Nonmass Enhancement on Breast MRI: Review of Patterns With Radiologic-Pathologic Correlation and Discussion of Management

OBJECTIVE. The purpose of this article is to review the varied appearances and associated diagnoses of nonmass enhancement on breast MRI with radiologic-pathologic correlation.

CONCLUSION. Knowledge of the distribution and internal characteristics of these findings is helpful to determine when core needle biopsy is indicated. Correlating imaging with pathologic findings is critical in making appropriate recommendations regarding clinical management.

As defined by the BI-RADS, nonmass enhancement is an area of enhancement on MRI that does not belong to a 3D mass or have distinct features of a mass [1]. These lesions are characterized by their distribution, internal enhancement pattern, and symmetry (or lack thereof). Although segmental, clumped, and linear nonmass enhancement is associated with malignancy, there is substantial overlap of benign, high-risk, and malignant processes in the breast that can show nonmass enhancement on MRI. Most often, core biopsy is required for accurate diagnosis. Determining concordance for nonmass enhancement is critical to ensure proper clinical management. As for other image-guided core biopsies, the diagnosis of malignancy, any atypia, complex sclerosing lesions, or fibroepithelial tumor warrants surgical excision. However, surgery is also indicated when the pathologic diagnosis does not definitively explain the MRI findings. In this article, we present a series of benign and malignant causes of nonmass enhancement on MRI with radiology-pathology correlation.

Benign Lesions

Pseudoangiomatous Stromal Hyperplasia

Seen as an incidental finding in up to 25% of biopsy specimens, pseudoangiomatous stromal hyperplasia (PASH) is a benign overgrowth of fibrous connective-tissue stroma most commonly seen in premenopausal and perimenopausal women [2]. Usually presenting as a circumscribed mass without associated calcifications or distortion on mammography, PASH can also be seen as a focal or developing asymmetry. On ultrasound, PASH is usually an oval hypoechoic mass with posterior acoustic enhancement and less frequently has mixed echogenicity or is ill defined [3]. On MRI, PASH is associated with focal or segmental clumped nonmass enhancement with persistent or plateau kinetics [4]. Often, low-signal fibrous stroma and high-signal cystic spaces may be seen on T2-weighted imaging sequences (Fig. 1). Histopathologically, PASH is composed of anastomosing slitlike spaces resembling small blood vessels that are either acellular or lined by spindle-shaped stromal cells. PASH does not require surgical excision, unless it enlarges, and of those that do require excision, 15–22% may recur.

Apocrine Metaplasia

Apocrine metaplasia is a variant of fibrocystic change related to monthly hormonal fluctuations. Apocrine metaplasia derives from the progenitor of cyst formation in which secretions from apocrine-line microcysts lead to increased intraluminal pressure and subsequent fusion and unfolding of the adjacent acini [5]. A new or enlarging lobular isodense mass with macrolobulated margins or a group of heterogeneous calcifications on mammography suggests the possibility of this diagnosis [6]. On ultrasound, typical presentation includes a cluster of cysts without a solid component, which favors a benign cause and warrants no further follow-up [7]. On MRI, apocrine metaplasia may be seen as either a mass or nonmass enhancement with...
enhancement kinetics ranging from below threshold to washout (type 3) [8] (Fig. 2). The association of high signal on T2-weighted sequences in the area of enhancement permits diagnosis by MRI for some cases; however, given the overlap with malignant causes, biopsy may be indicated, especially if the lesion shows washout kinetics, because these cases are more frequently associated with atypia or low-grade malignancies. It is important to correlate pathology with imaging and ensure that apocrine metaplasia is the target lesion and not an incidental finding. There is no increased risk of malignancy if only apocrine metaplasia is found on pathology, and excision is therefore not indicated.

Radial Scar and Complex Sclerosing Lesion

Typically seen in premenopausal women in the 3rd through 5th decades of life, radial scar (≤ 1 cm in size) and complex sclerosing lesion (≥ 1 cm in size) are benign breast lesions composed of a fibroelastic core with radiating ducts and lobules and are unrelated to trauma [16]. Most commonly, radial scar and complex sclerosing lesion are not palpable and are discovered incidentally on screening mammography or biopsy. They are associated with an elevated risk for subsequent development of breast cancer. On mammography, radial scar and complex sclerosing lesion can be seen as an asymmetry, mass, or distortion with central radiolucency. On ultrasound, imaging characteristics often mimic those of malignancy. On MRI, the lesions may present as nonmass enhancement, including in linear or clumped distribution, and are characterized by early rapid enhancement with plateau or delayed washout kinetics (type 2 or 3 curves) (Fig. 4). Clinical management of these lesions is controversial. On pathologic examination, radial scar or complex sclerosing lesion is often associated with wide range of pathologic findings including usual epithelial hyperplasia, adenosin, papillomatosis, atypical epithelial hyperplasia, DCIS, and early-stage invasive carcinomas [17]. Many studies have reported association of radial scar and complex sclerosing lesion with malignancy in up to 40% of cases [18–21]. Therefore, surgical excision is considered to be mandatory by many authors [22, 23]. In select patients, close observation may be substituted for surgical excision, in the absence of atypical hyperplasia on extensive biopsy sampling, including with vacuum-assisted large core biopsy devices [18, 24].

Flat Epithelial Atypia

A nonobligate precursor in the development of low-grade carcinomas and often seen in association with ADH and low-grade DCIS, flat epithelial atypia is characterized by the replacement of normal epithelial cells by a variable number of layers of atypical cuboidal to columnar cells with the characteristic pathologic finding of apical snouts [25]. Grouped calcifications represent the most common imaging presentation. More rarely, nonmass enhancement on MRI may be seen (Fig. 5). As with ADH and other high-risk lesions, there are no specific MRI predictors of subsequent upgrade rates on excision. When diagnosed on core biopsy, excision should be recommended given previously published upgrade rates to carcinoma of 0–21% [24].

Introductal Papilloma

Most commonly presenting with spontaneous unilateral bloody nipple discharge, papillomas are ductal neoplasms composed of a fibrovascular core lined with an epithelial outer layer that can be associated with hyperplasia, carcinoma in situ, or invasive malignancy. Typically arising in a central duct, intraductal papillomas on mammography are seen as small smooth masses with or without associated calcifications, a solitary dilated duct, or coarse or fine calcifications. On ultrasound, they present as hypoechogenic masses often within a dilated duct. On MRI, intraductal papillomas can be seen as a mass, focus, or linear nonmass enhancement typically located within 3 cm of the nipple. Kinetics vary from progressive to plateau—and even to washout [26]. Papillary lesions of the breast range between benign papilloma to papilloma with foci of atypical and papillary carcinoma. Cancer and high-risk lesions have been reported in up to 44% of benign papilloma diagnoses leading to upstaging at the time of surgical excision [27, 28]. Many authors advocate excisional biopsy of these lesions owing to the possibility of inadequate sampling leading to inaccurate diagnoses [29, 30]. Although some investigators deem close observation appropriate [31–33], presently, at our institution, all papillary lesions diagnosed on core biopsy undergo surgical excision (Fig. 6).

Malignant Lesions

Ductal Carcinoma In Situ

Currently accounting for approximately 20% of all new cancer diagnoses in the United States, DCIS comprises a spectrum of noninvasive malignant processes in the breast with the potential to develop into an invasive cancer. DCIS typically presents as grouped, segmental, or linear branching pleomorphic microcalifications, although in up to 14% of cases, a mass may be seen on mammography [34]. Mammographically occult DCIS occurs in 6–23% of cases [35]. The
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Invasive Ductal Carcinoma

Invasive ductal carcinoma (IDC) is the most common type of breast cancer, comprising approximately 65–75% of all breast carcinomas. A spiculated mass is the most common mammographic presentation, which may be associated with architectural distortion and microcalcifications, suggestive of an intraductal component. IDC may also present as a round or oval mass with variable margins, asymmetry, or architectural distortion. On ultrasound, IDC presents as a hypoechoic irregular mass with angular, spiculated, or microlobulated margins, variable posterior features and possible associated calcifications, corresponding to mammographic or palpable abnormality. IDC can develop independently or from the evolution of DCIS. IDC most commonly presents as an enhancing mass with plateau or washout kinetics on MRI; however, it can also manifest as nonmass enhancement or as a focus. When seen in association with nonmass enhancement, the distribution is variable, and internal enhancement can be heterogeneous, clumped, or stippled [41] (Fig. 8).

Invasive Lobular Carcinoma

Accounting for approximately 10–15% of all breast malignancies, invasive lobular carcinoma (ILC) is notoriously difficult to diagnostically assess and often is palpable on physical examination but has negative imaging findings. On mammography, when detected, ILC most commonly manifests as an indiscernable mass or asymmetry. On ultrasound, when detected, it typically is a vague indiscernible area of distortion or shadowing (or both). Sensitivities of mammography for detecting ILC are approximately 65%, which is improved by utilizing sonography, which can detect up to 75% of missed ILCs by mammography and remains the modality of choice for guiding biopsies [42, 43]. MRI is useful in defining disease extent and in the detection of multifocal, multicentric, and contralateral disease. The size and extent of ILC seen on MRI correlate well with size at pathology. Additional foci of disease are detected by MRI up to one third of patients in the ipsilateral breast and 7% of patients in the contralateral breast, leading to changes in clinical management [44, 45]. The most common manifestation of ILC on MRI is focal or regional nonmass enhancement. Washout kinetics are not commonly seen, and delayed progressive enhancement is more typical [46] (Fig. 9).

Conclusion

Nonmass enhancement can be seen on screening and diagnostic MRI studies. The differential diagnosis for nonmass enhancement on MRI includes PASH, apocrine metaplasia, flat epithelial atypia, intraductal papilloma, radiation effect, ADH, radial scar or complex sclerosing lesion, DCIS, IDC, and ILC. When seen on MRI, biopsy most often is performed because there is substantial overlap in the imaging appearances among the varied benign and malignant causes. As with other image-guided procedures, the radiologist must correlate the histopathologic findings with the MRI presentation to determine concordance. If the pathology does not explain the presence of nonmass enhancement on MRI, the radiologist should recommend surgical excision or biopsy given a discordant result. The radiologist is responsible for communicating the concordance or discordance of the MRI biopsy to the referring physician and the patient to ensure that the appropriate management takes place.

In summary, MRI can play a critical role in the detection, characterization, and clinical management of a wide range of benign, high-risk, and malignant entities, especially for diseases that may be occult on conventional mammography. Combined analysis of morphologic features, kinetics, distribution, and internal characteristics of the nonmass enhancement will facilitate better characterization of lesions.

References


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Fig. 1—35-year-old woman with prior history of right breast cancer. A and B, On screening MR images, enhancing area of asymmetry (arrow) is seen in left axillary tail on T1-weighted contrast-enhanced axial image, and region is primarily low signal (arrow) on T2-weighted imaging although higher in signal as compared with more-anterior dense glandular tissue. Ultrasound performed after MRI showed subtle area of mixed and increased echogenicity without internal vascularity corresponding to abnormality on MRI (not shown). C, Histology on ultrasound-guided core biopsy shows pseudoangiomatous stromal hypertrophy. Plump myofibroblasts are seen in stroma adjacent to artificial cleftlike spaces, simulating endothelial vascular spaces. Benign gland with columnar cell hyperplasia (arrow) is seen on left.

Fig. 2—53-year-old woman with prior left breast cancer. A, Axial T1-weighted contrast-enhanced subtraction images of right breast show 1.9 × 1.5-cm nodular clumped nonmass enhancement in upper inner quadrant with progressive kinetics (arrow). B, Histologic image of core biopsy shows apocrine metaplasia. Lobules are present, and enlarged apocrine-type epithelium is seen with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli.
Fig. 3—67-year-old woman with increasing breast mass, skin thickening, and erythema at lumpectomy site 15 years after breast-conserving therapy. 
A, Sagittal T1-weighted contrast-enhanced subtraction image shows vague nonmass enhancement involving entire right outer central and inferior breast (arrows). 
B, T2-weighted unenhanced image shows typical low-signal architectural distortion from prior lumpectomy. 
C, Histology shows benign breast tissue with changes consistent with radiation effects. Terminal duct lobular units show atrophy with sclerosis. Scattered large atypical cells can be seen but do not show any proliferative or mitotic activity.

Fig. 4—48-year-old woman with newly diagnosed left breast invasive cancer in whom MRI to determine extent of disease showed lesion in contralateral breast. 
A, Contrast-enhanced subtraction sagittal view shows abnormal 3-cm area of linear clumped nonmass enhancement with mixed kinetics including washout (arrow) adjacent to 1.3-cm cyst (arrowhead). Mammography (not shown) after MRI showed questionable area of distortion in left breast. 
B, Ultrasound image shows lesion as irregular hypoechoic mass with dominant vascularity.

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Fig. 4 (continued)—48-year-old woman with newly diagnosed left breast invasive cancer in whom MRI to determine extent of disease showed lesion in contralateral breast. 

C, Histology shows radial scar or complex sclerosing lesion. Multiple glands with usual ductal hyperplasia are seen radiating outward from central area of fibroelastic stroma.

Fig. 5—47-year-old with left breast pain and family history of breast cancer in whom mammography (not shown) revealed scattered fibroglandular tissues without suspicious grouped calcifications.

A, Axial contrast-enhanced subtraction image shows incidental 1.5-cm linear area of nonmass enhancement (arrow) in central inferior posterior right breast with mixed kinetics.

B, Histology shows flat epithelial atypia. Low-power image shows acinar structure dilated with rounded lumen. Multiple layers of rounded atypical monotonous epithelial cells are present with prominent apical snouts projecting into lumen.

Fig. 6—47-year-old woman with right upper outer quadrant palpable thickening who presented because of peau d’orange and skin color changes and had mother with history of breast cancer.

A and B, Axial T1-weighted contrast-enhanced (A) and subtraction (B) MR images show linear nonmass enhancement that appeared ductal and extended 3.5 cm (anteroposterior) with primarily progressive kinetics (arrows).

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Fig. 6 (continued)—47-year-old woman with right upper outer quadrant palpable thickening who presented because of peau d’orange and skin color changes and had mother with history of breast cancer.

C, Histology on core biopsy shows multiple papillary structures with abundant hyalinized pink stroma in fibrovascular cores. Papillae of epithelium lining are bland, and myoepithelial cell layer is easily identified below epithelium throughout lesion. Findings were considered consistent with multiple papillomas.

Fig. 7—57-year-old woman with family history of breast cancer (in mother at 44 years old) in whom mammographic findings (not shown) were normal.

A, Sagittal T1-weighted subtraction MR image shows clumped nonmass enhancement with mixed kinetics in medial mid left breast (arrow).

B, Histology shows ductal carcinoma in situ (DCIS) of solid type and high nuclear grade. Duct shown was involved by DCIS, spreading along duct in pagetoid pattern. Large atypical epithelial cells can be seen undermining normal epithelium, pushing smaller normal native epithelium upward toward lumen. Third row of myoepithelial cells can be seen surrounding duct.
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Fig. 8—52-year-old woman with spontaneous right breast bloody nipple discharge who had negative findings on recent mammogram and ultrasound (both not shown).
A, Axial T1-weighted subtraction image shows regional nonmass enhancement posterolaterally with mixed kinetics including progressive and plateau types.
B, Core biopsy shows infiltrating ductal carcinoma. Numerous small tubules and nests of neoplastic cells are present infiltrating through stroma and associated with cribriform pattern of ductal carcinoma in situ (arrows).

Fig. 9—46-year-old woman with left axillary node positive for carcinoma in whom mammography showed heterogeneously dense tissue with no suspicious findings, ultrasound of left axilla confirmed suspicious axillary nodes, and fine-needle aspiration of left axillary lymph node showed malignant cells.
A, Axial T1-weighted subtraction image of left breast shows irregular 3.6-cm area of nonmass enhancement in posterior outer inferior breast (arrow) with mixed kinetics. Similar abnormal areas were seen anteriorly in same breast.
B, Histology shows grade 1 invasive lobular carcinoma. Neoplastic lobular carcinoma cells are diffusely infiltrating stroma in single-file rows and single cells with surrounding small islands of lobular carcinoma in situ.
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