Screen Detected Papillary Lesions of the Breast-A Retrospective Review from a Single Institution

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Abstract

To identify the diagnostic accuracy of imaging, fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB) in identifying papillary lesions in the setting of a population based mammographic screening program. A retrospective analysis of mammographic screening detected lesions diagnosed as papillary lesions on surgical excision at Breast Screen Sydney West between 1993 - 2010 was performed. Imaging, FNAB and CNB diagnoses were correlated with surgical excision pathology to determine the performance indicators. Two hundred and seventeen papillary lesions were identified with imaging and corresponding excision pathology with a final total of 153 FNAB and 105 CNB performed on these.

Imaging - Of the 143 designated benign/ equivocal 27 (19%) were upgraded to malignant. Thirty two (43.2%) of 74 image-designated suspicious or malignant were benign on excision.

FNAB - Fourteen (12.4%) of the 113 designated benign/atypical were upgraded to malignant. Eleven (27.5%) of 40 malignant FNAB were downgraded to benign on excision.

CNB - Three of 43 benign lesions were malignant on excision (upgrade rate 7%). One of 24 (4%) suspicious/ malignant was downgraded to benign.

Complete sensitivity was high for FNAB and CNB- 95.2% and 91.7%, respectively. Absolute sensitivity was 42.8% for FNAB and 50% for CNB. Specificity for imaging, FNAB and CNB was 37.25%, 89.6% and 100% with accuracy rates of 60.4%, 85.3% and 95.0%, respectively.

Complete sensitivity, specificity and accuracy, indicating a benign CNB diagnosis is highly predictive of a benign papillary lesion on surgical excision.

ABBREVIATIONS

FNAB: Fine Needle Aspiration Biopsy; CNB: Core Needle Biopsy

INTRODUCTION

In Australia, population based screening mammography has been in practice since 1991. One of the most important objectives of this program is the reduction in mortality from breast cancer through early detection in the target population. This program requires double blind reading of all mammograms, and a third reader where there is discordance. Abnormalities confirmed by two readers will require recall for further workup and assessment. Achieving a high cancer detection rate under such a program is likely to be associated with a number of investigations including open surgical biopsy, which will ultimately in some cases prove to be unnecessary.

In order to minimize the latter BreastScreen Australia has a number of national accreditation standards in place, aiming to achieve a balance between cancer detection rates and the number of investigations that are performed for benign lesions. For example, these standards stipulate that the open diagnostic biopsy rate in which the final pathological diagnosis is benign, should be less than 4% for women undergoing their first screen and less than 3.2% for women undergoing their second or subsequent screens [1]. In practice this requires close collaboration between radiologists, pathologists and surgeons.

However, notwithstanding a highly regulated and high quality diagnostic breast screening service, there are some pathological lesions that pose significant diagnostic and management challenges. These are often related to the inherent biology of the lesions in question [2].

Papillary lesions of the breast are characterized by an arborescent fibrovascular core covered by a layer of epithelial cells with or without an underlying myoepithelial cell layer. These lesions account for approximately 5% of all biopsied breast pathology and encompass a diverse spectrum ranging from benign, to atypical and malignant (in situ or invasive) lesions [3-5]. Papillary lesions have overlapping and variable radiological features and will therefore frequently require percutaneous biopsy and histopathological correlation. However, definitive diagnosis even on core needle biopsy (CNB) may prove difficult, with several series in literature reporting significant upgrade rates of benign lesions to atypical and malignant categories [6]. In view of this difficulty on CNB the general approach adopted in many institutions is to excise all papillary lesions to establish a definitive diagnosis. This however, results in over-treatment of benign papillary lesions.

The diagnostic and management characteristics of these lesions, warrants review with the overall aim of addressing the existing policy of surgical excision of all histologically confirmed papillary lesions. To do this, radiological, fine needle aspiration biopsy (FNAB) and CNB results in a consecutive series of screening-detected breast lesions were reviewed and compared with the pathological diagnosis on surgical excision specimens.

MATERIALS AND METHODS

Patient population

The records of BreastScreen NSW Sydney West database were searched using the key words “papillary lesion”, “papilloma”, “papillary” and “papillary carcinoma” in the search fields of final diagnoses recorded on surgical excision specimens over the period August 1993 to August 2010, diagnosed through the Breast screening and assessment clinics. Of these, only cases that had previous percutaneous FNAB and/or CNB obtained through the screening service were included in this study. Cases without a definite papillary lesion and those without a pre-operative percutaneous biopsy result were excluded from the study. The final retrospective cohort comprised 217 papillary lesions diagnosed in 209 patients (8 patients had more than 1 lesion) on surgical excision histopathology with matched percutaneous FNAB and/or CNB results. The study was conducted with approval of the Western Sydney Local Heath District Human Research Ethics Committee (Westmead) and BreastScreen NSW. The use of health information in this study was compliant with local and state protocols for accessing patient data from the screening service.

Image Assessment and Biopsy Procedure

All percutaneous biopsies (FNAB and CNB) were performed in the setting of a BreastScreen NSW mammographic screening program. These biopsies were performed at a Screening and Assessment Clinic for further investigation of an abnormality detected on routine screening mammography, confirmed by two independent radiologists or an additional 3rd reader in cases with discordant results. The final imaging category was recorded as benign, equivocal, suspicious or malignant [7] similar to the Breast Imaging Reporting and Data Systems (BIRADS) criteria [8]. Core needle biopsies were generally performed under ultrasound guidance. For CNB, 14-gauge or 16-gauge needles were used, with a variable number of passes made through the lesion. For FNAB, needles ranged from 19-gauge to 25-gauge with 2 - 4 passes per lesion.

Histopathological Classification of Biopsied Specimens

The pathology of the FNAB, CNB and surgical excision specimens were reported by specialized breast pathologists. For FNAB a diagnostic code ranging from 1-5 followed by a descriptive diagnosis was used [9]. Briefly, the FNAB codes are: 1 – Inadequate/insufficient, 2 – Benign, 3 – Atypical/indeterminate, 4 – Suspicious of malignancy and 5 – Malignant. By protocol, code 3 (atypical/indeterminate) is frequently applied to lesions which on FNAB have a papillary appearance. The majority of CNB pathological diagnoses were assigned to one of three categories based on the WHO guidelines: [10] benign, (this included all lesions with a final diagnosis of papilloma with or without epithelial hyperplasia), atypical (included any papillary lesions with atypia falling short of ductal carcinoma in situ), and malignant papillary lesions (which included ductal carcinoma in situ arising in a papilloma, papillary ducal carcinoma in situ, intracystic or encysted papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma). Rarely a fourth category of suspicious for malignancy was used when a definitive diagnosis of malignancy was not possible. The surgical excision histopathological diagnoses were reviewed and assigned to one of the three main diagnostic categories detailed above: benign, atypical and malignant.

Upgrading of a lesion was defined as one that had been called benign (code 2) on imaging, or benign/ atypical (codes 2 & 3) on FNAB or benign on CNB but subsequently classified as malignant on surgical excision. Calculation of upgrade rate has been previously described [6].

RESULTS AND DISCUSSION

Results

A total of 217 papillary lesions were identified in 209 patients with a corresponding surgical excision pathological diagnosis (8 patients had more than 1 lesion). Of these, 108 had FNAB also, 58 had CNB and 51 had both FNAB and CNB. A final total of 153 FNAB (6 with inadequate material were not included) and 105 CNB (4 with inadequate material not included) were obtained for analysis. The age range was 42-84 years, with a median age of 60 years.

Comparison of imaging findings and surgical excision pathology

The comparison of the imaging category and surgical excision pathology diagnosis is shown in Table 1 and Figure 1. Of the 217 cases, 120 (55%) were categorized as equivocal on final imaging (which combines both ultrasound and mammography in the
designations, 61 (28%) as suspicious, 23 (11%) as benign and 13 (6%) as malignant.

Four of 23 (17%) cases designated as benign on imaging were upgraded to malignant on excision histopathology. Of the 13 lesions designated by imaging as malignant, 10 (77%) were confirmed on excision pathology, the remaining 3 lesions (23%) were downgraded to benign papillomas. The majority of the 120 lesions designated as equivocal by imaging (79%) were benign papillomas on excision, and 19% were malignant. There were 61 lesions categorized as suspicious on imaging, with approximately half of these (29/61) being benign and half (26/61) malignant on excision histopathology.

The commonest imaging presentation across all categories of papillary lesions was as a mass (with or without calcifications), and this was seen with similar frequencies in benign, atypical and malignant lesions. Benign lesions could also present as a
non-specific density (24%), more frequently than malignant and atypical lesions. The presence of calcifications or a stellate density was more frequently associated with in situ or invasive lesions than benign lesions.

Comparison of FNAB code and surgical excision histopathology

The FNAB diagnosis compared with the surgical excision pathology is shown in Table 2 and Figure 2. In 6 cases the material obtained on FNAB was inadequate for reporting. The majority of papillary lesions diagnosed on FNAB were designated atypical (code 3), (104 of the 153 lesions, 68%). The remainder of the lesions were designated as malignant (23 cases, 15%) or suspicious (17, 11%) or benign (9 cases, 6%).

Of the 104 lesions designated as atypical, the majority (84%) proved to be benign papillomas on surgical excision. The majority (27, 68%) of FNAB designated malignant/ suspicious of malignancy were confirmed on excision histopathology. The diagnosis was a benign papilloma in 11 of these cases (11 of 40, 28%) and atypical papillary lesion in 2 cases (5%).
nine cases designated as benign on FNAB, 1 was upgraded to a malignant papillary lesion on excision histopathology.

**Comparison of CNB diagnosis and final excision histopathology**

The CNB diagnosis compared with the surgical excision pathology is shown in Table 3 and Figure 3. A total of 109 lesions underwent CNB of which 4 cases had insufficient tissue for pathological assessment. A benign diagnosis was given in 43 (41%), atypical in 38 cases (36%), malignant in 18 cases (17%) and the occasionally used category of suspicious in 6 (6%) cases.

The majority of cases diagnosed as benign on CNB were confirmed in the surgical excision pathology (39 of 43 cases, 91%). Of these 43 cases, 3 lesions (7%) were upgraded to malignant and 1 case (2%) was diagnosed as an atypical papillary lesion. All lesions diagnosed as malignant on CNB (18 cases) were confirmed on surgical excision pathology. There were 6 cases designated as suspicious on CNB, 5 of which were confirmed malignant and 1 was downgraded to a benign papilloma on excision. The remaining 38 cases were designated as atypical on CNB, the majority of which (25 cases, 66%) were benign papillomas on excision, however, 26% (10 cases) proved to be malignant papillary lesions on excision.

**Comparison of Imaging, FNAB and CNB**

The performance indicators for imaging, FNAB and CNB are presented in Table 4. The sensitivity for imaging, FNAB and CNB are 90.0%, 65.8% and 85.7%, specificity 37.3%, 89.6% and 100% with accuracy rates of 60.4%, 85.5% and 95.0%, respectively. The absolute and complete sensitivity for FNAB was 42.8% and 95.2%, respectively. For CNB the absolute and complete sensitivity was 50% and 91.7%, respectively.

**DISCUSSION**

Current clinical protocols in BreastScreen Sydney West recommend surgical excision of all papillary lesions diagnosed on FNAB or CNB. In our practice most papillary lesions are designated as code 3 (atypical) on FNAB. Papillary lesions with overt cytological atypia or malignancy are coded as 4 or 5 (suspicious or malignant). The usual protocol for radiological lesions proven to be papillary on FNAB or CNB is to recommend surgical excision. This system ensures that all papillary lesions diagnosed on FNAB (codes 3-5) will be further evaluated for surgical excision.

In our study, similar to that reported by others, there was significant overlap in the imaging presentation of all categories of papillary lesion [2]. From a clinical point of view the distinction between papilloma with atypical ductal hyperplasia (ADH), papillary ductal carcinoma in-situ and papillary carcinoma is important in the screening setting as papilloma with ADH can be monitored with regular repeat screening without detriment to the patient [11]. Overall in this study, most lesions, whether benign or malignant, presented as a mass with or without calcifications. Presentation as just calcifications or a mass with calcification was more common in the atypical and malignant lesions. Those lesions that presented as a non-specific density were more likely to be benign. However, as with other studies, this study indicates that imaging alone cannot reliably distinguish benign, atypical or malignant papillary lesions. Benign surgical excision pathology was noted in 23% of lesions designated as malignant on imaging, and malignant surgical excision pathology was diagnosed in 17% of cases designated as benign on imaging.

The case numbers with an imaging designation of malignant and suspicious have been combined in this study. As a screening test, imaging proves suitable with high sensitivity (90%), but limited specificity (37.3%) and accuracy (60.4%). This is expected in view of the largely non-specific mammographic and sonographic features seen across the whole spectrum of lesions.

A benign FNAB diagnosis (code 2), usually reserved for non-papillary lesions, was rendered in 9 of 153 FNAB biopsied lesions (6%). These lesions may have been undiagnosed as papillary lesions if FNAB was used in isolation. These 9 cases include 1 case that was malignant on surgical excision histopathology. This may be attributable to sampling error in view of the heterogeneity seen in some papillary lesions [4,12,13]. Over 68% of lesions however, (104 out of 153) were designated at least atypical on FNAB. As mentioned earlier, an atypical diagnosis on FNAB is made when a papillary lesion is suspected with no definite evidence of malignancy or benignity. Overall FNAB was found to be highly specific with a high negative predictive value but limited sensitivity (65.8%) and only moderate positive predictive value (71%).

Core needle biopsy proved to be highly sensitive (85.7%) with an absolute sensitivity of 50% and complete sensitivity of 91.7% in the classification of papillary lesions into benign and malignant categories. All 18 malignant papillary lesions on surgical excision pathology were accurately classified by CNB and no false positive diagnoses were made. In 3 cases, where the CNB diagnosis was a benign papillary lesion, the surgical excision pathology was malignant. In those cases designated as suspicious or malignant on CNB (24 cases), the majority (23, 95.8%) were malignant on excision, indicative of the high specificity of the test.

Accurate classification of papillary lesions on FNAB and CNB can be challenging, due to the variable appearances and the difficulties associated with the interpretation of inherently friable and fragmented tissue samples [5,14,15]. In this study, lesions designated benign by imaging, FNAB and CNB, were upgraded to malignant in the surgical excision pathology in 17.4%, 11.1% and 7%, respectively.

Overall CNB showed higher rates of sensitivity, specificity and accuracy compared with FNAB. Fine needle aspiration biopsy has a number of advantages, however, including low cost, minimal invasiveness of the procedure, and the capability for rapid diagnosis. It does however require a skilled operator to obtain adequate material as well as a high degree of expertise in the interpretation [16]. High levels of accuracy were obtained in this study (85.5%). A benign or atypical diagnosis correlated well with a benign diagnosis on surgical excision pathology (negative predictive value of 87%, specificity of 89.6%), but there was fairly poor sensitivity for accurate identification of a malignant lesion with only 27 of 40 malignant papillary lesions classified as suspicious or malignant on FNAB.

Excision is frequently recommended for papillary lesions,
even when a CNB diagnosis of benign papillary lesion is made to mitigate the possibility of sampling error. A variety of classifications of papillary lesions is available in literature with some classifications including arbitrary measurements or proportion of involvement by a neoplastic population to designate lesions into benign, atypical or malignant categories [4, 12, 13]. In view of this, focal areas of atypia or invasion may be missed with a CNB sample, leading to misclassification of the lesion. However, surgical excision to avoid under diagnosis of a malignant lesion, may represent over treatment in the majority of patients diagnosed with a papillary lesion, given that most of these lesions are benign (66% of cases in this study were found to be benign papillomas on surgical excision).

The practice of surgical excision for all preoperatively diagnosed papillary lesions is given variable support in the literature. This is justified by upgrade rates following a benign core biopsy of up to 29% (range 0-29%) [6, 11]. In our study this was only 7% (following CNB), which is in keeping with other studies with over 100 cases in the series. Some studies have advocated imaging follow up rather than surgical excision for papillary lesions diagnosed as benign on CNB [11, 17, 18]. A moderate approach may be for vacuum assisted large gauge core biopsy removal of the lesion in those cases designated as code 2 or 3 on FNAB. This is supported by the negative predictive value of FNAB in this study. In addition larger gauge cores used with vacuum assisted techniques may avoid issues of sampling error and have been shown to improve accuracy in papillary lesions [19].

CONCLUSION

In the setting of a population-based breast cancer screening program, lesions such as papillary lesions are being seen more frequently. Management of these lesions requires an integrated approach with involvement of the radiologist, pathologist and surgeon. Imaging findings have limited ability to distinguish benign, atypical and malignant lesions. CNB has high complete sensitivity, specificity and accuracy, indicating a benign CNB diagnosis is highly predictive of a benign papilloma on excision. A more conservative approach, like a vacuum-assisted removal of the lesion in those cases designated as code 2 or 3 on FNAB may provide an alternative to surgical excision.

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REFERENCES