases.

An excisional biopsy was performed in all 21 patients within nine weeks of the CNB (range 2–9 weeks). 19 cases (90.5%) had all the tissue embedded while the remaining two cases had the entire grossly visible lesion and >90% of the fibrosis submitted for microscopic evaluation. The average block number 13 (range 6–23 blocks).

On excision, a FA was confirmed in all 21 cases. Fig. 1. The average FA size was 1.9 cm (range 0.5–2.4 cm). In addition to the FA, residual LCIS was present in 14 cases with residual ALH in 2 cases. Other associated pathology included calcifications in 11 cases, columnar cell change in 7 cases, epithelial hyperplasia (usual type) in 7 cases, atypical ductal hyperplasia in 2 cases and 2 cases had associated complex sclerosing lesions (Table 1).

One of the twenty-one cases (4.8%) was upgraded to invasive ductal carcinoma on excision. There was no known family history of carcinoma in this case and no prior excisions for high risk lesions had been performed. The CNB on this case showed a FA with adjacent tissue containing LCIS associated with calcifications. The patient underwent a wire guided diagnostic excision biopsy with all tissue submitted for histologic evaluation. Two foci of invasive ductal carcinoma were identified, both grade 2, each measuring 0.2 cm in maximum dimension. One focus was found adjacent to core biopsy site and a 0.7 cm FA and the second focus of invasion was identified more remote to this site. Extensive multifocal LCIS was present throughout the case. Ductal carcinoma in situ was not present.

Subsequent sentinel lymph node biopsy revealed isolated tumour cells which were identified on the immunohistochemical stain only. The case was therefore staged pT1aN0 (i+)(sn) multifocal as per the AJCC 7th edition [11].

#### Discussion

The true incidence of LN is unknown as there are no clinical or mammographic features. Nonetheless, LN is considered a risk factor for the development of invasive carcinoma with a relative risk of 4–5 times for ALH and up to 8–10 times for LCIS [12–14]. Challenges arise however as the presence of LN does not predict laterality of subsequent carcinoma and has no specific clinical or radiologic correlate. Currently there is considerable variation in management practice between institutions with no consensus guidelines on optimal management.

Upgrade rates for LN on subsequent excision also varies considerably in the literature ranging 0–35% in published studies [2,7,12,15–19]. The higher rates in some studies may be attributed to a number of reasons including the excision of LN in patients with radiologic pathologic discordance, inclusion of patients with higher risk histologic subtypes of LCIS such as PLCIS, LCIS with necrosis or those lesions considered to have overlapping features with DCIS (carcinoma in situ with mixed features), inclusion of lesions other

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