

Ultrasound in the diagnosis of papillary breast lesions

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Abstract

Papillary lesions are defined as an amalgam of various lesions which represent a diagnostic challenge, for both the radiologist and pathologist. They are diagnosed on the basis of a combination of clinical, imaging, and pathological findings and their features carry differing prognostic implications for the affected patients. The aim of this pictorial essay is to review the clinical and pathological findings in papillary breast lesions, to show the advantages and limits of each imaging method in their diagnosis with emphasis on the importance of ultrasound in the differential diagnosis. Also, the spectrum of ultrasound features (conventional, Doppler ultrasound and elastography) of papillary lesions of the breast will be illustrated.

Keywords: breast, papillary lesion, ultrasound, elastography.

Introduction

Papillary lesions are defined as an amalgam of various lesions which represent a diagnostic challenge, for both the radiologist and pathologist. Because of their wide morphologic spectrum, they are difficult to characterize as malignant or benign. They are diagnosed on the basis of a combination of clinical, imaging and pathological findings and their features carry differing prognostic implications for the affected patients [1,2].

Papillary benign lesions include papillomas. The malignant papillary lesions encountered are micropapillary ductal carcinoma in situ (DCIS), noninvasive papillary carcinoma, invasive papillary carcinoma, and invasive micropapillary carcinoma [1,2].

The main histopathologic feature of papillary lesions is represented by a finger-like projection composed by a central fibrovascular stalk that supports an arborescent

epithelial proliferation, without an intervening myoepithelial (ME) cell layer. The absence of ME cells is characteristic for carcinomas, but its presence does not exclude malignancy [3,4].

Cytologic findings are poorly correlated with histological findings, while core needle biopsy (CNB) plays an important role in the diagnosis of papillary lesions, despite its limits [2,3]. A correlation between CNB results and mammographic and sonographic findings is crucial in the diagnosis.

In this pictorial essay we will review the clinical, pathological and imaging findings in papillary breast lesions, and we shall illustrate the spectrum of ultrasound features (conventional, Doppler ultrasound and elastography) of these lesions.

Mammography

Mammography has a low sensitivity and specificity in the diagnosis of papillary lesions since they may be occult (especially benign papillomas) or may present with discrete or nonspecific findings: area of increased density (micropapillary DCIS), dilated duct (intraductal papilloma or malignancy), or a solitary mass with benign or malignant features [1,5]. Its value consists of depicting the malignant calcifications that can accompany a papillary malignant lesion [5] (fig 1).

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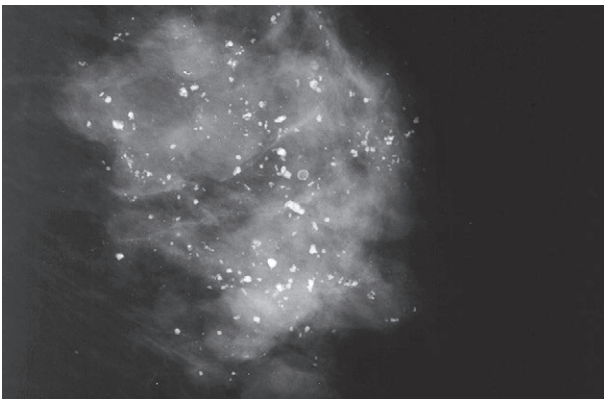


Fig 1. Mammography of a patient with invasive papillary carcinoma, showing multiple calcifications with heterogeneous morphology.

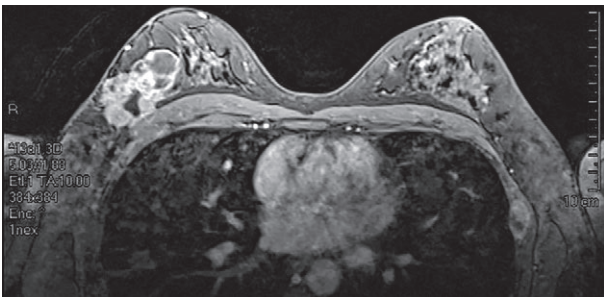


Fig 2. Breast MRI (T1 sequence after intravenous administration of gadolinium) in a patient with extensive invasive papillary breast carcinoma. In the outer quadrants there is an irregular mass, with rim enhancement, apparently developing from a cyst with internal septae, the cyst also presenting rim enhancement.

Magnetic resonance imaging

Magnetic resonance imaging is useful when a papillary lesion is suspected on the basis of other imaging techniques because of its ability to demonstrate ductal relation of the lesions and also for its increased accuracy in diagnosing the extension of malignant lesions [1,5] (fig 2). Even if appears that MRI could be useful in differentiating benign from malignant lesions, just as in the case of mammography, there are overlaps in the morphologic and dynamic features of the papillary lesions [6].

Ultrasound

Breast ultrasound is of great value in the diagnosis of papillary lesions. Performed by an experienced mammographer, conventional ultrasound, combined with Doppler ultrasound and elastography allows an accurate diagnosis of papillary lesions in most cases. When performed for further evaluation of masses depicted on mammography,

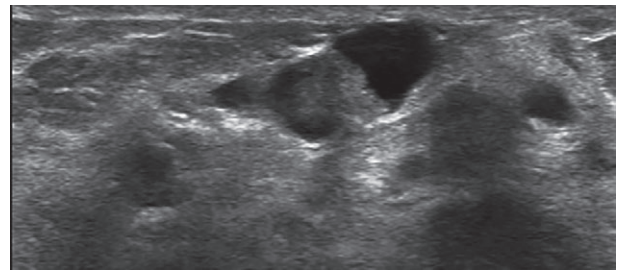


Fig 3. Conventional ultrasound showing a parenchymal intraductal proliferation.

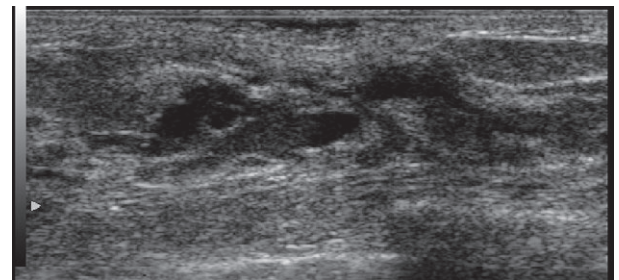


Fig 4. Ultrasound performed in a patient with nipple discharge. In the retroareolar region, there are more dilated ducts, one with intraductal proliferation (after excision, pathology revealed an intraductal papilloma).

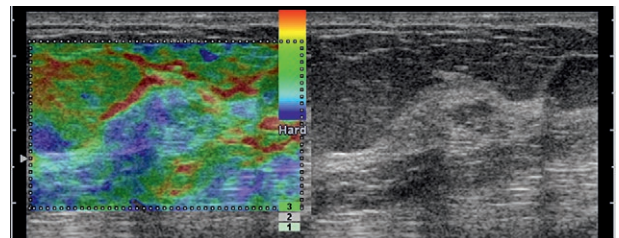


Fig 5. Elastography in a patient with mammographically depicted microcalcifications. The area with suspected microcalcifications shows increased stiffness at sonoelastography which increases the degree of suspicion and allow the ultrasound guidance of preoperative localization.

it is superior to mammography in diagnosing intraductal or intracystic parenchymal proliferations (fig 3).

Also, in patients with occult mammography, presenting with nipple discharge, careful ultrasound examination of the central part of the breast can reveal a pathological duct or a central mass [7] (fig 4).

Even if ultrasound is not indicated for further evaluation of mammographically depicted microcalcifications, targeted ultrasound can reveal the microcalcifications, alone or associated with other lesions. Elastography in these patients, by showing increased stiffness of the area with microcalcifications, can increase the degree of suspicion of malignancy and guide the interventional procedures [8] (fig 5).

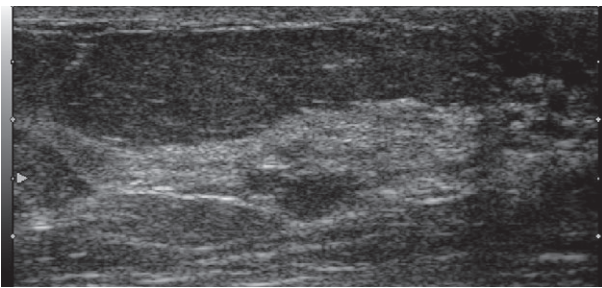


Fig 6. Solid nodule with homogeneous structure and well defined borders, proven to be a solitary papilloma.

It is important, when suspecting a papillary lesion, to keep in mind that benign and malignant lesions have overlapping features and even if ultrasound can rise or affirm the suspicion of malignancy, the final diagnosis is based on core or excisional biopsy [9].

Benign papillary lesions

Solitary or central papilloma represents a solitary lesion located centrally in the breast, within the large subareolar lactiferous ducts and patients may present clinically with serous or bloody spontaneous nipple discharge [3]. Mammography can show a small, circumscribed subareolar mass, rarely with associated calcifications or a solitary dilated retroareolar duct but, in most cases, the lesion is occult on mammography. On ultrasound, a solitary papilloma appears as a dilated duct with a hypoechoic content, as a parenchymal proliferation inside a dilated duct [10] or as a solid mass with well defined borders [1,7,9,11] (fig 6).

Doppler ultrasound and elastography, by showing the presence of blood vessels inside the intraductal content (fig 7) or the stiffness vs BGR sign specific for fluid filled lesions, can differentiate intraductal lesions by apocrine metaplasia or dilated ducts with viscous content (fig 8-10).

The differential diagnosis should also be made with intraductal or invasive carcinoma. Elastography, by showing an increased stiffness of the lesions or elasticity similar to the surrounding tissue can suggest the correct diagnosis and the proper clinical management [12] (fig 11, fig 12).

However, due to the risk of associated atypia or ductal carcinoma in situ of these lesions and to frequent upgrade to high-risk lesions or cancer of papillomas diagnosed on core needle biopsy, excision should be recommended for all papillary lesions [2,3,13]

Multiple or peripheral intraductal papillomas, also known as papillomatosis, is characterized by papillary proliferations within multiple terminal ductal lobular

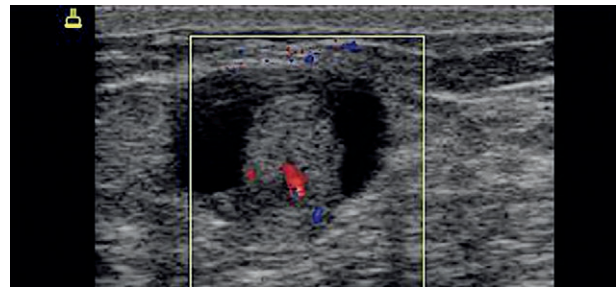


Fig 7. Intracystic parenchymal proliferation, with central blood supply at Doppler evaluation.

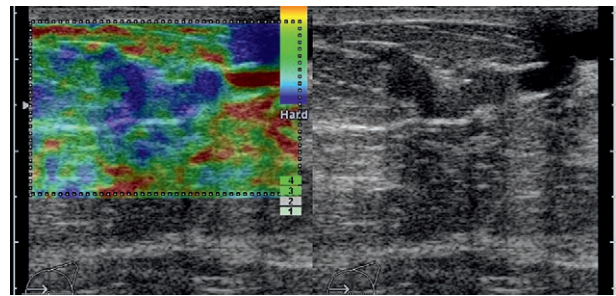


Fig 8. Intraductal papilloma, appearing as a dilated duct with hypoechoic content, stiff at elastographic examination.

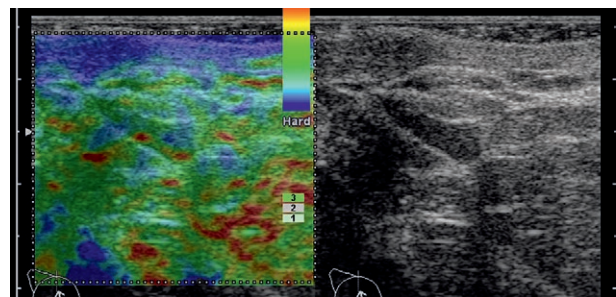


Fig 9. Dilated duct with apocrine metaplasia, with similar elasticity as the surrounding parenchyma at sonoelastography.

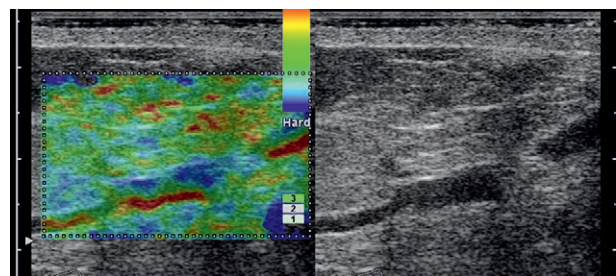


Fig 10. Dilated duct with hypoechoic content, at sonoelastography with the BGR sign typical for fluid content.

units or in the distal branches of the ductal system. Papillomatosis is more likely to occur bilaterally, in the 4th-5th decade of life and is more frequently associated with

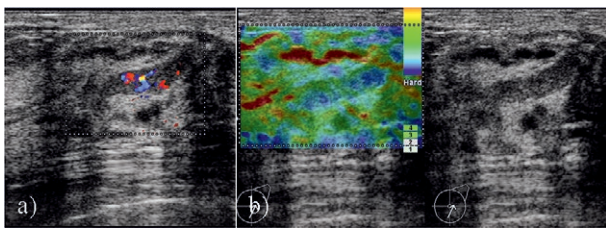


Fig 11. Intraductal parenchymal proliferation, with intense blood supply at Doppler examination (a) but elasticity similar with the surrounding tissue, with an elasticity score of 1 (b), proved at pathology to be a benign intraductal papilloma.

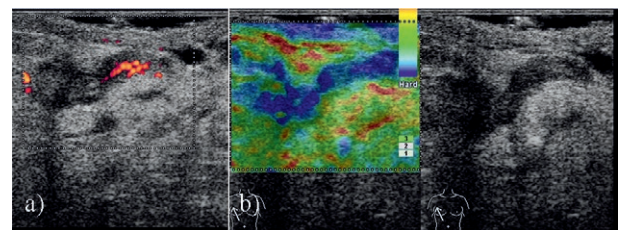


Fig 12. Intraductal parenchymal proliferation, with intense blood supply at Doppler examination (a), stiff at sonoelastography, with an elasticity score of 4 (b), proved at pathology to be an intraductal carcinoma.

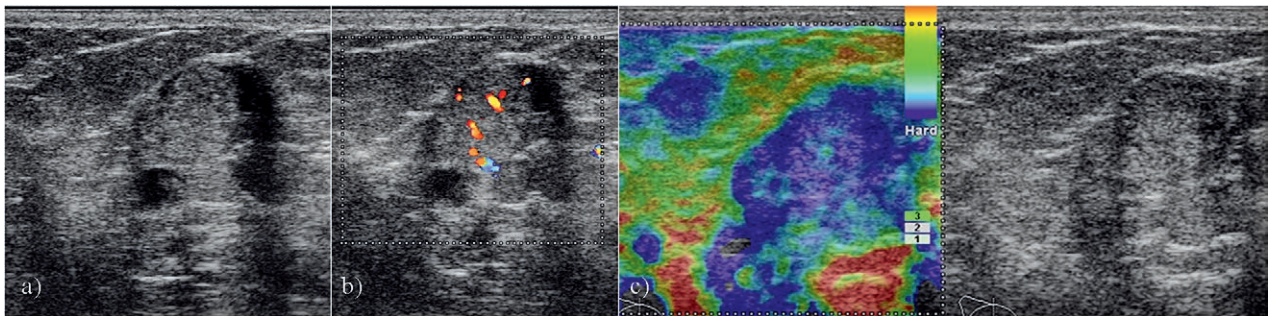


Fig 13. Papillomatosis, presenting on ultrasound as a solid, complex mass, with cystic inclusions (a); Doppler examination, showing intense blood supply (b) and elastography, showing the stiffness of the mass with an elasticity score of 4 (c) raised the suspicion of malignancy.

hyperplasia, atypia, DCIS, or invasive carcinoma [1,3]. Lesions may be occult or patients can present with palpable masses or, rarely, with nipple discharge [3]. Because these patients have a higher risk of developing breast cancer (3 to 7 times) patients with multiple papillomas should be carefully followed [3,11].

On mammography, round, oval, slightly lobulated, well-circumscribed or spiculated mass, with or without associated calcifications can be seen. On ultrasound, the lesions can be solid, round or lobulated, or can present as complex masses (fig 13a) [1,5,11]. The diagnosis is made on the basis of core or excisional biopsy; the lesions have no specific features, on neither Doppler ultrasound or elastography and they are often mistaken with other benign or malignant lesions [12] (fig 13b,c).

Juvenile Papillomatosis (Swiss cheese disease) occurs almost exclusively in young adult women. It manifests as a solitary, firm, unilateral breast mass that is often mistaken for a fibroadenoma. Many of the patients have a family history of breast cancer and about 10 to 15% also present a higher risk of developing a subsequent carcinoma. Because of the young age of the patients, mammography is not routinely indicated and, when performed, it has low sensibility due to the increased density of the breast. On ultrasound, juvenile papillomatosis appears as an illdefined, hypoechoic mass, with inhomogeneous

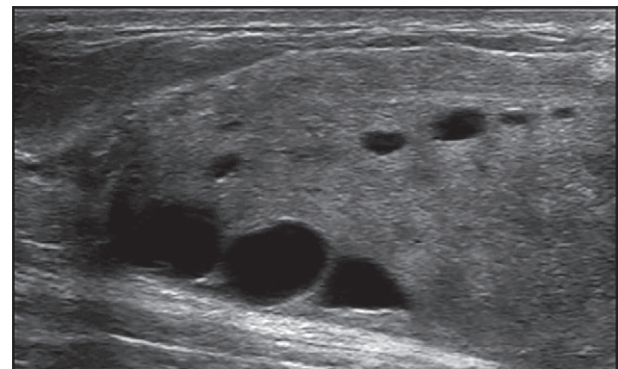


Fig 14. Juvenile papillomatosis, with inhomogeneous structure due to multiple cysts within the lesion.

structure due to multiple cysts within the lesion [1,14] (fig 14).

Malignant papillary lesions

Papillary DCIS, a variant of DCIS that should be differentiated by papillomas with atypia or DCIS within a papilloma, occurs in patients between 50 and 59 years and is usually not palpable. The most sensitive exam is mammography (area of asymmetric density, with or without calcifications). On ultrasound, the lesion presents as

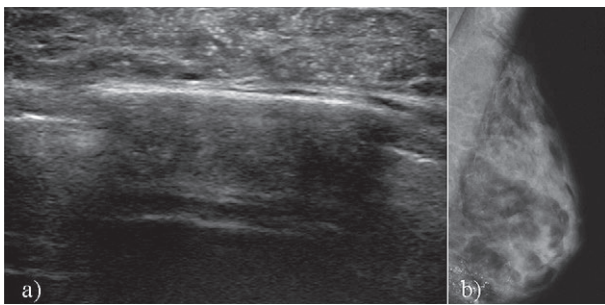


Fig 15. a) Ultrasound performed as a first step examination in a young patient revealed the presence of microcalcifications on the hypoechoic background; b) Mammography showing the granular, heterogeneous morphology of the microcalcifications in a papillary DCIS.

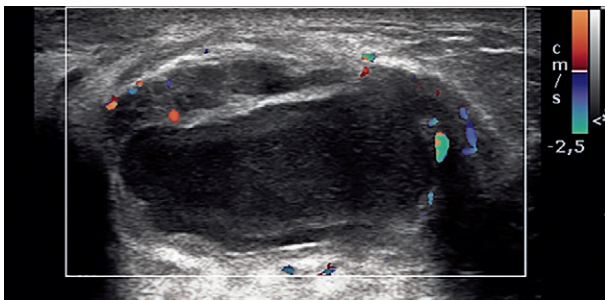


Fig 16. Intracystic carcinoma. There is irregular wall thickening in a cystic mass, with the presence of blood vessels in the cyst wall.

a hypoechoic mass or multiple small lesions, but is usually not detected sonographically [15]. In young patients, when ultrasound is performed as a first step examination, it can detect the associated microcalcifications, especially when the underlying breast tissue is diffuse hypoechoic [11]. In these situations, no matter what the patient's age is, mammography should be indicated in order to analyze their morphology. Calcifications seen in papillary DCIS are linear, granular or mixed [14] (fig 15).

Encapsulated (Intracystic) Papillary Carcinoma is a rare entity, accounting for 0.5-2% of all breast carcinomas. It occurs in older patients (60 years and older) and has a good prognosis. It is located centrally in the breast, the patients presenting usually on clinical examination a 2-3 cm mass in the retroareolar region. At least one third of the patients have bloody nipple discharge [14,16].

On mammography, it may appear as an ill-defined, lobulated mass, usually with no calcifications but, more frequently, it appears as a circumscribed lesion with benign features, similar to those found in fibroadenomas, cysts, phyllodes tumor or in certain malignancies (medullary or mucinous carcinoma, metastases) [1]. Ultrasound is of crucial importance in raising the suspicion of intracystic carcinoma by showing focal, irregular wall

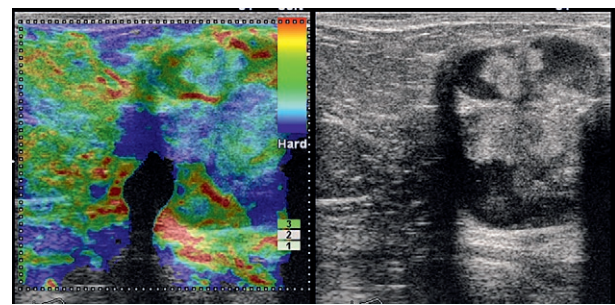


Fig 17. Intracystic parenchymal proliferation, with morphology suggestive of malignancy but with a score of 2 at sonoelastography, suggesting the benign nature. Both tru-cut biopsy and excisional biopsy revealed a benign intracystic papilloma.

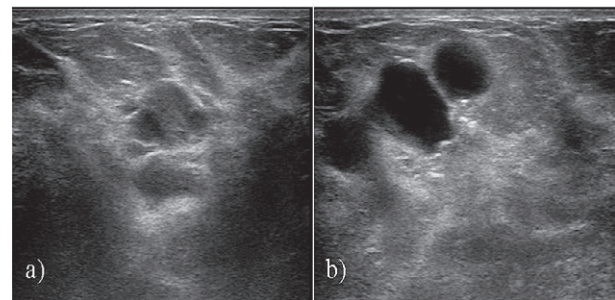


Fig 18. Invasive papillary carcinoma. On ultrasound, multiple hypoechoic (a) and cystic masses, with associated microcalcifications (b) are seen.

thickening in a cyst (fig 16) or an intracystic parenchymal proliferation with features suggesting malignancy: microlobulated contour, inhomogeneous structure, thick internal septae, and intense blood supply [16].

Even if not always possible to establish on ultrasound the benign or malignant nature of the intracystic proliferation, the addition of elastography to 2D ultrasound can highly improve the diagnosis [12] (fig 17). An elastic appearance of the intracystic mass may suggest a benign nature and, in cases of negative results after percutaneous biopsy, surgical excision of the lesion instead of repeated biopsy could be indicated.

Invasive Papillary Carcinoma accounts for 2% of breast cancers. It represents a particular type of invasive ductal carcinoma that occurs in elderly patients (63-71 years) and has a favorable prognosis. Almost 50% of invasive papillary carcinomas occur in the central part of the breast and manifest themselves with nipple discharge [14].

On mammography, invasive papillary carcinoma appears as a rounded or lobulated mass, often with associated calcifications. On ultrasound, it appears as a hypoechoic mass or complex cyst (fig 18).

Anechoic areas within the mass are due to the cystic components or intralesional hemorrhage [5]. The dif-

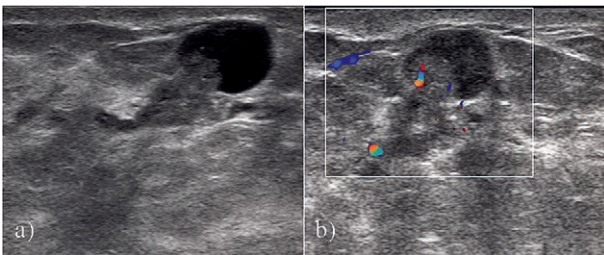


Fig 19. Ultrasound in a case of micropapillary invasive carcinoma showing a solid hypoechoic, irregular mass, with ill defined margins and cystic component (a), hypervascularized (b).

ferentiation from benign lesions relies on its irregular contours and on the detection of suspect axillary lymph nodes on mammography or ultrasound [15].

Invasive Micropapillary Carcinoma represents a rare, clinically aggressive variant of invasive carcinoma. Its incidence varies from 0.9% in its pure form to 7% in mixed forms. The age of the patients ranges between 25 and 92 years and cases have also been reported in male patients. The patients usually present with a palpable mass and in most of the cases, at the time of the diagnosis there is lymph node involvement due to its marked lymphotropism [14, 17].

On mammography it usually appears as a high-density, irregular mass with speculated borders, with or without malignant calcifications. On ultrasound, the findings are similar to those from invasive papillary carcinoma: a solid hypoechoic, irregular or multilobulated mass, with ill defined margins, with cystic component [17-19] (fig 19).

Conclusions

Papillary lesions of the breast are commonly encountered in routine practice but still remain one of the most problematic areas in breast pathology. In the evaluations of these lesions radiological, clinical, and histopathological correlations are essential. Ultrasound has proven its diagnostic value and Doppler ultrasound and elastography improve the specificity of 2D ultrasound, by differentiating papillary lesions from other breast lesions.

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