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CASE STUDY

Intracystic mural nodules of the breast: benign versus malignant; a multidisciplinary imaging and management approach

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Abstract

This case report illustrates the presence of intracystic mural nodules within the breast, a benign proliferative disorder associated with the fibrocystic spectrum: papillary apocrine metaplasia. The aim of this paper is to provide a comprehensive understanding of the physical and histological attributes of benign intracystic mural nodules, and the ability to distinguish these from a malignant papilloma and carcinoma. Also, the technical and patient considerations, as well as the appropriate imaging and interventional methods required to ensure correct patient management pathway are discussed, extending into an analysis of the psychological effects felt by patients undergoing assessment.

Case History

A 71-year-old post-menopausal woman presented for routine screening mammography and was subsequently recalled for further assessment. Recall was required due to an asymmetric density in the upper outer quadrant of the right breast, which had significantly increased in size over a 4-year period. The patient had no significant history of familial breast cancer or previous breast surgery. The patient reported the use of hormone replacement therapy, with cessation in 2009, 5 years prior. The asymmetric density had been assessed in 2012, 2 years previously and had undergone a fine needle aspiration biopsy (FNA) with cytology reporting benign apocrine and papillary apocrine metaplasia (PAM).

Bilateral mammography demonstrated predominantly fatty replaced breast tissue, consistent with a post-menopausal breast (see Fig. 1), equivalent to pattern I of Tabár's classification. The mammogram depicts a uniform proportion of all components of breast tissue with a minor predominance of fibrous tissue.[1]

On returning for assessment, a clinical examination was performed and palpation of a 70 mm non-tender lump was identified, corresponding to the mammographic lesion. No dedicated mammographic images were taken at the time of assessment, as it was deemed that no additional mammographic detail would be gained from performing spot magnification views. Previous assessment mammographic images were available for correlation with recent screening images.

After correlation of mammographic and clinical examination findings, a targeted ultrasound examination of the right upper outer quadrant identified a large oval shaped, thin walled cyst; defined by its anechoic appearance, bright circumference, posterior enhancement and low-level internal echoes (see Fig. 2). Provisional diagnosis was reported as a complex cyst, with the manifestation of multiple eccentric wall thickenings,

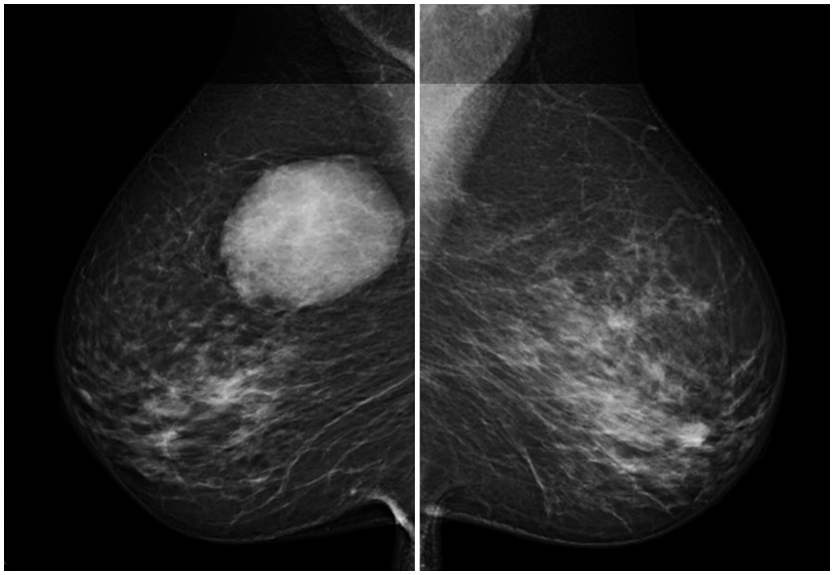

Figure 1. Mediolateral oblique (MLO) projection showing a well-defined oval mass. Image courtesy of BreastScreen ACT.

appearing incurvated and parallel to the cyst wall.[2] The nodules were described as isoechoic, homogeneous and microlobulated. Utilising colour Doppler to assess associated vascularity, the appearance of a fibrovascular stalk could not be excluded (see Fig. 3).

Provisional imaging diagnosis: intracystic papilloma (multiple)

In comparison to the ultrasound performed in 2012, the cystic lesion had increased in size by approximately 21 mm and additional mural nodules were noted (see Fig. 4a and b).

After multidisciplinary discussions between radiologist and pathologist, the patient was referred for further interventional procedures, including a FNA biopsy and ultrasound-guided core biopsy.

Under ultrasound guidance, a FNA biopsy was performed and 40mm of fluid within the cystic lesion was removed for histology review. A small amount of fluid was left within the cystic walls, to provide an anechoic sonographic landmark surrounding the mural nodule for accurate placement of the core biopsy apparatus. After introduction of local anaesthetic, a core needle biopsy was performed, utilising a 14-gauge needle with a spring-loaded automatic biopsy device and a coaxial introducer. Five core tissue samples were obtained and placed in formaldehyde solution for histopathological analysis.

Marker clip insertion within the biopsy region was performed for both mammographic correlation

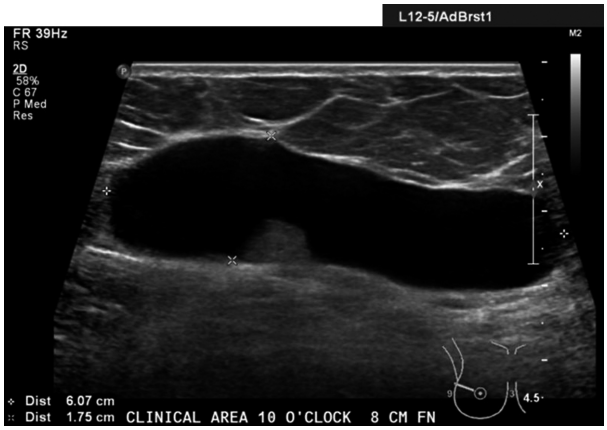

Figure 2. Ultrasound image showing a complex cyst with associated mural nodule. Image courtesy of BreastScreen ACT.

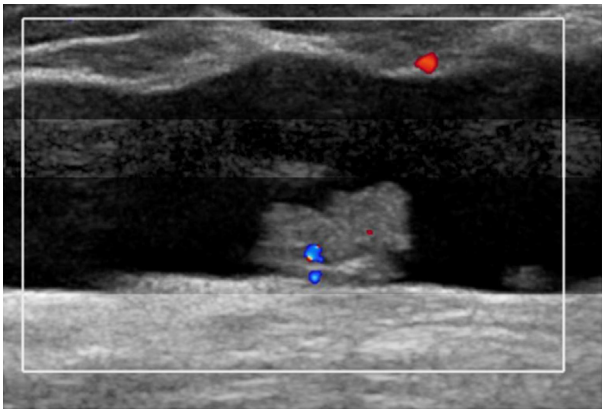

Figure 3. Ultrasound image demonstrating mural nodule with vascularity. Image courtesy of BreastScreen ACT.

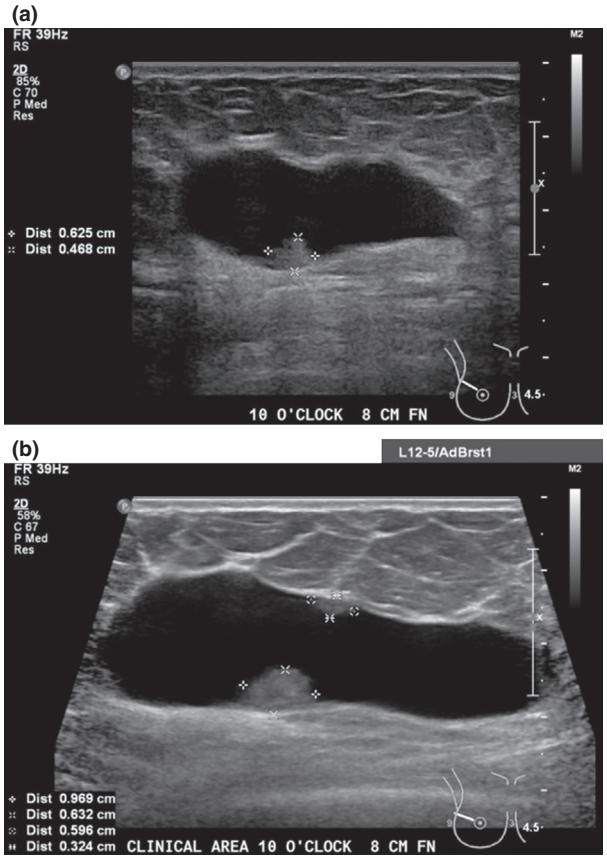

Figure 4. Ultrasound images taken in 2012 (a) and 2014 (b), demonstrating the increased size and additional nodules. Image courtesy of BreastScreen ACT.

and as a reference point for any future surgical intervention.

Histological analysis of the cystic fluid reported thick inspissated proteinaceous material, and an abundance of apocrine cells occurring singly. Definitive diagnosis: benign cyst fluid.

Microscopic histology of core samples described fragments of benign breast tissue showing cystic changes with areas of apocrine metaplasia with focal papillary hyperplasia. Definitive diagnosis: benign cyst lining.

A benign diagnosis was established, and in view of draining the large cystic portion of the lesion, further surgical intervention was avoided. The patient was returned to routine two yearly screening and advised that if there was any recurrence of the region of interest, further advice should be sought from her general practitioner or that she should undergo surgical review.

Discussion

Complex cysts are defined as cysts with associated thickened walls, thick internal septa, intracystic masses or discrete solid masses. Additionally, the presence of intracystic mural nodules within the breast is associated with a benign proliferative disorder on the fibrocystic spectrum: PAM.[2]

Benign versus malignant: imaging and management

The difference between mural nodules caused by intracystic papillomas or carcinomas and those caused by fibrocystic changes (FCC) with PAM is influenced by its sequence of evolution. It must be determined which pathology preceded the other; was there a pre-existing cyst, or did the development of the papilloma within a draining duct force the existence of a cyst. Determining the order of proliferation is important in indicating the imaging and management pathway for a patient. To differentiate, it is suggested that scanning complex cysts in a radial manner can define the relationship of the mural nodules with nearby ducts.[2]

The sonographic appearance of intracystic papillomas or carcinomas is depicted by two main characteristics. Firstly, evaluation of the wall of the cystic lesion to which the mural nodule attaches will appear irregular, with interruption to the echogenic wall at the point of attachment. Secondly, the presence of duct extension; whereby the papilloma or carcinoma extends into the draining duct causing distension. This changes the shape of the cyst from spherical or oval, to a keyhole shape.[2]

For mural nodules developing from apocrine metaplasia within a pre-existing cyst, the site of attachment to the cystic wall remains preserved, with the thin capsule fully visible. Additionally, mural nodules do not extend into the ducts, causing no distortion or obstruction within the duct, allowing the cyst shape to remain unchanged.[2] Characteristics such as internal echotexture and vascularity can aid differentiation between benign and malignant intracystic mural nodules.

Disparities between the internal echotexture of intracystic papillomas or carcinomas and that of mural nodules are due to histological differences. Intracystic papilloma lesions are considered to be echogenic and course due to their multifrondular presentation. The fronds appearance contains layers of epithelium, myoepithelium, basement membranes and a loose fibrous core with fluid layers. In contrast, PAM predominantly grows across the cystic lumen in gracile, bridges which are one or two cells wide. The fluid between papillae appear to be much wider, thus the echotexture appears less echogenic and less heterogeneous.[2]

In terms of vascularity, papillomas and carcinomas are among the most vascular lesions found within the breast; even the smallest of lesions (a few millimetres) will have a

fibrovascular stalk appearance. For PAM, its appearance seldom displays colour when using Doppler.[2]

If one or more of these factors are evident on ultrasound, biopsy of the lesion is recommended.

Technical considerations

To accurately evaluate the full extent of the lesion, technical considerations, such as image quality factors, patient positioning and scanning techniques are vital. With the use of SonoCT and WideScan, the lesion can be completely captured in one image. This function also allows a smoother, more uniform image, eliminating artifactual echoes causing reverberation and low level echoes within the cystic lesion.

Patient positioning is also important to allow access to the upper outer quadrant of the breast. The patient is covered with a gown and positioned supine, uncovering only the right breast, with a 45° sponge underneath the right shoulder, and the right arm raised above the head. This allows the breast to evenly spread across the chest wall, maintaining adequate depth aiding technical considerations.[2]

The breast is scanned in a radial/anti-radial rotation to adequately illustrate the entire lesion, and to aid the detection of any associated intraductal lesions. Scanning in the radial plane best tracks along the ducts of the breast and can assist in demonstrating intraductal lesions.[2]

A suitable degree of compression is required to scan the breast, for cystic lesions to determine their compressibility reaction. A lesion that has some extent of distortion under compression indicates a benign cystic area.[3]

Biopsy techniques

When sonographic evaluation demonstrates a complex cystic lesion with associated mural nodules, ultrasound-guided 14-gauge core biopsy with marker deployment is recommended. Where a large cystic lesion is present, it is suggested that a FNA biopsy be performed to remove a portion of the cystic fluid for histology. This alone, however, is not sufficient to gain a diagnosis due to the significant false-negative rate associated with cytological studies.[2] Providing the nodule is still visible within the cyst, a core biopsy should also be performed.

Due to removing a portion of the cystic fluid, limitations can be encountered in differentiating the mural nodule from adjacent tissues; technical considerations to aid better visualisation must therefore be recognised. One such technique takes advantage of the needle used of the FNA biopsy, which is left in place, in order to create a vacuum effect on the cyst to maximise visualisation of the nodule whilst positioning the co-axial introducer. The 14-gauge needle is positioned, within the introducer aligned with the region of interest. Visualisation of the nodule will become significantly difficult after the first tissue sample is taken, due to the deflation of the cyst (pierced by the needle), and the bright artefact effect along the track of the needle after excision. Extra care and consideration of the lesion, compared with surrounding tissue structures, must be taken to ensure tissue samples are of diagnostic quality.

Due to the uncertainty of a benign versus malignant diagnosis, marker clip insertion is necessary as a reference point for screening mammography and future surgical investigations.

Patient considerations

An understanding of not only the physical attributes of undergoing an assessment and biopsy procedure but a patient's psychological state before and after a procedure also needs to be considered. Kamath et al. conducted a clinical study investigating symptom distress, quality of life as well as affective states before and after breast biopsy procedures. The study outlines the heightened distress experienced by women whom are recalled for assessment and subsequent biopsy, after the screening mammography. It is determined that the psychological state is affected more so pre- to post-biopsy when compared with screening due to its close proximity to a potential breast cancer diagnosis.[4]

In reference to the patient, her psychological state after being recalled for assessment on multiple occasions must be considered. It may be expected that a patient would experience heightened distress symptoms due to the region of interest having grown significantly in size, particularly after receiving a benign result when assessed in 2012. It must be considered that the initial choice of biopsy in 2012 could have hindered a definitive diagnosis for the patient, has the potential to cause undue distress, given the need for re-assessment. In 2014, the biopsy procedures chosen, after good communication between multidisciplinary teams, has not only provided a definitive diagnosis but also avoided any further surgical intervention which may have been necessary if an inconclusive result was achieved due to unreliable technique.

Kamath et al. have described that it is possible that even a negative biopsy result will not completely resolve any psychological distress symptoms or heightened anxiety resultant from a recall to assessment.[4] Therefore, it is important to care for a patient's psychological state before and after a biopsy, as well as

the processes of an abnormal mammogram requiring further assessment.

Discussion prior to and after the assessment visit indicated that patient was evidently experiencing signs of heightened distress due to the recall. Before the assessment, the patient exhibited anxiety and apprehension due to previous experiences but maintained a positive rapport with all members of the multidisciplinary team. Post-biopsy discussions included the potential diagnosis, as well as pathways of treatment. The patient remained positive, evidently relieved that the appropriate techniques for diagnosis were conducted. At the time of results, the patient was alleviated of some anxiety when reassured of the benign nature of the lesion, and was encouraged to remain vigilant with routine breast checks, including routine screening. The patient noted that she was well informed throughout the whole process which she attributed to a well-functioning multidisciplinary team, taking pride in optimising patient care.

Conclusion

The appearances of intracystic mural nodules of the breast vary clinically, radiologically and pathologically. It is imperative to have a comprehensive understanding of benign and malignant features to ensure consideration of appropriate interventional investigations are undertaken, in order to achieve a definitive diagnosis and facilitate sound future management. Finally, by including the patient as a part of the multidisciplinary team, the negative psychological factors, such as heightened distress symptoms, can be managed and minimised, whilst optimising patient care and management.

Ethics Statement

I hereby maintain that all research and information contained within this study has been carried out in accordance with the ethical standards outlined by the Declaration of Helsinki (2000) and the Declaration of Istanbul (2008). Additionally, all individuals involved in this study have provided full informed consent, and any personal information has been omitted ensuring confidentiality and anonymity.

Conflict of Interest

The author declares no conflict of interest.

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