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BEST PRACTICE APPROACHES BREAST RADIOLOGY-PATHOLOGY CORRELATION AND MANAGEMENT (J SCHEEL AND MR KILGORE, SECTION EDITORS)

A Multidisciplinary Approach to Managing Uncertainty

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Abstract

Purpose of Review Image-guided percutaneous breast biopsy of both palpable and non-palpable findings has become standard of care. These minimally invasive breast procedures can avoid a surgical procedure for patients who have benign findings and can also guide pre-surgical management for malignant pathology. Establishing radiology-pathologic concordance is critical to guide appropriate management and is often performed between the radiologist and pathologist. However, the role of a multidisciplinary team and understanding the overall clinical context can better guide clinical care, particularly when imaging and pathologic findings may be uncertain.

Recent Findings This article presents a series of difficult cases where multidisciplinary input is needed to help guide subspecialty decision-making.

Summary A multidisciplinary team that has an understanding of what information is needed to guide subspecialty decision making and recommendations can improve patient management, particularly in uncertain radiology-pathology situations.

Keywords Radiology-pathology correlation · Multidisciplinary · Concordance

Introduction

Imaging-guided percutaneous breast biopsy of both palpable and non-palpable findings is now standard of care, and establishing radiology-pathologic concordance is critical to guide appropriate management. However, there are imaging and pathologic situations where the findings are uncertain. In these cases, the role of a multidisciplinary team and understanding the overall clinical context can better guide clinical care. Practices with multidisciplinary radiology-pathology conferences have been shown to result in changes to patient management in up to 5.3% of cases [1]. The purpose of this article is to present a series of cases where multidisciplinary input is needed as either the imaging, pathology, and/or management scenarios are not straightforward.

This article is part of the Topical Collection on *Best Practice Approaches Breast Radiology-Pathology Correlation and Management*

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Case 1: Intraductal Atypical Papillary Proliferation in an Elderly Patient with Comorbidities

A 90-year-old woman with multiple comorbidities, including severe dementia and heart failure, and breast history of remote right mastectomy for invasive ductal carcinoma (IDC) presented with a left breast palpable abnormality. A diagnostic left breast mammogram and targeted ultrasound showed an irregular solid mass with microlobulated margins (Fig. 1). This mass was highly suspicious for malignancy and assessed as American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS)

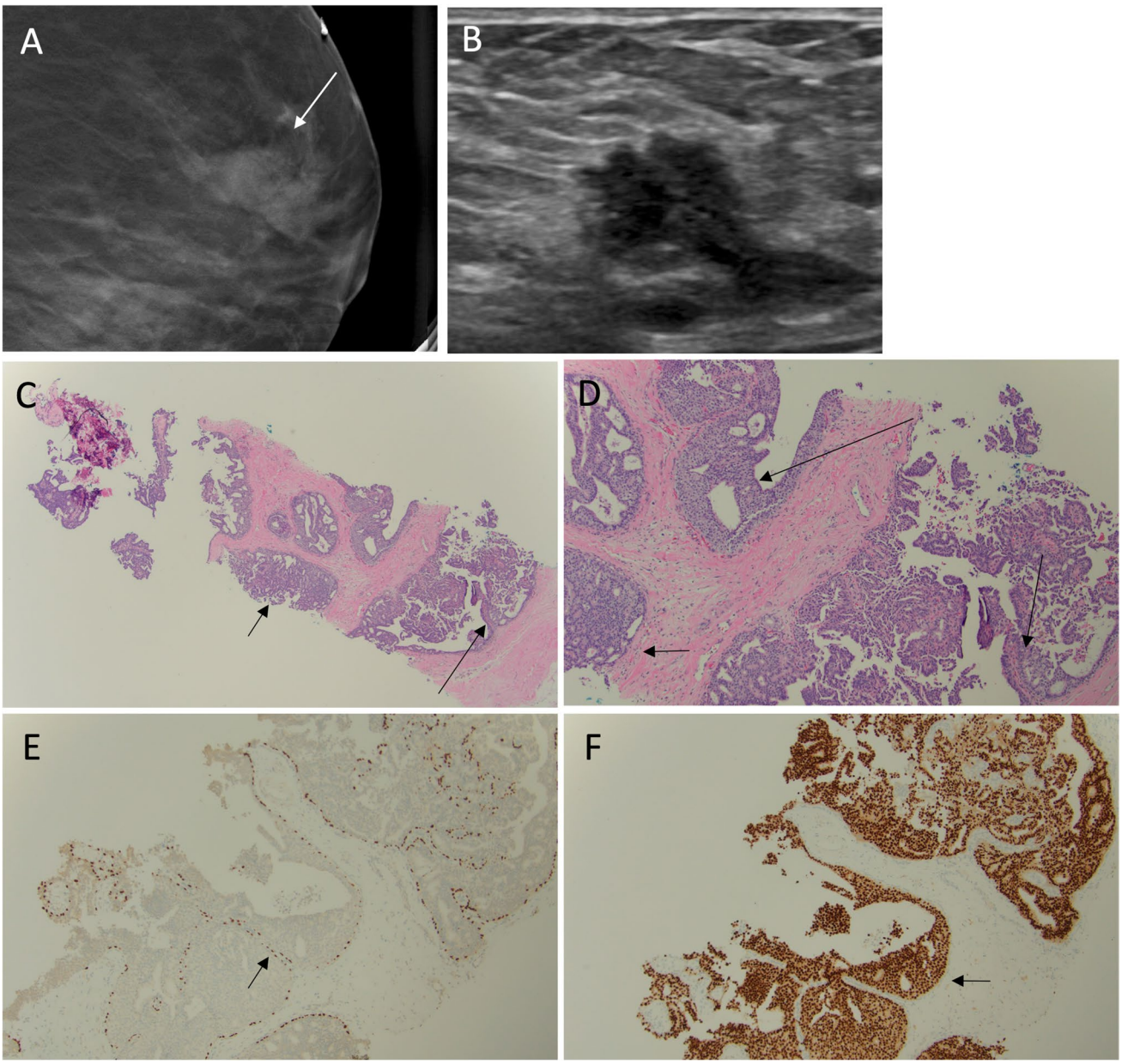

Fig. 1 Intraductal atypical papillary proliferation. Diagnostic left breast spot ML mammogram (**A**) and targeted ultrasound (**B**) showed a solid round mass with microlobulated margins measuring 11 mm in the subareolar position. Histology (40× in **C**, 100× in **D**) showed an intraductal epithelial proliferation (short arrow) with papillary architecture (medium arrow indicates fibrovascular cores) and a somewhat monotonous appearance (**D**, long arrow). Immunostain for the myoepithelial marker p63 (**E**, 100×) highlights myoepithelium surrounding the expanded ducts (short arrow) supporting that the proliferation is intraductal. Immunostain for ER (**F**, 100×) showed that the intraductal proliferation overexpresses ER (short arrow)

category 5 [2••]. Biopsy pathology revealed intraductal epithelial proliferations with a monotonous appearance and focal papillary architecture. The combination of monotonous, low-grade appearance of the proliferation and overexpression of estrogen receptor (ER) warranted an interpretation of atypia [3]. The intraductal nature of the proliferation is supported by the presence of surrounding myoepithelial cells on p63 immunostaining (Fig. 1). Overall, the features are that of an atypical papillary lesion without evidence of invasive carcinoma.

Multidisciplinary Discussion

A major goal of the ACR BI-RADS was to reduce confusion in breast imaging interpretation and management recommendations through standardized reporting. Each BI-RADS

assessment category indicates the likelihood of malignancy based on imaging features. A BI-RADS category 5 indicates a > 95% chance of malignancy of the assessed lesion with the associated management plan of core needle biopsy [2••]. It can be debated whether pathology revealing a high-risk lesion (atypical papillary proliferation) of a BI-RADS category 5 lesion should be categorized as concordant versus discordant; however, in this particular patient scenario, this was deemed as radiology-pathology concordant with a clear recommendation to refer to a surgeon for surgical excision.

Papillary lesions with atypia are associated with upgrade to ductal carcinoma in situ (DCIS) or invasive carcinoma in 36.9% of cases in a recent meta-analysis [4]. Therefore, there is a general consensus in the literature that papillary lesions with atypia should undergo surgical excisional biopsy, particularly if there is a palpable finding, as this has been shown to be independently associated with upgrade [5]. Upgrade to DCIS is more common than invasive carcinoma [6–8]. If there is no upgrade on excisional biopsy, the long-term risk of breast cancer associated with atypical papillary lesions mirrors other high-risk atypical lesions, and close follow-up with the option of chemoprevention is warranted. In this case, the patient was elderly with multiple comorbidities, including heart failure and dementia. Therefore, alternatives to excision were discussed, including expectant care with short-term interval imaging follow-up and clinical breast exam.

Case 2: Intraductal Epithelial Proliferation in a Patient with Prior Ipsilateral and Synchronous Contralateral Breast Cancer

A 65-year-old postmenopausal woman with a history of *right* breast cancer status post lumpectomy, radiation, and chemotherapy 15 years ago was subsequently diagnosed with multifocal *left* breast invasive lobular carcinoma. A breast MRI performed for determining extent of disease showed a focus of enhancement measuring 5 mm in the *right* breast (Fig. 2). This was assessed as BI-RADS category 4 and an MRI-guided biopsy was performed.

Pathology revealed a focal intraductal epithelial proliferation (0.1 cm) arising in a background of atrophic epithelial changes. The small proliferation is somewhat monotonous and on immunostaining is seen to overexpress ER and to have heterogeneous expression of cytokeratin CK5. Low-grade atypical proliferations overexpress ER and exhibit loss of CK5, while benign epithelium typically will have variable ER expression and a mosaic pattern of expression for CK5. In this case, the patient's post-menopausal status must be taken into consideration because overexpression of ER can be seen not only in low-grade atypical proliferations but also in post-menopausal breast epithelium [9]. Therefore, given the patient's post-menopausal status (which can explain the ER overexpression) and the heterogeneous expression of CK5, this is interpreted as a small focus of intraductal epithelial proliferation that is negative for atypia and carcinoma.

Multidisciplinary Discussion

Intraductal epithelial proliferations of the breast are characterized by an increased number of cells perpendicular to the basement membrane and range from benign epithelial hyperplasia to malignant lesions [10]. In this case, it was necessary to incorporate clinical information (i.e., the patient's post-menopausal status) for clear pathological reporting, which led to a pathologic diagnosis of benign post-menopausal epithelium without atypia or carcinoma. This finding was radiology-pathology concordant and the radiologist recommendation was to follow up with her cancer treatment team for her known current left breast cancer.

Case 3: Atypical Apocrine Adenosis

A 60-year-old woman who is high risk for developing breast cancer due to family history had a screening breast MRI that showed a suspicious left breast mass measuring 16 mm in the lower inner quadrant at 7:00 and a separate mass measuring 5 mm in the upper outer quadrant at 12:00. A targeted ultrasound was performed and found correlates for both the masses (Fig. 3) and a two-site biopsy was performed.

Pathology of the left breast 7:00 site revealed IDC, and pathology of the left breast 12:00 site demonstrated a small focus of adenosis. The adenosis has characteristic apocrine features with abundant eosinophilic cytoplasm, round nuclei, and focal snouting. In addition, some of the nuclei were significantly enlarged and hyperchromatic, which warranted an interpretation of atypia (Fig. 4) [11]. Overall, the findings were consistent with atypical apocrine adenosis.

Multidisciplinary Discussion

Atypical apocrine adenosis is a rare diagnosis that is made when there are overlapping findings of apocrine adenosis and apocrine atypia. Given the rarity, there are few studies that have reported risks of upgrade and disease progression. Several small studies (12–51 patients with long-term follow-up) demonstrated no increased breast cancer risk when atypical apocrine adenosis was present in isolation, and no upgrade upon surgical excision [11–15]. Given the scarcity of data regarding atypical apocrine adenosis, there is variability in management of findings with some breast surgeons offering an excisional biopsy due to the finding of

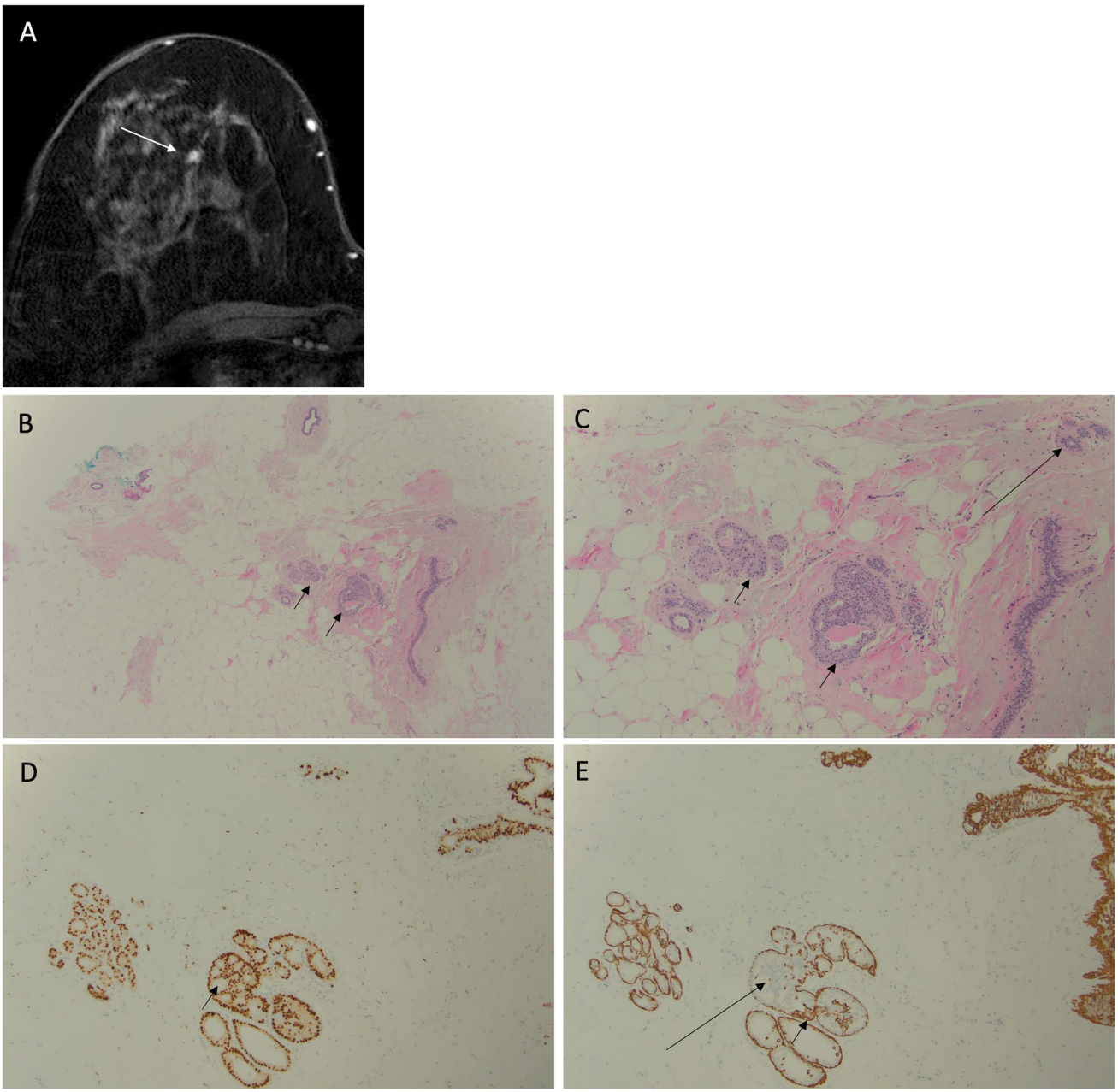

Fig. 2 Intraductal epithelial proliferation without atypia. Contrast enhanced T1-weighted fat saturated image from a breast MRI showed a focus of enhancement in the right breast (**A**, arrow). On low power (**B**, 40×), the right breast biopsy showed a focus of intraductal epithelial proliferation (short arrows). On higher power (**C**, 100×), this focus is seen to be comprised of a monotonous population of cells (short arrows). Of note, the background glandular epithelium appears atrophic (long arrow). Immunostain for ER (**D**, 100×) showed that the intraductal proliferation overexpresses ER (short arrow). Immunostain for CK5 (**E**, 100×) showed that the intraductal proliferation has heterogeneous (mosaic pattern) of CK5 (short arrow indicate cells that express CK5, long arrow indicates cells that do not express CK5)

atypia while others opt for clinical follow-up. After a discussion with this patient, the decision was made to excise only the known IDC with breast conserving therapy and plan for surveillance of the atypical apocrine adenosis on imaging. The patient's imaging surveillance included both mammography and breast MRI with specific attention to the area of atypical apocrine adenosis on future imaging exams.

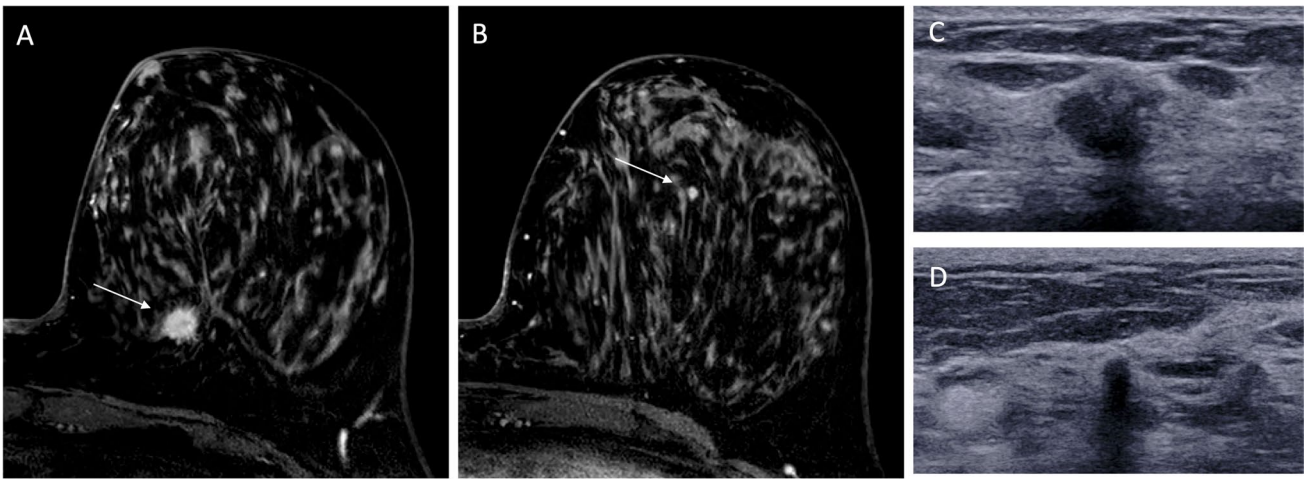

Fig. 3 Contrast enhanced T1-weighted fat saturated breast MRI image showed a suspicious round mass with spiculated margins at 7:00 (**A**, arrow) and a separate suspicious oval mass with circumscribed margin at 12:00 (**B**, arrow). A targeted ultrasound demonstrated two masses corresponding to the MRI findings. There was an irregular mass with indistinct margins and posterior acoustic shadowing at 7:00 (**C**), and a round mass with indistinct margins at 12:00 (**D**). Pathology showed IDC for the mass at 7:00 and atypical apocrine adenosis for the mass at 12:00

Case 4: Discordant Biopsy of Calcifications

A 45-year-old woman with pre-pectoral silicone implants had screen detected right breast calcifications. On diagnostic mammography, there were fine pleomorphic calcifications in the subareolar position. A stereotactic biopsy was performed; however, given the location (subareolar position), small breast size, and pre-pectoral implant, this was a very technically challenging biopsy and only one potential calcification was seen on specimen radiographs (Fig. 5).

Pathology revealed focal fibrosis without calcifications, which was discordant with the imaging findings (Fig. 5). A repeat biopsy was recommended given the radiology-pathology discordance; however, the patient was lost to follow-up until 6 months after initial biopsy.

When the patient returned 6 months after her initial imaging, diagnostic imaging demonstrated an increase in the number of calcifications and new architectural distortion in the upper outer quadrant. A targeted ultrasound at the area of distortion showed a solid mass. Pathology results revealed IDC with associated calcifications (Fig. 6).

Multidisciplinary Discussion

Radiology-pathology discordance is present when the histologic findings do not provide an acceptable explanation for the breast imaging findings. There is a false negative rate of stereotactic biopsy of approximately 1–2%, with the majority of the studies using 10, 11, and 14 gauge devices [16–20]. At our institution, a 9-gauge vacuum-assisted device is used, which can also decrease a false negative biopsy given larger sample size. In this case, given the highly suspicious morphology of the calcifications and lack of calcifications on specimen radiographs, additional sampling was warranted, either by attempted repeat core needle biopsy or excisional biopsy. In cases where image-guided core needle biopsy is technically challenging or not possible, such as too thinly compressed breasts for stereotactic core needle biopsy or findings close to the skin on mammogram-only findings, a surgical excisional biopsy may be necessary.

This case not only highlights the necessity of radiologic-pathology concordance, but also highlights the importance of patient follow-up in breast imaging. Multiple attempts were made by the breast imaging clinic staff to contact the patient, both by phone and by certified mail. The patient's primary care provider was also alerted regarding the suspicious finding and need for additional biopsy.

Case 5: Architectural Distortion Showing Entrapped Glands in Fibrotic Stroma

A 41-year-old woman had a baseline screening mammogram which showed architectural distortion in the lower outer quadrant. A diagnostic mammogram showed persistence of the architectural distortion with a corresponding mass on targeted ultrasound (Fig. 7). This finding was biopsied under ultrasound guidance.

Pathology revealed entrapped glands in fibrotic stroma with a background of proliferative changes including usual ductal hyperplasia (UDH) and columnar cell change (CCC)/hyperplasia. The stroma was fibrotic with

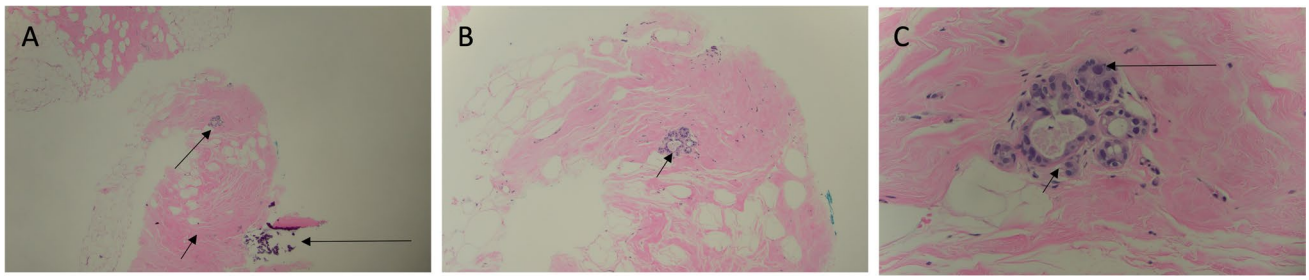

Fig. 4 Atypical apocrine adenosis. On low power (**A**, 40×), the breast tissue has abundant stroma (short arrow) with a small focus of glandular epithelium (medium arrow). In addition, there is a focus of detached calcification (long arrow). On higher power (**B**, 100× and **C**, 400×), the focus of glandular epithelium (short arrow) is seen to be atypical with enlarged and hyperchromatic nuclei (**C**, long arrow)

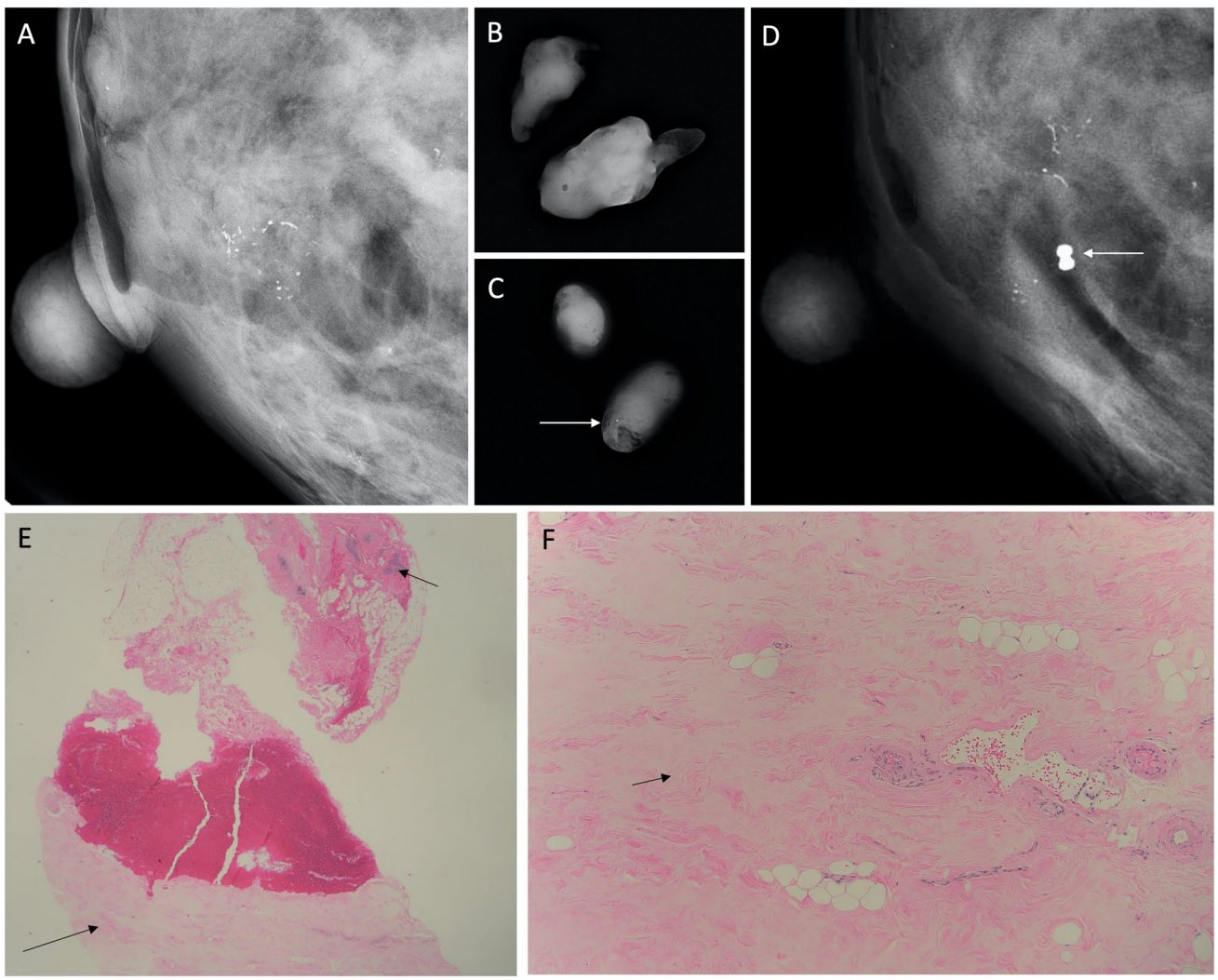

Fig. 5 Group of pleomorphic calcifications. Spot magnification true lateral view showed a group of pleomorphic calcifications in the subareolar position (**A**). Two representative specimen radiographs after successive stereotactic sampling showed only 1 potential calcification (**B**, **C**, arrow). A post-biopsy mammogram showed the biopsy marker clip in the area of the calcifications (**D**, arrow). On low power (**E**, 20×), the breast tissue has focal glandular epithelium (short arrow) and abundant fibrous stroma (medium arrow). On higher power (**F**, 100×), the stroma is confirmed to be highly fibrous (short arrow). Calcifications were not identified

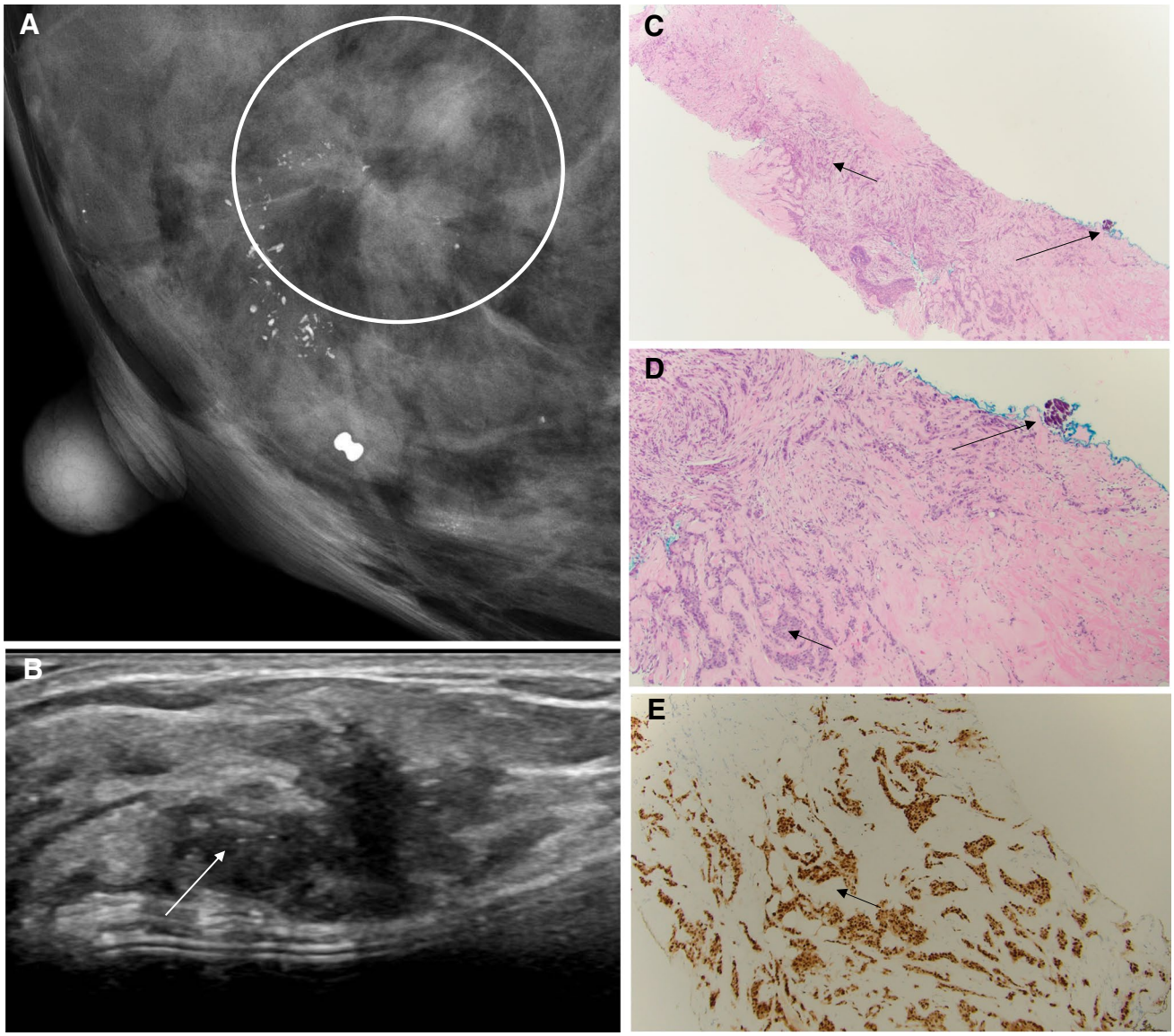

Fig. 6 Architectural distortion and solid mass at site of prior calcifications. Spot-magnification mammographic view showed a new area of architectural distortion (**A**, circle) near the site of prior calcifications, which have increased compared to prior exam. The prior biopsy marker clip is at the inferior aspect of calcifications. A targeted ultrasound was performed of this area, which showed a solid irregular mass with spiculated margins and associated calcifications (**B**, arrow). On low power (**C**, 40×), irregular nests of atypical epithelium infiltrate the fibrous stroma, diagnostic of invasive carcinoma (short arrow). There is associated calcification (medium arrow). On higher power (**D**, 100×,) the impression of invasive carcinoma is confirmed and ductal features are noted (short arrow) with cohesive nests of carcinoma. There are associated calcifications (medium arrow). Immunostain for ER (**E**, 100×) showed that the invasive carcinoma expresses estrogen receptors (short arrow indicates nuclear brown staining immunoreactivity)

areas of elastosis, which in combination with the irregular, entrapped glands raised the possibility of a complex sclerosing lesion. Myoepithelial cells were variably present around the glands, which made this challenging to interpret given the fibrotic background (Fig. 8). Definitive evaluation for this lesion, which had features that suggest a complex sclerosing lesion/radial scar, required additional sampling [21].

Multidisciplinary Discussion

Given the inability to make a definitive diagnosis on core needle biopsy, the options for management included repeat core needle biopsy versus surgical excisional biopsy. UDH and CCC are considered proliferative lesions associated with a mildly elevated breast cancer risk approximately 1.5 to 2.0-fold. If they do not have a component of cytologic atypia and

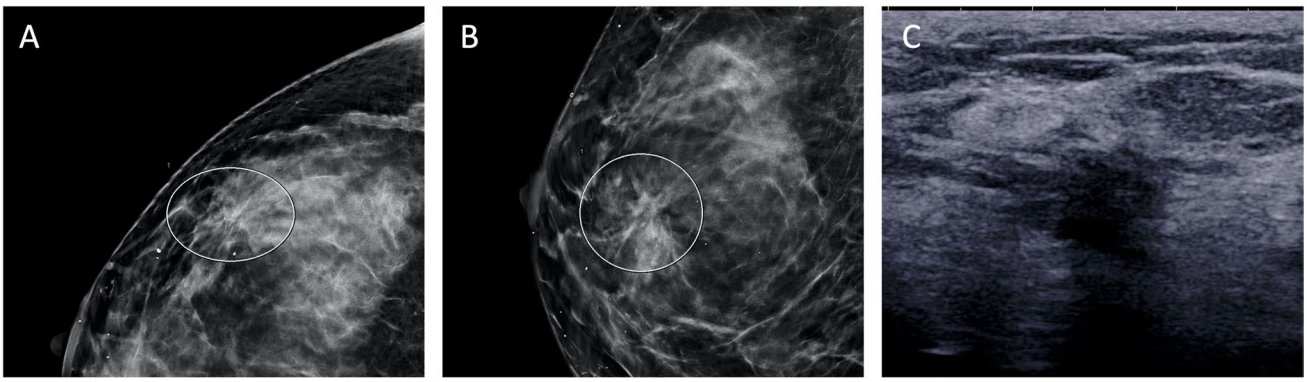

Fig. 7 Architectural distortion with corresponding sonographic mass. Diagnostic mammogram spot CC (**A**) and ML (**B**) views showed architectural distortion (circle). A targeted ultrasound showed an irregular hypoechoic mass with irregular margins measuring 11 mm at the site of the mammographic distortion (**C**)

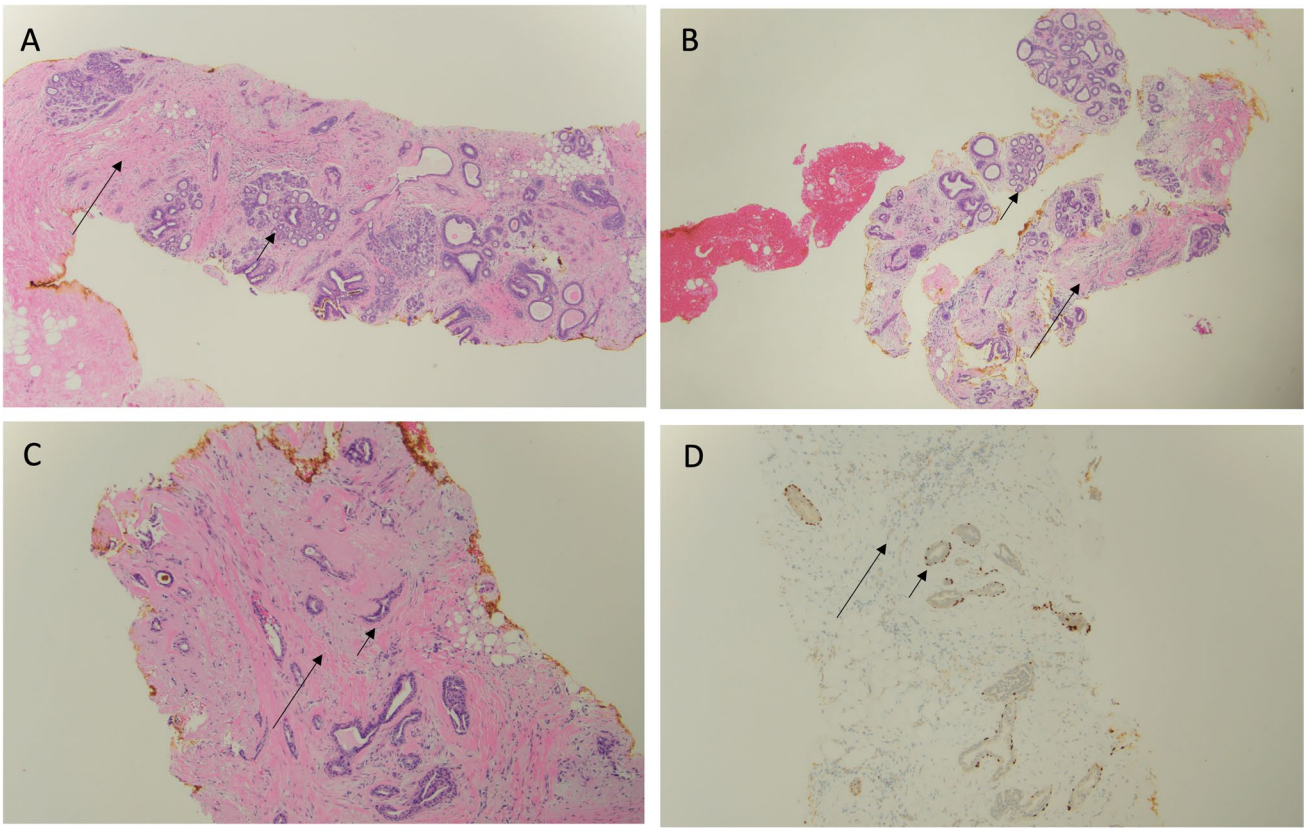

Fig. 8 Breast parenchyma with entrapped glands in fibrotic stroma. The background breast tissue (**A** and **B**, 40×) has abundant glandular epithelium (short arrow) in a mildly fibrotic stroma (long arrow). An area (**C**, 100×) with irregular glands (short arrow) in fibrotic stroma with focal elastosis (long arrow) raises the possibility of a sclerosing lesion. Immunohistochemistry for myoepithelial marker p63 (**D**, 100×) showed intact staining around most glands (short arrow) but loss around focal glands (long arrow)

there is radiologic-pathologic concordance, excision is not necessary. Complex sclerosing lesions and radial scar are terms used to describe similar histologic findings with some authors distinguishing between them based on the size of lesion (radial scar < 1 cm, complex sclerosing lesion > 1 cm) [22]. These lesions are significant because they can mimic invasive carcinomas on mammographic, gross, and microscopic examinations. On microscopic examination, one potential pitfall is that due to the degree of glandular distortion by the sclerotic stroma, myoepithelial immunoreactivity

may be diminished, which can make the distinction with invasive carcinoma challenging, particularly in the biopsy setting [23]. They can also be associated with upgrade to DCIS or invasive carcinoma on surgical excision. In a recent meta-analysis, upgrade rates of radial scar without atypia were 7.5%, and those with atypia were 26% [24]. One caveat to understanding upgrade rates is that because these lesions can have significant overlap with other entities (for examples: fibrocystic changes), understanding upgrade rates can be challenging. Current recommendations are for excision of these lesions given high upgrade rates; however, prospective multi-center trials are ongoing to better define upgrade rates for radial scars without atypia. In this case, excisional biopsy was recommended given the findings of likely radial scar on core needle biopsy.

Surgical pathology showed a complex sclerosing lesion with a focus of atypical lobular hyperplasia (Fig. 9). Atypical lobular hyperplasia is a high-risk lesion that confers elevated risk of breast cancer in either breast of 9–25% at 10 years [25–27]. Depending on extent and involvement, chemoprevention can be considered to reduce future risk of estrogen-receptor positive breast cancer [25, 27]. Imaging

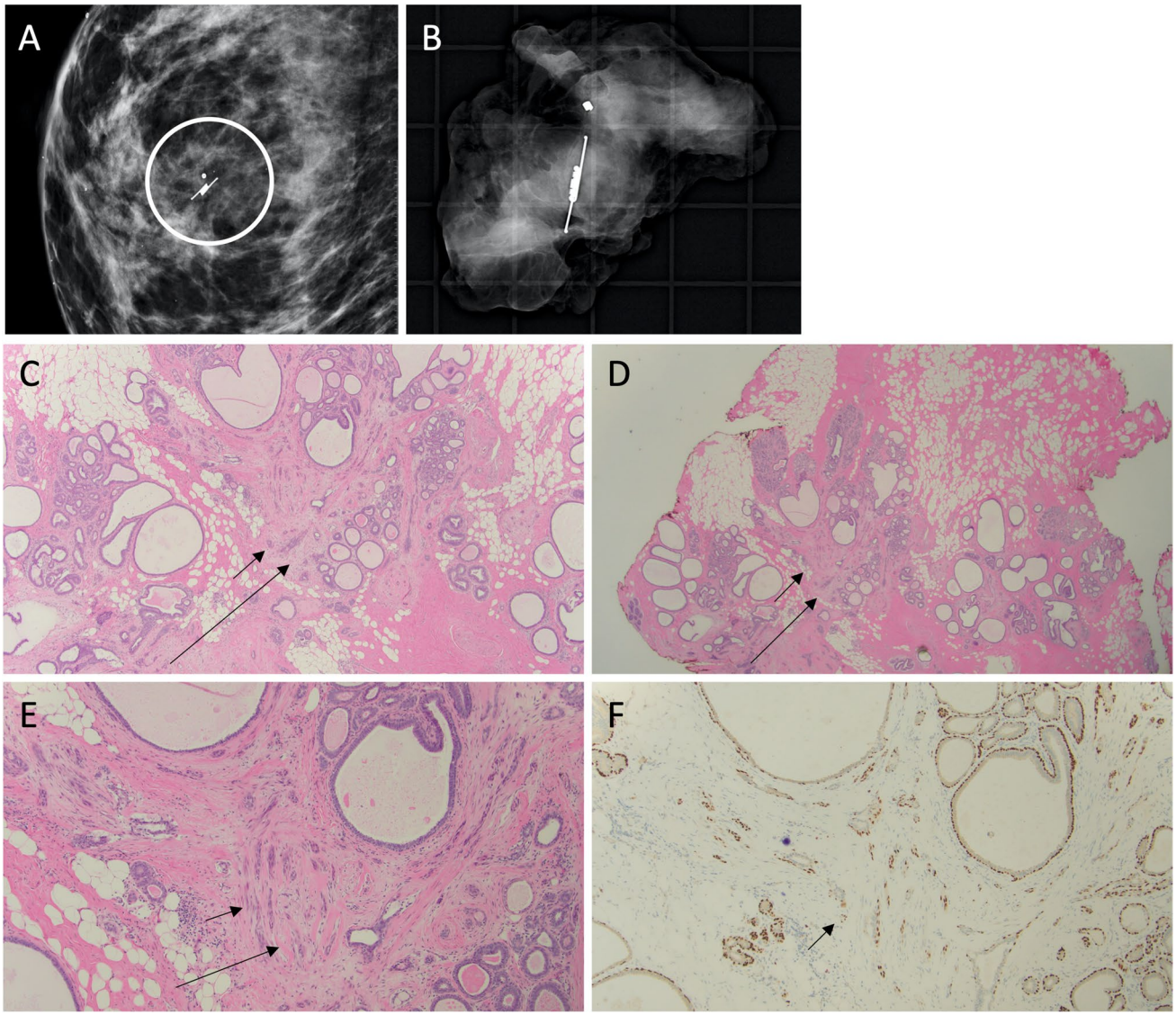

Fig. 9 Surgical excision showed complex sclerosing lesion. Post-localization mammogram showed the localization reflector next to the biopsy marker clip (**A**, circle). Excisional biopsy specimen showed the targeted reflector and biopsy marker clip (**B**). There is breast tissue (**C**, 20×) with irregular glands (short arrow) in fibrotic stroma with focal elastosis (long arrow) consistent with a sclerosing lesion. On higher power (**D**, 40×and **E**, 100×), the features of sclerosing lesion are better appreciated including irregular glands (short arrow) in fibroelastotic stroma (long arrow). Immunohistochemistry for myoepithelial marker p63 (**F**, 100×) showed intact staining around most glands (short arrow)

follow-up should consist of at least annual mammography with consideration for high-risk MRI screening based on other factors such as family history.

Case 6: Lymph Node with Metastatic Carcinoma Including Extracapsular Extension

A 41-year-old woman presented with a right breast palpable abnormality which showed an 18 mm mass in the upper outer quadrant on mammography. On ultrasound, this mass measured 14 mm. Biopsy revealed IDC with lobular features. MRI showed a unifocal mass measuring 23 mm with no lymphadenopathy (Fig. 10).

She subsequently underwent lumpectomy with sentinel lymph node biopsy, which showed a 28-mm IDC with negative margins. One of three sentinel lymph nodes was positive for macrometastatic carcinoma with associated extracapsular extension (spanning 0.4 cm). Extracapsular (otherwise known as extranodal) extension (ECE) is defined as carcinoma that extends beyond the capsule of the lymph node. Establishing an interpretation of ECE can be challenging if identifying the capsule is difficult (i.e., in a lymph node with fatty replacement, carcinoma effacing normal architecture, or when the carcinoma involves the hilum, which does not have a well-defined capsular component). Once an interpretation of ECE has been rendered, there is no consensus regarding the utility of quantifying ECE to risk stratify patients, although some consider ≥ 0.2 cm as "gross" ECE with the clinical implication of likely additional nodal disease [28].

Multidisciplinary Discussion

Results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial demonstrated that completion axillary lymph node dissection did not prolong survival or decrease the risk of regional recurrence among women with < 3 positive lymph nodes and T1 or T2 invasive breast carcinomas who underwent breast conservation therapy [29••]. However, patients with extracapsular extension were excluded from this study. A recent study evaluating the significance of extracapsular extension in women who otherwise met Z0011 criteria demonstrated that the presence and extent of ECE were associated with greater axillary disease burden [30]. Twenty percent of patients with ECE had additional positive nodes on completion axillary lymph node dissection compared to 3% of women without ECE. On multivariate analysis, ≥ 2 mm of ECE was the strongest predictor of ≥ 4 positive nodes at completion ALND (odds ratio 14.2). This patient had 4 mm of ECE, and therefore, completion axillary lymph node dissection was recommended.

Historically the presence of ECE has been linked to a higher risk of locoregional failure in the absence of adjuvant

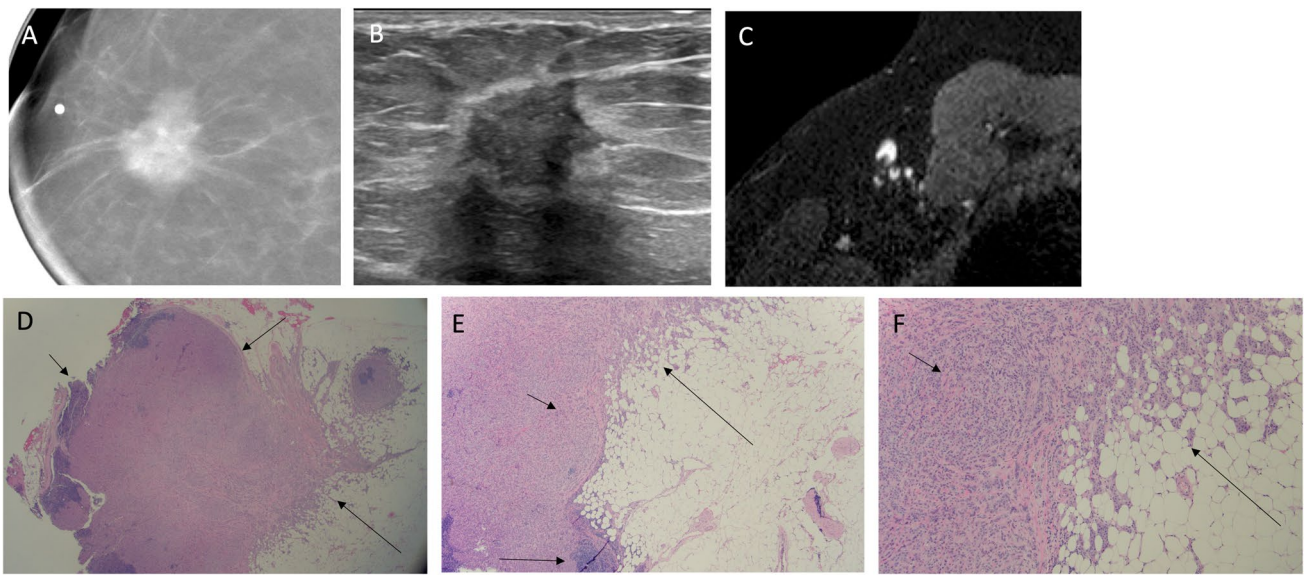

Fig. 10 Mammographic spot-magnification view with BB over the site of palpable abnormality showed an irregular mass with spiculated margins (**A**). A targeted ultrasound of this mass showed an irregular mass with spiculated margins (**B**). On subsequent breast MRI, there was no lymphadenopathy (**C**). Histology of the sentinel lymph node biopsy showed on low power (**D**, 20×) there is residual intact lymphoid tissue (short arrow) which is involved by macrometastatic carcinoma (medium arrow). There is infiltration of this metastatic carcinoma into adjacent adipose tissue (long arrow), consistent with extracapsular extension. On higher power (**E**, 40× and **F**, 100×), the metastatic carcinoma (short arrow) is seen infiltrating beyond the lymphoid tissue (medium arrow in **E**) and into the adjacent adipose tissue (long arrow). This is consistent with extracapsular extension

radiotherapy in breast cancer [31]. Furthermore, in conjunction with other unfavorable pathologic features, it may be a prominent negative prognostic factor [32]. More recently, phase III data support the use of less invasive axillary surgeries; however, they fall short in providing guidance on the role of regional nodal irradiation in this population, especially with respect to the presence of ECE [33, 34]. In this case, radiation treatment would encompass the entire breast including the low axilla using high tangential fields with the option to include a third field for regional nodal coverage.

Trials evaluating the utility of genomic testing for chemotherapy treatment decisions for node positive breast cancers were agnostic regarding ECE; however, they limit the use to women with 1–3 positive lymph nodes (N1 disease) [35, 36]. Given that ECE predicts for > N1 disease, it is worthwhile to consider this when making systemic therapy decisions.

Case 7: Biopsy of a Suspicious Mass After Neoadjuvant Chemotherapy

A 40-year-old woman with left breast triple negative 35-mm IDC at 1 o'clock, upper outer quadrant was noted to have an additional suspicious 9-mm mass in the medial breast approximately 50 mm away from index malignancy on extent of disease breast MRI. An MRI-guided biopsy was recommended; however, 1.5 months of neoadjuvant chemotherapy (NAC) was completed prior to biopsy. At the time of MRI-guided biopsy, pre-biopsy post-contrast images showed resolution of the prior 9-mm mass; however, a biopsy using landmarks of this area was performed with pathology showing benign breast tissue. Without a pathologic finding to explain the radiologic impression of a mass lesion, this was deemed discordant (Fig. 11).

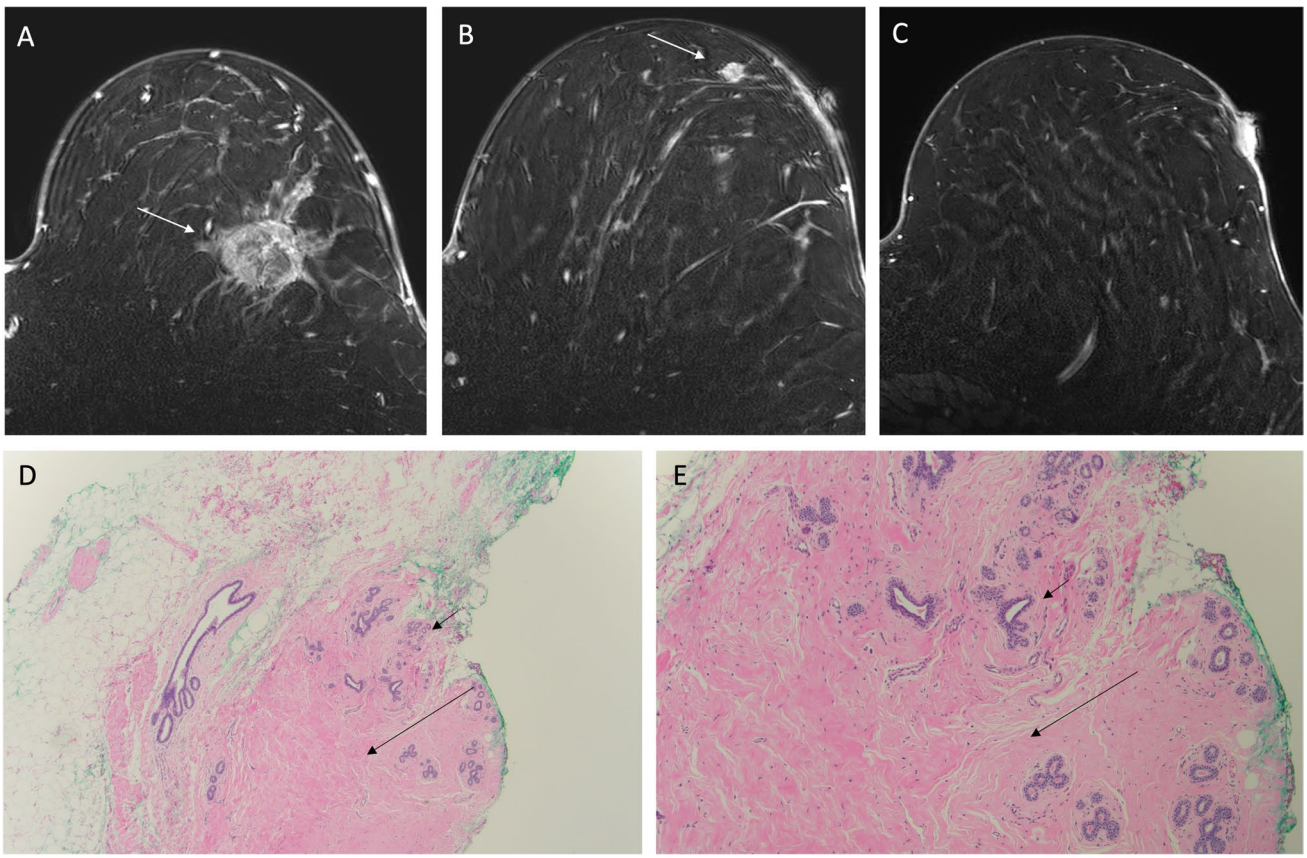

Fig. 11 Contrast enhanced T1-weighted fat saturated breast MRI image showed an irregular mass with heterogeneous internal enhancement in the left breast upper outer quadrant at the site of known cancer (**A**, arrow). There is an additional suspicious round mass with irregular margins at 9:00 (**B**, arrow). Post-NAC MRI performed showed no abnormal enhancement at the prior mass (**C**) in addition to complete imaging response of the biopsy proven index mass (not shown). Histology from the left breast mass at 9:00 showed breast tissue without obvious pathology and no histologic correlate to the radiologic finding of a mass lesion (**D**, 40× and **E**, 100×). Glandular breast tissue was present (short arrow) in a background of typical fibrous stroma (long arrow). Residual in situ and/or invasive carcinoma was not identified

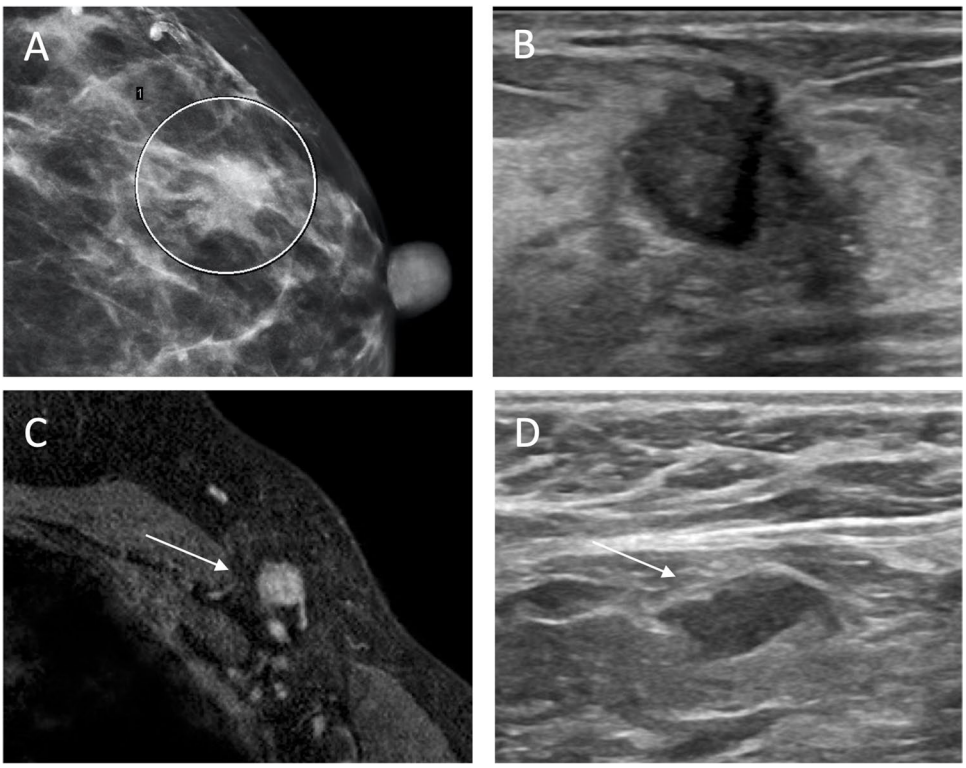

Fig. 12 Single abnormal axillary lymph node. Mammographic CC view (**A**, circle) showed an oval mass with spiculated margins. There is a corresponding irregular shaped mass on ultrasound with indistinct margins (**B**). Post-contrast breast MRI (**C**, arrow) showed a single abnormal left axillary level 1 lymph node with corresponding abnormal lymph node seen on ultrasound (**D**, arrow)

Multidisciplinary Discussion

This radiologic and pathologic discordance could either have been due to a sampling error or possibly interval resolution of a neoplastic process. The absence of any sort of tissue response, such as marked fibrosis or histiocytic inflammation (i.e., treatment related changes), in this biopsy argues against the latter. A post-NAC breast MRI was performed, which confirmed that the suspicious additional mass had resolved and the biopsy marker clip was in the area of prior mass lesion. The known index cancer in the upper outer quadrant had also resolved. Options for surgical management included breast conservation of the primary carcinoma in the upper outer quadrant with close surveillance MRI for recurrence of the second mass versus mastectomy.

In regard to adjuvant radiation therapy, whole breast radiotherapy would be recommended after breast conservation surgery. A tumor bed boost would be delivered after completing the whole breast course based on pre-chemotherapy imaging and surgical clips. Post-mastectomy radiation therapy would not be recommended unless there was evidence of a large tumor bed or previously positive lymph node on final pathology. In this situation, a lumpectomy was performed after discussion with the patient. Final pathology revealed complete pathologic response, negative for carcinoma with biopsy site changes and treatment effect. Given the complete pathological response, no further systemic therapy was indicated for this triple negative IDC; however, close monitoring on follow-up imaging was recommended.

Case 8A and 8B: Number of Abnormal Axillary Lymph Nodes on Initial Imaging in Women Who Receive Neoadjuvant Chemotherapy for Invasive Breast Cancer

The following two cases describe the importance for the radiation oncologist to understand the number of abnormal lymph nodes prior to NAC in order to determine treatment field.

Case 8A: Single Abnormal Lymph Node

A 64-year-old woman with known left breast unifocal IDC (ER + /PR − /HER2 +) and DCIS had a single abnormal left level 1 axillary lymph node identified on breast MRI (Fig.). A targeted ultrasound with ultrasound-guided biopsy and biopsy marker placement of this lymph node

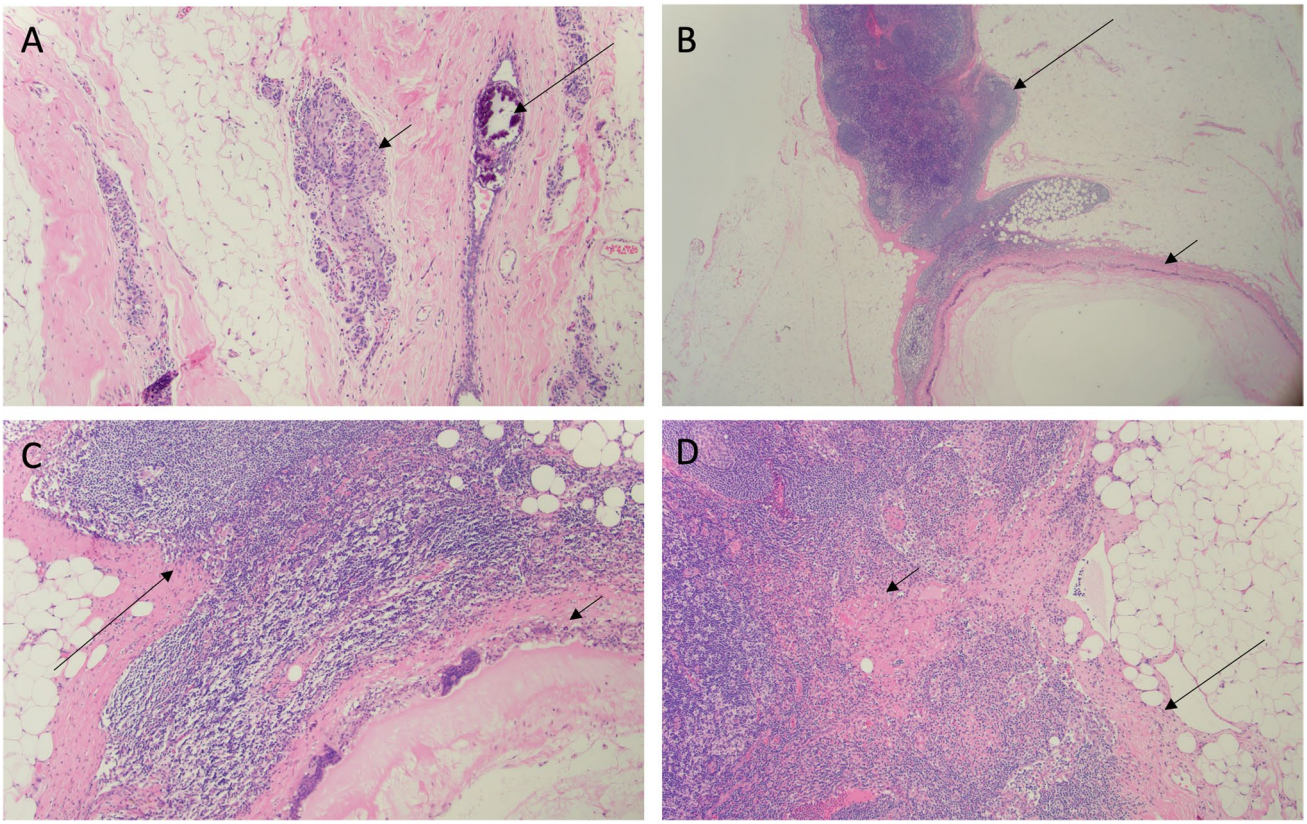

Fig. 13 In the breast (**A**, 100×), there is focal residual treated DCIS (short arrow) with nearby calcification (long arrow); there is no residual invasive carcinoma. In a lymph node (**B**, 20×and **C**, 100×), there is biopsy site change (short arrow) with a cystic space lined by synovial-type hyperplasia with associated foreign body giant cells, fibrosis, and lymphocytic inflammation. Residual lymphoid tissue (long arrow) is present without definite treatment effect. In a different lymph node (**D**, 100×), there is focal fibrosis (short arrow); however, this appears to be in continuity with the overlying capsule (long arrow) and therefore is not interpreted as treatment effect

was performed which revealed axillary lymph node metastasis. The patient then had NAC with resolution of the index mass and abnormal lymph node by ultrasound (Figs. 12 and 13).

The patient preferred to undergo mastectomy and had a sentinel lymph node biopsy. Pathology from the left breast mastectomy showed focal residual high-grade DCIS. The sentinel lymph node excision specimen did not identify residual carcinoma or treatment-related changes, such as marked fibrosis or histiocytic inflammation. However, biopsy site changes were present in the lymph node (Fig. 13).

Case 8B: ≥ 3 Abnormal Axillary Lymph Nodes on Initial Imaging

A 39-year-old woman had a right breast IDC (ER − / PR − /HER2 +) spanning the upper outer and upper inner quadrants measuring up to 68 mm. In addition, she had biopsy proven metastatic disease in a right axillary lymph node. A subsequent breast MRI was performed which showed at least 3 abnormal right level 1 lymph nodes (one of which contained the biopsy marker) as well as an abnormal level 2 lymph node (Fig. 14). The patient received NAC with complete imaging response in the breast and lymph nodes.

Post-treatment surgical pathology revealed no residual invasive carcinoma in the right mastectomy specimen. There were four sentinel lymph nodes excised without residual carcinoma. There was evidence in one lymph node of biopsy site and treatment-related changes (Fig. 15).

Multidisciplinary Discussion

In women who undergo NAC with biopsy-proven axillary metastasis, it is particularly important for the radiation oncologist to understand how many lymph nodes may have originally been affected with carcinoma prior to NAC. This helps guide the radiation treatment fields. For example, if a patient had pathologic complete response

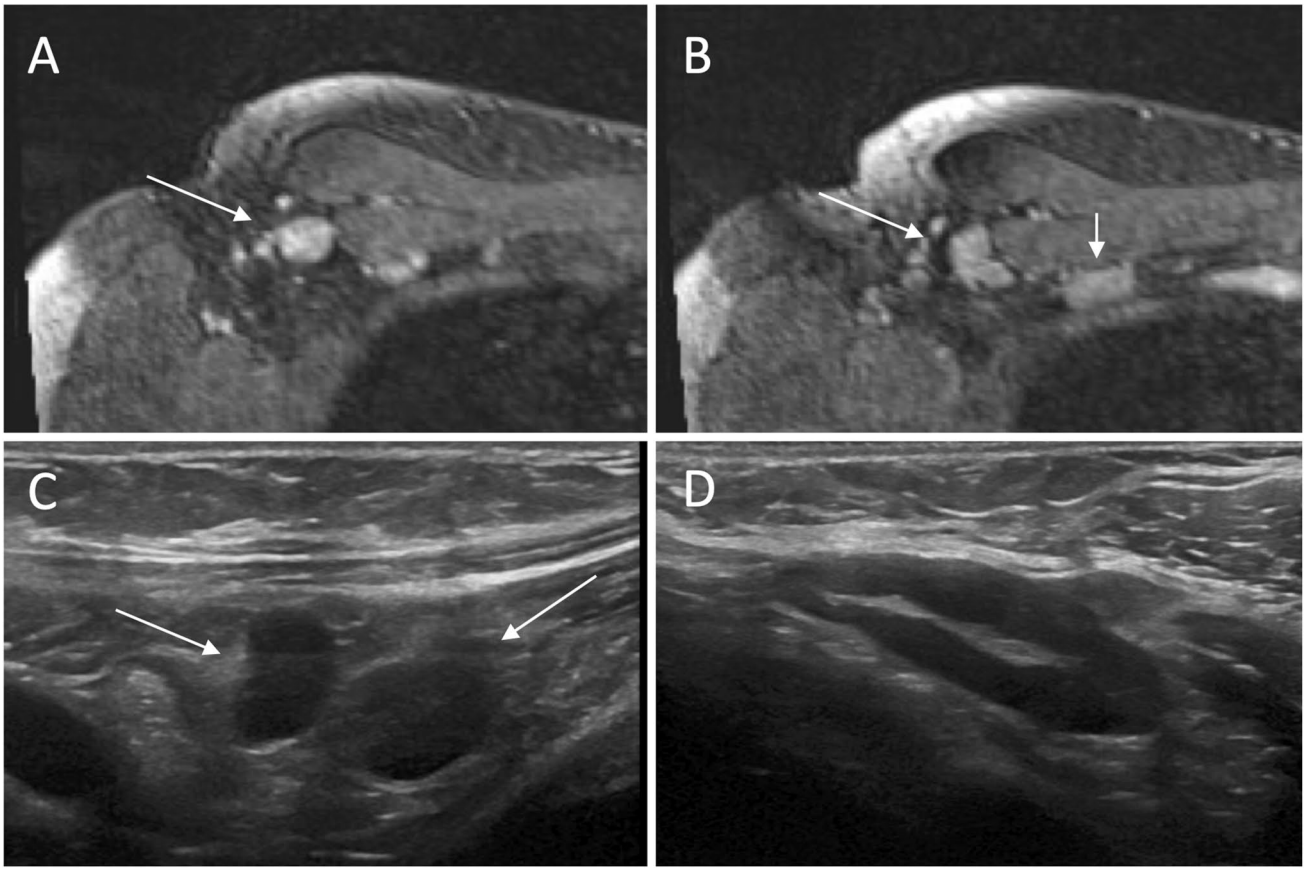

Fig. 14 ≥ Three abnormal axillary lymph nodes. Contrast enhanced T1-weighted fat saturated breast MRI images showed at least 3 morphologically abnormal right axillary level one lymph nodes (**A**, **B**, long arrow) in addition to an abnormal right axillary level 2 lymph node (**B**, short arrow). A targeted ultrasound showed the two abnormal left level 1 lymph nodes in different planes (**C**, arrows and **D**)

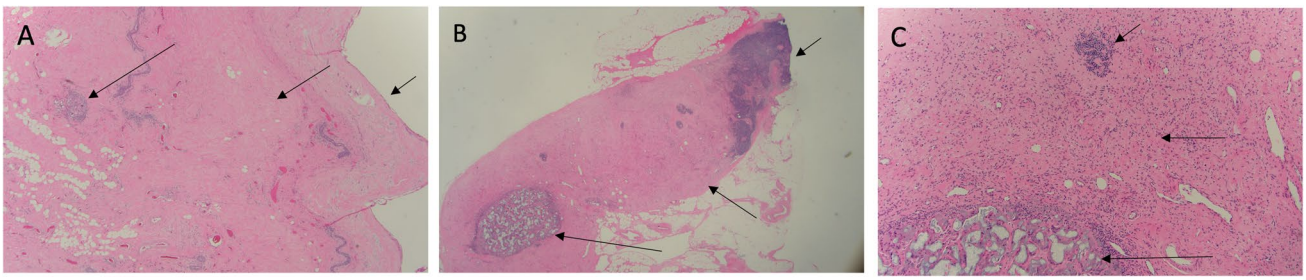

Fig. 15 The breast (**A**, 40×) showed biopsy site changes (short arrow) with background fibrotic stroma (medium arrow) and mild inflammation (long arrow); there is no residual in situ or invasive carcinoma. One of the sentinel lymph node specimens (**B**, 20×and **C**, 100×) has focal residual lymphoid tissue (short arrow), predominantly a fibrotic stroma indicative of treatment changes (medium arrow), and biopsy site changes (long arrow) comprising a discrete area with foreign body giant cells and associated fibrosis. There is no residual metastatic carcinoma present in the lymph node

with 5 negative lymph nodes upon sentinel lymph node biopsy, however, they all had treatment effect, the radiation oncologist might choose to treat the regional lymphatics. In contrast, if there were 5 negative lymph nodes without treatment effect, less comprehensive treatment may be warranted. Furthermore, based on future study results, these women may potentially not need radiation therapy [37]. The most significant predictor of long-term outcomes among women who undergo NAC is their response to therapy. Those with a

pathological complete response have the best prognosis, and recommended therapy is completion of 1 year of HER2-directed antibody therapy without a change to ado-trastuzamab emtansine [38, 39].

Conclusion

This manuscript describes several challenging radiology-pathology correlations for which a multidisciplinary team is helpful. Understanding the overall clinical context can better guide clinical management.

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