Benign mucocoele-like lesions of the breast: revisited

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Mucocoele-like lesions of the breast are ruptured ducts that discharge their contents into the stroma. They constitute a spectrum from benign to atypical to malignant. The current management of these lesions diagnosed on core biopsy is excision. The goal of our study was to evaluate the necessity of this practice for benign mucocoele-like lesions. Retrospective review of the pathology database from 1 January 2000 to 1 June 2008 identified 61 cases, with follow-up information available in 50 cases. Clinical, radiological, and pathological information was correlated. Core biopsies were reviewed to confirm the diagnosis and verify previous biopsy site. In all, 45 patients underwent surgery, whereas 5 patients were followed for >1 year and remained stable. Patient's ages ranged from 44 to 76 years. Most benign mucocoeles were diagnosed stereotactically while targeting calcifications (93.3%); rarely, the lesion was a sonographically detected mass. Most excisions had no residual mucocoele (37/45 = 82%). In seven cases (15.6%), atypical duct hyperplasia was present, three with residual mucocoele. In one case, the residual mucocoele showed a continuum from florid to atypical duct hyperplasia at the core biopsy site. The other six cases showed atypical duct hyperplasia adjacent to but not directly at the core biopsy site. The sizes of the benign mucocoeles ranged from incipient to 0.6 cm, all containing calcifications except one, which was incidental. Radiological–pathological correlation was concordant in all cases except one with suspicious calcification, which was ductal carcinoma *in situ* on excision. In this series, the largest of its kind, the upstage rate of benign mucocoeles diagnosed on core biopsy was 17.8%. With the exception of the ductal carcinoma *in situ* case, no radiological or morphological features were predictive of atypia. Thus, because of associated atypical duct hyperplasia, sampling reasons, and intralesional heterogeneity, we continue to recommend excision of benign mucocoele-like lesions diagnosed on core biopsy. *Modern Pathology* (2011) 24, 683–687; doi:10.1038/modpathol.2010.235; published online 14 January 2011

Keywords: benign mucocoele-like lesion; core needle biopsy; excision

Historically, mucocoele-like lesion of the breast was first described in 1986 by Rosen.¹ He established the definition of mucocoele-like lesions as ‘mucin containing cysts lined by flat or low cubical epithelium with or without extravasated mucin’. Subsequent series found that mucocoele-like lesions may be accompanied by a spectrum of pathological findings ranging from benign to atypical to malignant.^{2,3} In fact, in their series on benign and malignant mucocoele-like lesions, Hamele-Bena *et al*² found half of the cases associated with malignancy either in the form of intraductal carcinoma or invasive mucinous carcinoma. Thus, they recommended excisional biopsy for all mucocoele-like lesions.

These lesions were also felt to be precursors to mucinous carcinomas, given that mucocoele-like lesion associated with atypia occurred a decade earlier than mucinous carcinoma and usually in the same region, when it preceded it.

It was also recognized that mucocoele-like lesions were usually associated with calcifications and thus could be detected by mammography. With improved mammography, digital mammography, and the advent of image-directed biopsy specimens, most mucocoele-like lesions are detected because of mammographic microcalcifications rather than a mass. A diagnosis of mucocoele-like lesions on core biopsies is followed by a recommendation for excision because of the spectrum of lesions associated with mucocoele-like lesions and sampling error. Although this practice may seem straightforward in cases with accompanying atypia or malignancy, the necessity of excising purely benign lesions diagnosed on core needle biopsy has been recently questioned.

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Received 25 August 2010; revised 2 November 2010; accepted 23 November 2010; published online 14 January 2011

The few series that have addressed this issue have had mixed results with upstage rates ranging from 0 to 43%.^{4–9} Four of the six series^{4,6,8,9} showed atypia on excision, whereas two others showed no change between the core needle biopsy and excision findings of benign mucocoele-like lesion. Based on their findings, the latter group has questioned the necessity of excising benign mucocoele-like lesion diagnosed on core needle biopsy. With the exception of two recent series,^{8,9} none showed malignancy on excision, further justifying this practice. The goal of this study was to evaluate our experience and follow-up of benign mucocoele-like lesions diagnosed on core needle biopsy.

Materials and methods

Using the pathology computer database of all core needle biopsy performed at our institution from 1 January 2000 to 1 June 2008, we identified 61/23 969 cases (0.25%) of benign mucocoele-like lesions, all biopsied by radiologists. All specimens were received fixed and processed routinely. Of the 61 patients, 45 underwent surgical excision, whereas 5 refused surgery and have remained stable for over 1 year. Also, 11 patients were lost to follow-up. All core biopsies were reviewed to confirm the diagnosis of benign mucocoele-like lesion defined by the presence of mucin-containing dilated ducts that ruptured, with resultant extravasation of mucin into surrounding stroma (Figure 1). All excision specimens were reviewed to confirm the final diagnosis and document biopsy site changes. Clinical, radiological, and pathological correlation was performed.

Results

The age of the patients ranged from 44 to 76 years (mean = 54.6 years). The method used to diagnose

benign mucocoele-like lesion included stereotactic core needle biopsy using 11–14 gauge needle done for calcifications in 57 patients and ultrasound guided biopsy (USG) for a mass using 14–18 gauge needle in 4 patients. Systematic review of the imaging studies showed that the description of the calcifications was as follows: clustered = 37, new = 10, indeterminate = 3, coarse = 3, linear = 1, granular = 1, pleomorphic = 1, and suspicious = 1. On core biopsy, the benign mucocoele-like lesion ranged in size from 0.1 to 0.6 cm.

Biopsy site changes were identified in all patients who underwent excision (45; 42-stereotactic, 3-ultrasound guided). A total of 37 patients had benign findings (82%) such as fibrocystic changes with residual benign mucocoele-like lesion in only 4 of the patients (Figure 2). In all, seven patients (16%) had associated atypical duct hyperplasia, 3 with residual mucocoele-like lesions (Figure 3).

Figure 2 Residual benign mucocoele-like lesion present at previous biopsy site changes.

Figure 1 Benign mucocoele-like lesion associated with calcifications diagnosed on core biopsy.

Figure 3 Excision specimen showing residual mucocoele-like lesion associated with atypical duct hyperplasia and calcifications.

Only 1 patient (2%) was noted to have malignancy in the form of intraductal carcinoma associated with mucocoele-like lesions. Thus, residual mucocoele-like lesions were present in only 8 out of 45 cases (18%) and ranged in size from 0.2 to 0.5 cm.

We analyzed the clinical and morphological features of the cases with atypical duct hyperplasia and intraductal carcinoma and found that all of them were diagnosed stereotactically. Beginning with the atypical duct hyperplasia cases, with the exception of one case, the calcifications in all these cases were found to be present in the benign mucocoele-like lesion on core biopsy (Figure 1). In the one exception case, the calcifications were present in fibrocystic changes and the benign mucocoele-like lesion was incidental, measuring 0.1 cm (Figure 4). On excision, there was no residual mucocoele-like lesion, but residual calcifications in atypical duct hyperplasia were identified. With the exception of two cases, the benign mucocoele-like lesion ranged in size from 0.2 to 0.6 cm. The two cases included: the incidental one already mentioned above and a second case that was incipient (Figure 5), that is, a mucin-filled cyst measuring 0.1 cm that had not yet ruptured. In the latter case, no residual mucocoele-like lesions or calcifications were identified on excision, but there was atypical duct hyperplasia present adjacent to the biopsy site.

Residual calcifications were identified in five of the atypical duct hyperplasia cases. In three of these cases, no residual mucocoele-like lesions were present, and the calcifications were present in atypical duct hyperplasia (two cases) and fibrocystic changes. In the remaining two cases with residual mucocoele-like lesion, calcifications were identified in mucocoele-like lesions in one case and both

atypical duct hyperplasia and mucocoele-like lesions in the other case. We next studied the relationship of the biopsy site to the pathology and found only one case of atypical duct hyperplasia at the biopsy site, continuous with an area of mucocoele-like lesions with florid duct hyperplasia. In the remaining six cases, the atypical duct hyperplasia was adjacent to, but not at the biopsy site.

The indication for biopsy in the intraductal carcinoma case was suspicious and widespread calcifications. On core biopsy, the benign mucocoele-like lesion measured 0.3 cm and was associated with calcifications (Figure 6), but did not entirely correlate with the finding of suspicious calcifications. There was also adjacent atypical lobular hyperplasia (Figure 6). The excision specimen showed residual mucocoele-like lesions with atypical duct hyperplasia and lobular carcinoma *in situ* admixed with focal low-grade intraductal

Figure 5 Incipient mucocoele-like lesion.

Figure 4 Incidental benign mucocoele-like lesion characterized by minute size (0.1 cm) found on stereotactic core biopsy done for calcifications as seen exclusively in the fibrocystic changes (see arrow).

Figure 6 Core biopsy showing benign mucocoele-like lesion with adjacent atypical lobular hyperplasia, both associated with calcifications.

Figure 7 Excision specimen of Figure 6 showing residual mucocoele-like lesion with adjacent *in situ* carcinoma (a). High power shows mixed ductal and lobular features (b).

carcinoma associated with mucin and calcifications (Figure 7).

Discussion

The early series describing mucocoele-like lesions were primarily in specimens that consisted of excisional biopsies, lumpectomies, and mastectomies. These studies provided evidence that a morphological spectrum existed from benign to atypical to malignant, and thus complete excision of these lesions was recommended.^{1,2} With the advent of core needle biopsies, the practice of excising mucocoele-like lesions was similarly continued primarily because of issues related to sampling a heterogeneous lesion. Although the diagnosis of mucocoele-like lesions proved challenging on limited fragmented core biopsy material, it was nevertheless feasible as proven by Renshaw,⁴ although in a small series consisting of only 22 cases. In his series, although there was no misdiagnosis of any benign cases to malignancy or *vice versa*, one of three (33%) excised benign mucocoele-like lesions proved to have atypical duct hyperplasia on excision. Similarly, Wang *et al*⁶ showed in their series that the majority of mucinous lesion can be accurately diagnosed by core biopsy. Given that all their benign mucocoele-like lesions remained benign on excision, they questioned the necessity of surgical excision. On the other hand, Carder *et al*⁵ showed an upstage of benign mucocoele-like lesion to atypical duct hyperplasia in three out of seven cases (43%) from core biopsy to excision. Based on their results, they advocated excision on mucocoele-like lesions diagnosed on core biopsies, even benign mucocoele-like lesion because of the associated risk of atypical duct hyperplasia on excision. In the excisions of benign mucocoele-like lesion diagnosed on core in Nguyen *et al*,⁷ there was no upstaging to atypia or malignancy. Thus, it was felt that follow-

up alone was appropriate for benign mucocoele-like lesion; however, this series was limited by only six cases that were excised. On the other hand, in the study of Phillips *et al*,⁸ of seven benign mucocoele-like lesions that were excised, one was upstaged to atypical duct hyperplasia and another to intraductal carcinoma. Thus, this group recommended excision of all benign mucocoele-like lesions, particularly if they presented as a mass. Similarly, in the most recent study of mucocoele-like lesions by Begum *et al*,⁹ two out of 39 cases of benign mucocoele-like lesions were upstaged; one was upstaged to colloid carcinoma and had been composed of acellular mucin pools on core biopsy, whereas the other case's excision showed atypical duct hyperplasia. Based on this study, the authors felt that if the entire radiological lesion was completely removed by a large core biopsy, particularly calcifications, surgery could be avoided. However, they cautioned that radiological-pathological correlation and further validation of these findings in larger studies is necessary. Thus, as can be seen by the results of these series, there are varying opinions and no true consensus regarding the management of benign mucocoele-like lesion diagnosed on core biopsy.

To attempt to resolve this issue, we looked at our study composed of 61 benign mucocoele-like lesions, the largest of its kind. We found that benign mucocoele-like lesion tends to occur in older women, usually detected because of clustered calcifications rather than a mass. Our upstage rate was 18%, compared with 0–43% in the literature as described above. In our series, it was primarily because of atypical duct hyperplasia (88%), with only one case of intraductal carcinoma, all diagnosed stereotactically. Despite the low upstage to malignancy on excision, a mere 2%, we would still recommend excision of mucocoele-like lesion because of the 16% associated risk of atypical duct hyperplasia. This is because it is hypothetically recognized that atypical duct hyperplasia and intraductal carcinoma are part

of an evolving spectrum. Excising atypical duct hyperplasia is akin to excising the precursor lesion to malignancy, thus preventing the theoretical progression to malignancy. In fact, a diagnosis of atypical duct hyperplasia is an important factor in the Breast Cancer Risk Assessment Tool (the Gail model). Additionally, the diagnosis of atypical duct hyperplasia confers a four- to five-fold increased risk over that of the general population for the development of malignancy in either breast. Consequently, patients with a diagnosis of atypical duct hyperplasia are offered more frequent screening and some, depending on their risk factor index, are also offered antihormonal treatment such as tamoxifen. Thus, the upgrade from mucocoele-like lesion on core biopsy to atypical duct hyperplasia may not be as significant as malignancy but, nevertheless, has relevant clinical implications.

Most mucocoele-like lesions were removed by the core biopsy with no appreciated residual component on excision (82%). Unlike other studies, we did not find the biopsy needle gauge size, cellularity of the mucocoele-like lesions, residual mucocoele-like lesions or calcifications, size of the mucocoele-like lesions, or whether it presented as a mass or calcifications as being predictive of residual mucocoele-like lesions, atypia, or malignancy. In fact, with regard to size, in two of our cases upstaged to atypical duct hyperplasia, the mucocoele-like lesions were incidental and incipient, measuring <1 mm.

In the atypical duct hyperplasia cases, the finding of atypical duct hyperplasia close to but not at the biopsy site in most cases suggests an association between mucocoele-like lesions and atypia. Although some have advocated the use of large gauge needles as an alternative to excision of benign mucocoele-like lesion provided radiological–pathological correlation is performed, our series shows the contrary. Both incidental and incipient mucocoele-like lesions that were entirely removed by core needle biopsy were found to have associated atypical duct hyperplasia on excision. This then justifies the practice of excising the area immediately contiguous to the benign mucocoele-like lesion because of associated atypia, despite no residual mucocoele-like lesions or even calcifications.

The single intraductal carcinoma case stresses the necessity of radiological–pathological correlation in all these cases. Given the discordance between the presence of mammographically suspicious calcifications and the finding of benign mucocoele-like lesion with calcifications, excision was done. Residual suspicious calcifications were present. Excision of these calcifications showed a spectrum of findings from residual mucocoele-like lesions with atypical duct hyperplasia, lobular carcinoma *in situ*, and

intraductal carcinoma. Thus, discordance between radiology and pathology must always be resolved by excision.

Conclusions

The excision of benign mucocoele-like lesion has been questioned by some. In our series, although most benign mucocoele-like lesions were removed by the core biopsy, a residual component was present in ~18% of cases and an upstage occurred in 18%. In terms of malignancy, we only had one case of intraductal carcinoma, which was because of radiological–pathological discordance. We agree with previous studies that it is prudent to continue to excise all benign mucocoele-like lesions diagnosed on core needle biopsy because of sampling phenomena, intralesional heterogeneity, and associated atypia or malignancy.

Disclosure/conflict of interest

The authors declare no conflict of interest.

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