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PICTORIAL ESSAY

The nipple-areolar complex: anatomy, methods and pathologic findings, between senologist and dermatologist

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Abstract

The purpose of this presentation is to show the ultrasonography findings of normal variants and benign and malignant diseases that affect the nipple-areolar complex. Many of which have unspecific clinical and radiological presentations that can present a challenge for medical specialists. Experienced specialists need to know the different imaging modalities used to study the nipple-areolar complex and the aspect not exactly senology, as well as dermatologist who approach the ultrasound must know the anatomy of this complex area. We will show you a combined clinical and radiological approach to evaluate the nipple-areolar complex, the findings for the normal morphology and the most common benign and malignant diseases that can affect this region. We discuss the characteristics of the different ultrasonography findings and provide guidance on how to avoid artifacts and pitfalls.

Keywords Nipple · Nipple-areolar complex · Breast disease · Sonography · Zuska's disease · Montgomery gland's abscess · Nipple adenoma · Nipple ductal carcinoma in situ · Paget's disease

Abbreviations

TDLU	Terminal ductal lobular unit
US	Ultrasound/ultrasonography
DCIS	Ductal carcinoma in situ
MSCT	CT multi-slices

Introduction and anatomy

The nipple-areolar complex is a specialized region of the mammary gland. It is a major anatomic landmark of the breast, where the lactiferous ducts draining the 15 to 20 lobes of the mammary gland converge, these lobes are oriented radially toward the nipple, and each lobe is made up of several lobules. From each lobule departed a lactiferous duct that in turn branches and ends in the terminal ductal lobular unit (TDLU), which is the functional unit of the breast gland [1]. In the subareolar region, the ducts expand to form the lactiferous sinus just before it enters the nipple of the breast [2]. This area contains the Montgomery glands, large intermediate-stage sebaceous glands that are embryologically transitional between sweat glands and mammary glands and are capable of secreting milk (Fig. 1) [3].

Ultrasound

Ultrasound is very common in the study of the nipple-areolar complex, the reason are being widely available and not requiring ionizing radiation. The nipple can cause a posterior acoustic shadow [1](Fig. 2), to avoid this problem are described various techniques for evaluating the nipple-areolar complex with ultrasound: it is helpful to angle the probe radially so that the ultrasound beam hits the major axis of the duct perpendicularly to enable the entire length of the duct to be seen or peripheral compression and traction with the probe itself is the one that achieves the best angle of incidence on the subareolar ducts [4] (Fig. 3). More useful and detailed vascular information on breast lesions can be done by the advent of new technology such as the microvascular flow imaging, a new ultrasound technique with better ability than color Doppler imaging to identify small vessels that have slow blood flow, and it permits better evaluation of the

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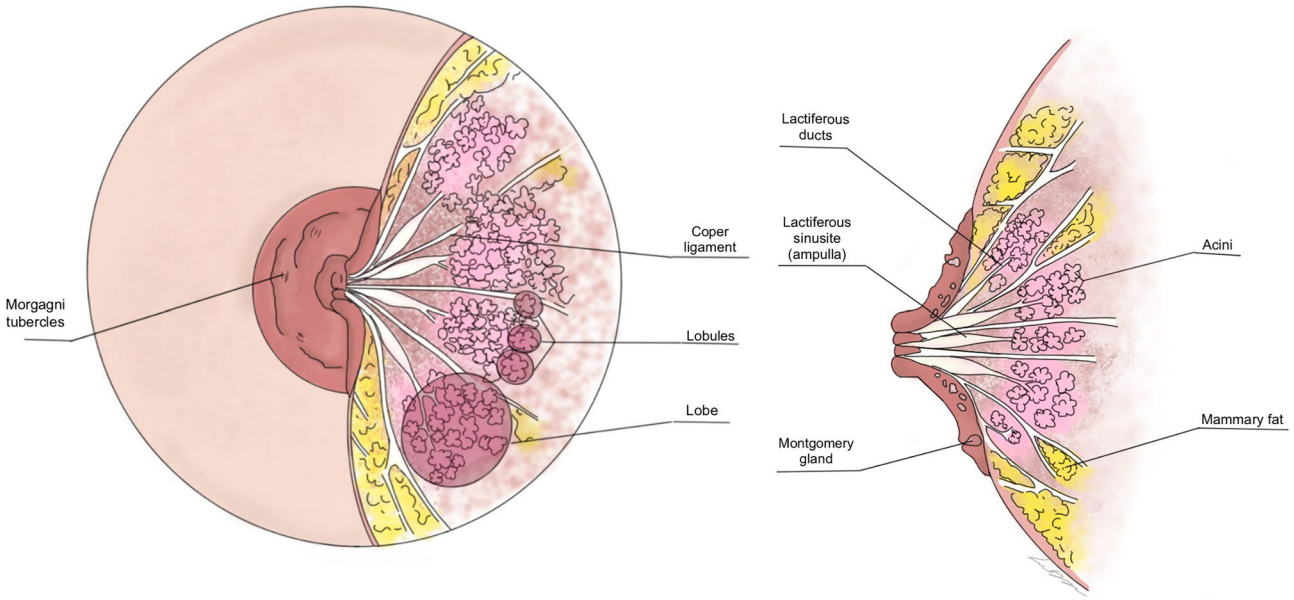

Fig. 1 Anatomy of the nipple-areolar complex

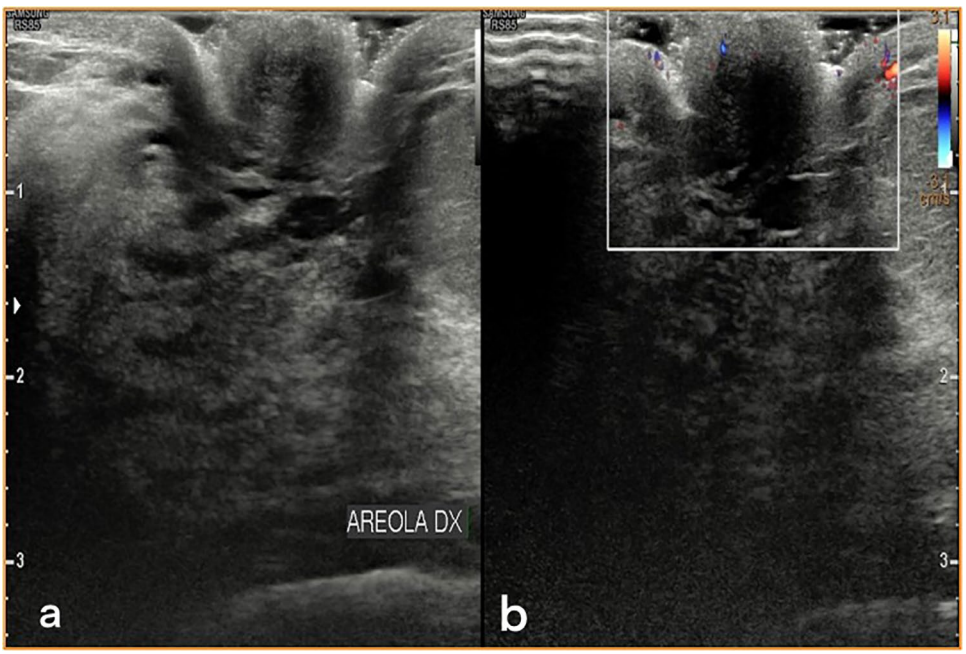

Fig. 2 **a** Normal representation of the nipple-areolar complex. **b** Normal vascularization of the nipple

features, especially microvascular architecture, of various lesions[5].

Benign disease

Zuska's disease

The pathogenesis of Zuska's disease involves squamous metaplasia of the cuboidal epithelium lining the lactiferous ducts. The squamous lining produces large amounts of keratin that obstructs and dilates the ducts, leading to acute inflammatory infiltrates and cellular debris. These ducts become secondarily infected as a result of stasis and bacterial invasion, which leads to abscess formation. The abscess may drain spontaneously and can develop into a periareolar cutaneous fistula [6, 7]. It predominantly affects non-lactating middle-aged women, and is directly associated with tobacco smoking, that is thought to have a direct toxic effect on the retroareolar ductal

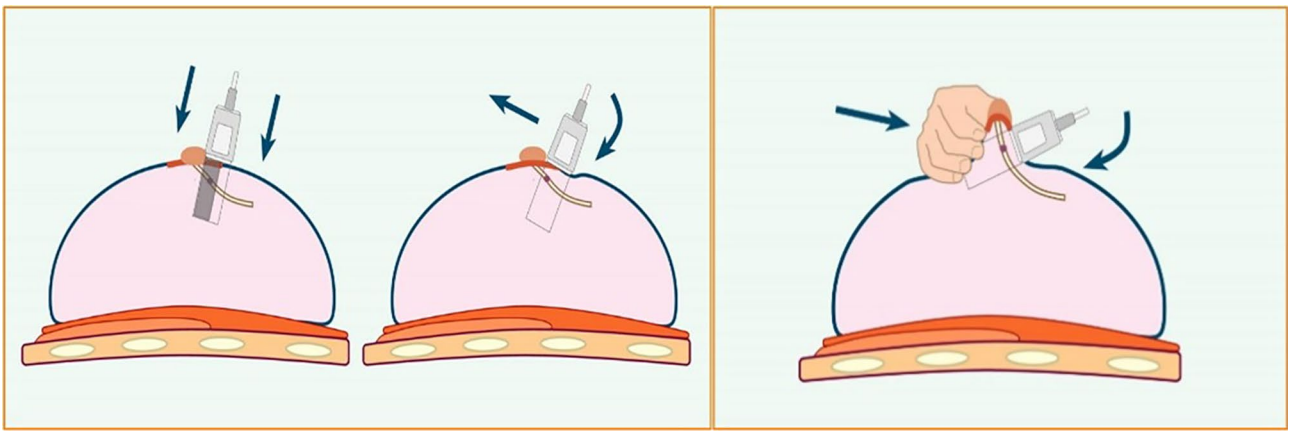

Fig. 3 US techniques to best demonstrate the subareolar and intraniple ducts; first image the rolled-nipple technique: transducer parallel to long axis of the duct then slid toward the nipple, gradually rolling over the NAC. Second image the two-hand compression technique: transducer positioned parallel to the long axis of the disease duct; compression is then applied to the lateral end of the transducer which flattens the NAC

epithelium or an indirect effect via the hoemonal stimulation of breast secretion, thus predisposing to Zuska's disease [8, 9]. It presents as a painful, erythematous subareolar mass and recurring fistula at the edge of the areola [6]. The diagnosis is clinical, but ultrasound is useful for assessing the extent of the disease (Fig. 4).

Infection and abscess of montgomery glands

An abscess is an accumulation of pus that arises due to an obstructed Montgomery gland. Hormonal activity affects the function and therefore the size of sebaceous glands [10]. This glands represents an entrance to bacteria (staphylococcus aureus and other gram +) [11]. Patients may present clinically with pain associated with a palpable superficial mass (Fig. 5a). The gland will appear on US imaging as a round, iso-/hypoechoic, mass with circumscribed or indistinct margins(Fig. 5b). The ultrasound is also important to guide the percutaneous puncture and the antibiogram. [11]

Abscess from foreign bodies

Nipple piercing is a growing fashion trend among young people and has shown an increase over the last years. More frequent are the abscess that may occur between 2 week or months after the operation. US imaging show hypoechoic lesion (Fig. 6) [12]

Ductal ectasia

Asymptomatic or incidental mammary ductal ectasia is thought to occur secondary to the involution process of

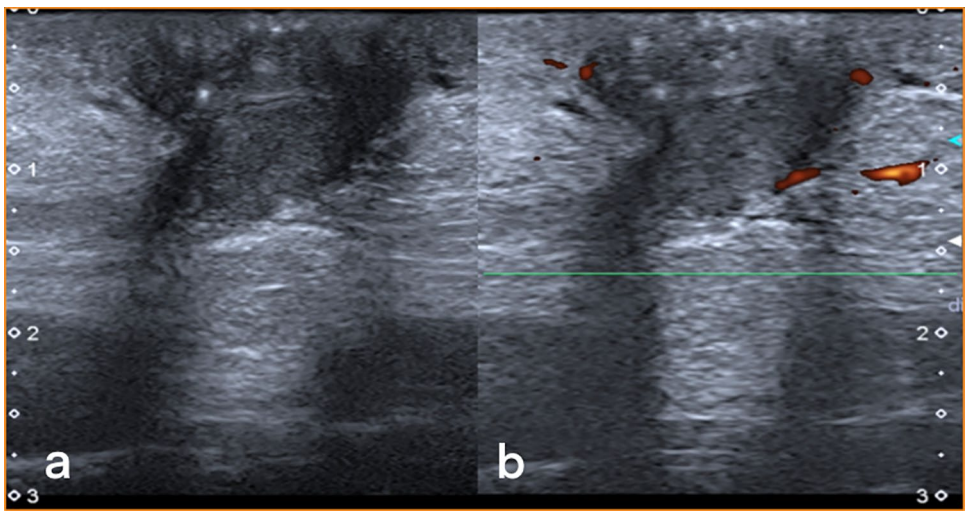

Fig. 4 **a** Ultrasound shows a irregular lesions, with poor heterogeneous internal echoes and skin thickening is a very, with increased peripheral color-Doppler signal (**b**)

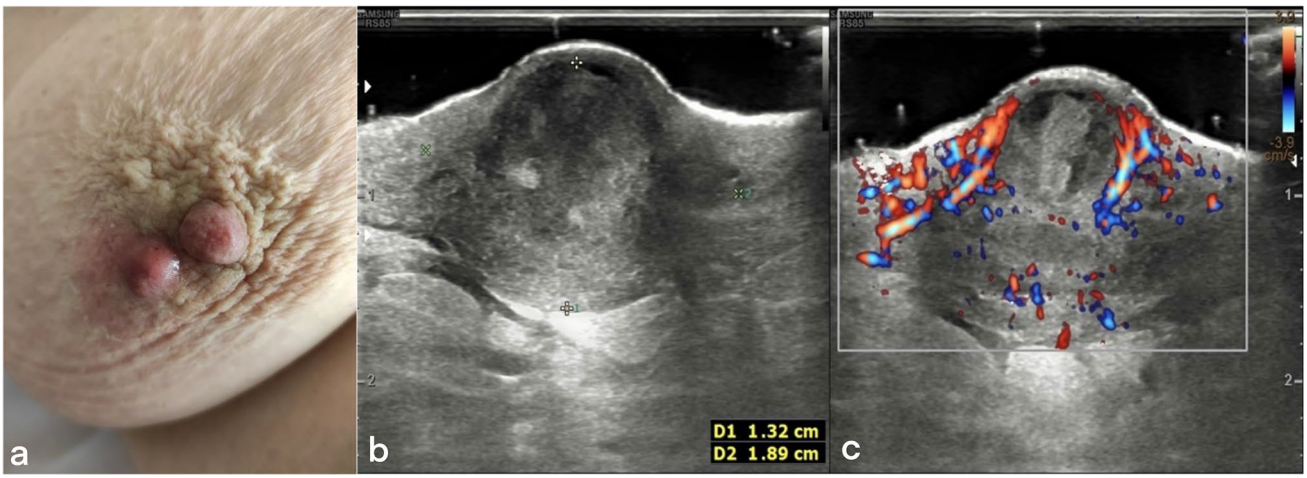

Fig. 5 **a** abscess of the montgomery's gland. **b** US image shows a heterogeneous hypoechogenic intradermal collection compatible with an abscess with increased peripheral color-Doppler signal (**c**)

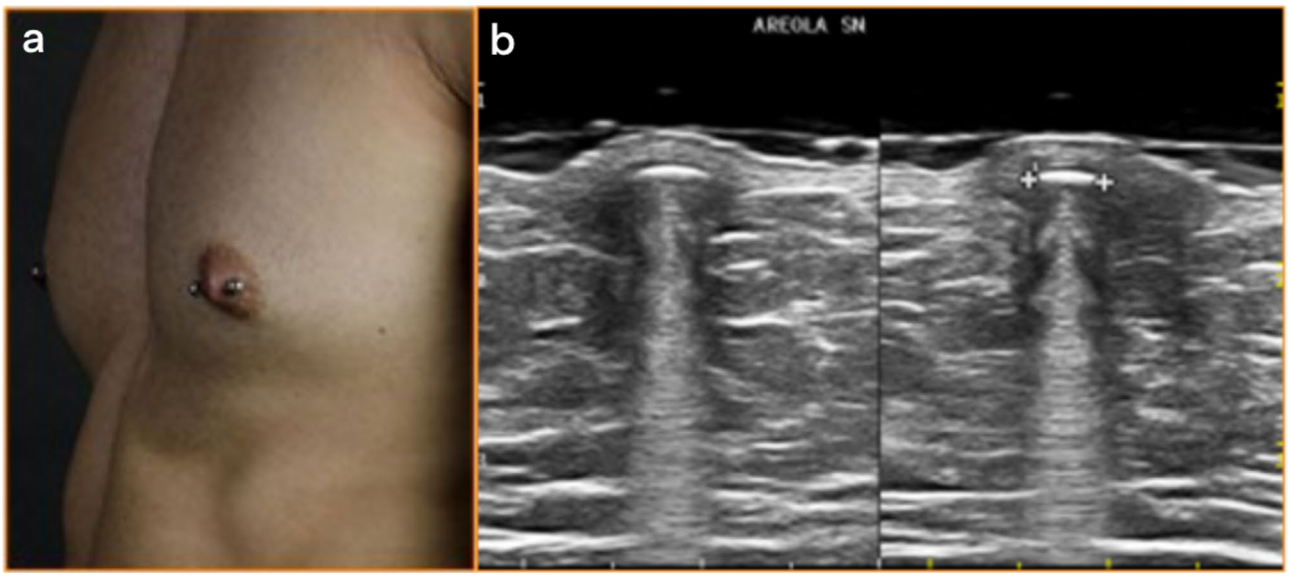

Fig. 6 **a** Nipple piercing, with hyperechogenic artifacts of the metallic reverberations (**b**)

the breast, which begins at menopause. The development of symptoms with mammary duct ectasia is proposed to result from the accumulation of secretions resulting in an inflammatory response [13]. The ductal ectasia can also may develop secondarily to ductal obstruction from thickened secretions associated with the inflammatory response in periductal mastitis [14]. Mammary ductal ectasia is defined as benign dilatation of the ductal system > 3 mm in diameter. On sonography, dilated ducts are filled with fluid, and concentrated secretions and debris are visible as circumscribed hypoechoic mass with internal echoes, which are difficult to differentiate from intraductal tumors [15] (Fig. 7).Movement of echogenic materials on realtime sonography may be a diagnostic feature of ductal ectasia [16]. Apart from compressing the duct to check to see whether it collapses, Doppler studies can be very useful because intraductal masses can have flow signals inside them that indicate vascularization [17]. Asymmetric ductal ectasia is associated with a higher risk of malignancy and warrants further work-up with ultrasonography and potentially biopsy, particularly if a ductal wall abnormality such as thickening or irregularity is identified or intraductal hypoechoic contents are identified [18].

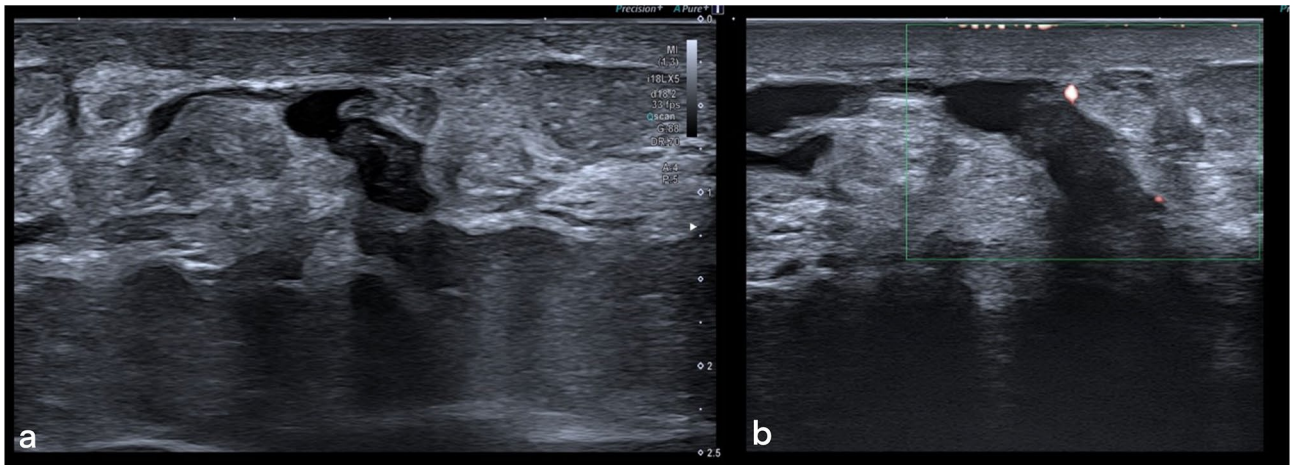

Fig. 7 **a** Ultrasound shows skin thickening and retroareolar ductal ectasia with echogenic contents and increased periductal Doppler signal (**b**)

Papilloma

Intraductal papillomas are relatively common benign neoplasms originating from proximal ducts or retroareolar mammary ducts, usually within a central duct near the nipple[19]. Clinically, patients may present with pain, a palpable abnormality, or nipple discharge, which is typically clear or serosanguinous. Intraductal papillomas are the most common cause of pathological nipple discharge and occur most commonly in perimenopausal women[20]. Papillomas are known to occur anywhere within the ductal system and are classified into central and peripheral types [21]. As opposed to a solitary central intraductal papilloma, multiple peripheral papillomas arising in the terminal ductal lobular units are associated with higher rates of atypia and malignancy [19]. Ultrasound findings of an intraductal papilloma include a circumscribed or irregular eccentric solid mass within a dilated duct (Fig. 8). It can have the appearance of a mural nodule [21]. Colour Doppler imaging can differentiate inspissated secretions from a papilloma by identifying flow within the fibrovascular stalk of the papilloma [22]. Strain elastography for imaging lesion stiffness is being used as a diagnostic aid in the malignant/benign discrimination of breast diseases that's because malignant masses in the breast tend to be harder than the surrounding normal tissue. [23]

Adenoma

Nipple adenoma is an uncommon benign tumor, a rare variant of a papillary lesion, with unknown prevalence [24]. Histologically, an epithelial proliferation with a retained myoepithelial cell layer occupies the surrounding stroma of lactiferous ducts [24]. Clinically, it manifests with pain as a palpable nipple, and possibly skin changes that simulates Paget disease or fibroadenomas and it is rarely associated with bloody nipple discharge. It is visualized as a round, homogeneous, hypoechoic mass with circumscribed margins with micro or macro-calcification and internal vascularity

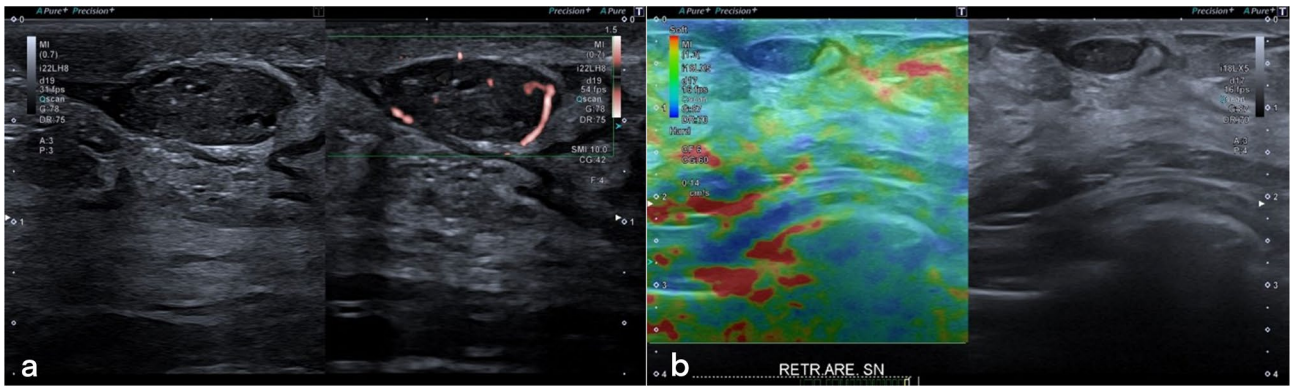

Fig. 8 **a** Ultrasound shows a cystic lesion with a solid nodule inside with increased peripheral Doppler signal, adjacent to the nipple and the imaging of the stiffness with the aid of strain elastography (**b**)

on colour Doppler images [25] (Fig. 9). Complete surgical excision is recommended given the non-specific clinical presentation and differential considerations including Paget disease [26].

Fibroadenomas

Fibroadenomas are the most common benign tumors of the breast. They are composed of epithelium and stroma of terminal ductal-lobular units [27]. They are classically round or oval in shape, firm and rubbery in consistency, smooth, and very mobile, they are generally not painful, but they can be associated with some tenderness[28].

US findings of fibroadenomas usually show round, oval, or lobulated shapes, which are sharply defined by a pseudocapsule of compressed parenchyma (a poorly defined margin or an irregular shape is associated with a malign disease). Therefore, fibroadenomas are typically well-circumscribed round or oval solid masses, compressible but not easily deformed with the probe, associated with smooth contours and homogeneous internal echoes on sonography [28]. However, some fibroadenomas have atypical sonographic findings, such as posterior shadowing, phyllodes, collagen bundles, adenosis, and microcalcifications (Fig. 10) [29]. Ultrasound is also an accurate method of assessing the size of the lesion and permits size to be monitored in women treated conservatively.

Malignant pathology

Paget's disease

Paget disease is a rare malignancy of the breast characterized by infiltration of the nipple epidermis by adenocarcinoma cells, presumably through ductal proliferation.

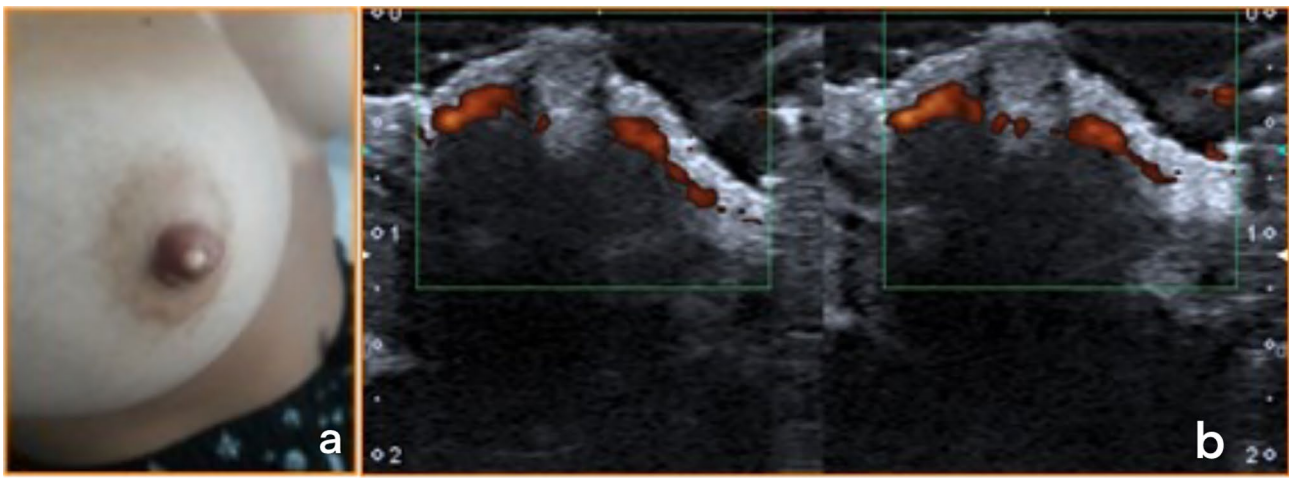

Fig. 9 **a** Woman presented with nipple erythema, the US shows a circumscribed, oval, hypoechoic solid mass with internal vascularity and posterior enhancement. Gel stand-off and light transducer pressure were used to acquire the image (**b**)

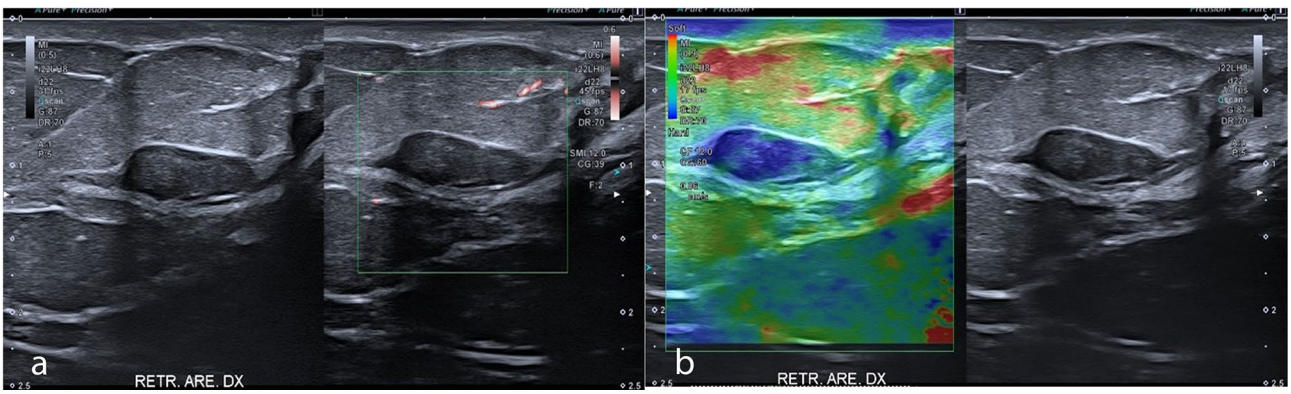

Fig. 10 **a** US show with the color Doppler internal vascularity, important to aid in the therapy management. **b** The strain elastography show a homogenic stiffness or a mosaic pattern

Clinical presentation of Paget disease may include unilateral pruritus, eczema, erythema, skin erosion or ulceration, nipple retraction or inversion, or nipple discharge [30] (Fig. 11).As opposed to benign eczema, which is typically bilateral, Paget disease will be unilateral [30]. More than 90% of cases of Paget disease are associated with an additional underlying breast malignancy like ductal carcinoma in situ (DCIS) [30]. Nevertheless, ultrasound or mammographic findings such as skin thickening with or without underlying microcalcifications, ductal ectasia, or a mass (Fig. 11), may be negative in up to 50% of cases, that's the reason for the utility of magnetic resonance (MR) imaging, in patients with Paget disease for evaluation of the nipple-areolar complex and identification of an additional underlying malignancy in the breast [31, 32] (Fig. 11).

Invasive ductal carcinoma

Invasive ductal carcinoma is the most common malignant tumor of the breast. Occasionally, it can be located immediately behind the nipple or it can originate in another location and extend to the nipple [33]. In cases involving the nipple-areolar complex, the most common clinical manifestation is unilateral nipple retraction and distortion of the areola. Invasive ductal carcinoma generally presents as an ill-defined retroareolar mass, hypoechogenic, with irregular or spiculated defined borders, rich internal vascularity at the color Doppler [34]. Male breast cancer can occasionally develop in the subareolar region, but most breast cancers and other breast conditions occur in other parts of the breast and tend to spare the subareolar region and nipple [35] (Fig. 12). The infiltrating ductal carcinoma is the most common histologic subtype of male breast cancer (approximately 80% of breast cancer cases in men) that is usually unilateral, occurring

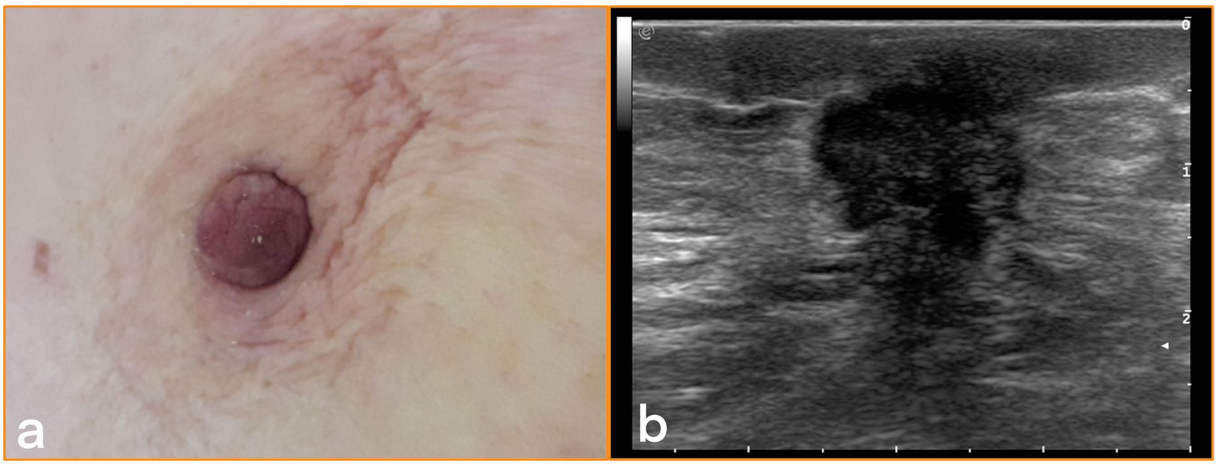

Fig. 11 **a** this case presented with erosions and swollen nipple. **b** US reveals globally enlarged nipple, the us finding are aspecific

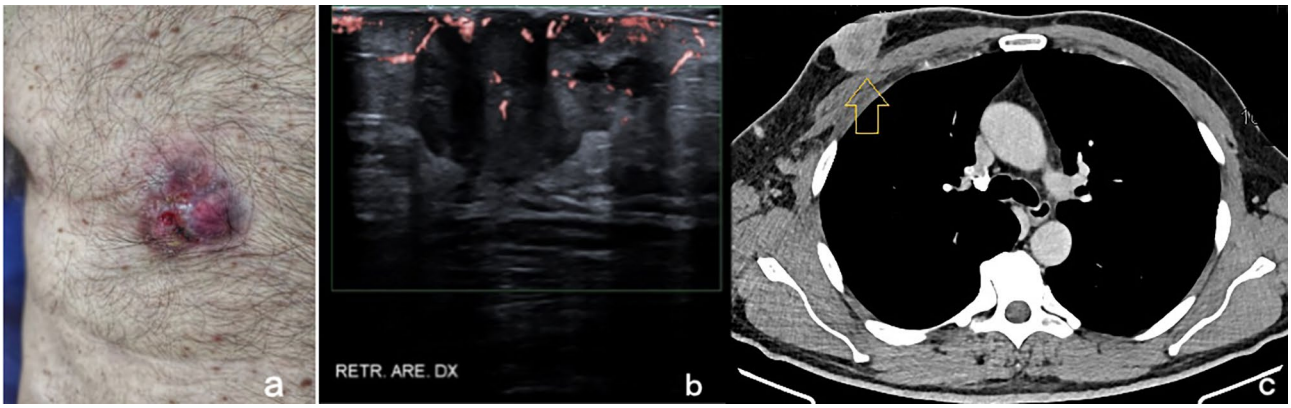

Fig. 12 **a** Invasive ductal carcinoma, on ultrasound, (**b**) the lesion is hypoechogenic and ill-defined, with irregular borders and internal vascularity at the color Doppler. **c** Confirmed at the MSCT, the infiltration of the muscle

bilaterally in less than 1% of cases [36]. Male breast cancer most commonly manifests as a painless palpable mass, other signs and symptoms include nipple ulceration or retraction, nipple discharge, skin thickening, and palpable axillary lymph nodes [37] (Fig. 12).

Conclusion

Summarily, nipples may be affected by various benign and malignant pathologies, several of which have similar clinical and imaging presentations. Imaging studies play an essential role in the diagnostic workup of conditions involving the nipple-areolar complex. Radiologists and dermatologist must be accustomed to meticulous management of the different imaging presentation. It is essential to evaluate the clinical, radiological, and histological findings together to establish an accurate diagnosis.

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Declarations

Conflict of interest The authors declare that there are no financial or other relations that could lead to a conflict of interest.

Ethical statement This study was approved by the local research ethics committee and all the subjects enrolled were informed about the examinations and the procedure, and their written consents were obtained before the US examination.

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