Atypical Features of Fibroadenoma, Correlation between Ultrasound and Pathology

Thesis

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List of Abbreviations

Abb.	Full term
ADH	*Atypical ductal hyperplasia*
BIRADS	*Breast imaging reporting and data system*
BLES	*breast lesion excision system*
BMI	*Body mass index*
CIS	*Carcinoma in situ*
CNB	*Core needle biopsy*
CT	*Computed tomography*
DCIS	*Ductal carcinoma in situ*
ER	*Estrogen*
FAD	*Fibroadenoma*
FNAC	*Fine needle aspiration cytology*
GH	*Growth hormoone*
HIFU	*High intensity focused ultrasound*
MRI	*Magnetic resonant imaging*
PR	*Progesterone*
RFA	*Radiofrequency ablation*
RR	*Relative risk*
TDLU	*Terminal ductal lobular unit*
TNBC	*Triple negative breast cancer*
US	*Ultrasonography*

INTRODUCTION

Fibroadenoma is the most common benign tumor in the breast. Ultrasound is commonly used for evaluation and follow up of breast fibroadenoma ***(Nassar, 2014).***

It is preferred because it is easy, available and not invasive. It is accurate in visualizing abnormalities in dense breast and so recommended for young women. Also ultrasound lacks the hazards of radiation so it is preferred in pregnant women and in situations where frequent follow up examinations are warranted ***(Irimia and Gottschling, 2016).***

Fibroadenomas arise from the epithelium and stroma of the terminal ductal-lobular unit, and consist of proliferative fibrous stroma and secondarily increased epithelial ductal structures ***(Kook et al., 1999; Pinto et al., 2014).***

Mostly fibroadenomas present as a sharply demarcated, firm mass, usually not more than 3 cm in diameter. The cut surface is solid, grayish white, and bulging, with a whorl-like pattern and slit-like spaces ***(Thakur and Misra, 2014).***

Histologically it consists of two components (epithelial and fibroblastic).

Depending on the proportion and the relationship between these two components, there are two main histological features: intracanalicular and pericanalicular. Often, both types

are found in the same tumor. Intracanalicular fibroadenoma: stromal proliferation predominates and compresses the ducts, which are irregular, reduced to slits. Pericanalicular fibroadenoma: fibrous stroma proliferates around the ductal spaces, so that they remain round or oval, on cross section. The basement membrane is intact ***(Nassar, 2014).***

More than 70% of fibroadenomas present as a single mass, and 10%-25% of fibroadenomas present as multiple masses. It may also be small enough that it is only seen on microscopic examination or it may be larger than 10 cm and cause breast asymmetry and significant esthetic deformation of the breast. The size of the fibroadenoma may shrink or expand spontaneously, or it may be hormonally responsive and vary in size in conjunction with the menstrual cycle. Fibroadenomas may also vary in clinical presentation, ranging from being asymptomatic to causing debilitating pain ***(Lee et al., 2015).***

In ultrasound Fibroadenomas appear oval, and their width is larger than their anteroposterior diameter. Gentle lobulations (typically fewer than 4) may be present, but the margins should be circumscribed.

Internal echogenicity may be homogeneous, and findings may range from isoechoic to lobules of fat to hypoechoic. The through-transmission of the tumor is variable. A thin echogenic capsule is typical of a fibroadenoma and indicates that the

lesion is benign. Fibroadenomas do not have a true capsule; the thin echogenic capsule seen on ultrasonograms is a pseudocapsule caused by the compression of adjacent tissue.

When using color-flow Doppler or power Doppler imaging, the amount and distribution of vascularity among fibroadenomas is highly variable. Therefore, the vascularity of solid masses does not help distinguish a cancer from a fibroadenoma ***(Kovatcheva et al., 2015).***

Giant fibroadenoma is an uncommon variant of fibroadenoma characterized by rapid growth. Peak incidence occurs in late adolescence. The size of the lesion is usually more than 5 cm but is encapsulated and benign. The underlying mass may cause a major distortion to the breast contour ***(Fallat et al., 2008).***

Fibroadenomas usually seen in late teens and less so common in postmenopausal women where breast cancer may look like fibroadenoma on imaging. So we should have a high index of suspicion for FAD in the postmenopausal ladies and triple assessment should include thorough tissue sampling in the form of FNA and core biopsy ***(Khout et al., 2011).***

Complex fibroadenoma is a sub type of fibroadenoma harbouring one or more of the following: epithelial calcifications, papillary apocrine metaplasia, sclerosing adenosis or cysts larger than 3 mm ***(Nassar, 2014; Gogoi and Borgohain, 2015; Pinto et al., 2014).***

Complex fibroadenomas are usually smaller than simple fibroadenomas (1.3 cm compared with 2.5cm in simple fibroadenomas).

In ultrasound, they may show angular or irregular margin this may happen because of infarction or hyalinization, it may show more than 3 lobulations, also acoustic shadowing could be seen due to hyalinization and calcification.

With the above mentioned features, fibroadenomas may mimic malignancy and core biopsy is warranted to confirm the diagnosis ***(Selvi, 2015; Namazi et al., 2017; Greenberg et al., 2018).***

To assess the relation between fibroadenomas and breast cancer we should address two main questions: whether or not a fibroadenoma is a marker for increased risk of breast cancer, and whether breast cancer can evolve from the epithelial component of a fibroadenoma. The first question was originally assessed in several retrospective studies, which demonstrated increase risk of breast cancer in women with fibroadenomas compared with the general population.

Complex fibroadenoma were associated with a 3.1 elevated risk of breast cancer. The relative risk for women with a familial history of breast cancer and complex fibroadenoma was 3.72, yet malignant transformations in the epithelial components of fibroadenomas are considered rare ***(Greenberg et al., 1998).***

Aim of the Work

The purpose of our study is to assess the diagnostic accuracy of ultrasound in complex fibroadenoma.

Chapter 1

BREAST ANATOMY AND EMBRYOLOGY

The breast or mammary gland is a modified type of apocrine sweat gland, which begins to develop at approximately the fifth week of fetal development. An array of local and systemic growth factors and hormones regulate this sequence of highly ordered events. The breast originates from paired linear ectodermal ridges or mammary ridges ***(Moore and Persaud, 1998; Hunt et al., 2010).***

Ectodermal ridges are thickened strips of ectoderm extending bilaterally on the ventral surface of the embryo from the axillary to the inguinal regions. These epithelial cords initially appear as 15–20 buds. During the seventh week in utero, these buds undergo apoptosis in human embryos, with a single pair of solid buds persisting at the fourth or fifth intercostal space: the primary mammary buds ***(Sabel, 2009).***

The breasts subsequently begin to develop as these primary buds of ectoderm penetrate downward into the underlying mesoderm. By the 12thweek of gestation, the primary mammary buds burgeon into secondary buds, which will eventually form the mammary lobules. In the fifth month in utero, the mammary ridge penetrates the underlying mesoderm, sending 15–20 branching ingrowths radially into the developing breast ***(Moore and Persaud, 1998).***

Small lumina develop within the mammary buds, forming the lactiferous ducts and their branches. The lactiferous ducts converge to open into a shallow mammary pit, which transforms into a nipple during infancy. During the second trimester, the breast development continues with the formation of sweat glands, sebaceous glands, and apocrine glands, which will eventually form the Montgomery glands. The areola also develops at approximately 5 months of gestational age. At birth, males and females have identical breasts, formed by the major lactiferous ducts. Shortly after birth, the nipple begins to protrude from the areola, encompassing 10–15 terminal duct outlets ***(Pandya and Moore, 2011).***

During puberty, the breast mound increases in size. Subsequent enlargement and outward growth of the areola result in a secondary mound. Eventually, the areola subsides to the level of the surrounding breast tissue, leaving a single breast mound. At full development, the nipple-areolar complex overlies the area between the 2nd and 6th ribs, with a location at the level of the 4th intercostal space being typical for a nonpendulous breast. The adult breast consists of approximately 15–20 segments demarcated by mammary ducts that converge at the nipple in a radial arrangement. Like the number of segments, the number of mammary ducts may vary. The collecting ducts that drain each segment, which typically measure about 2 mm in diameter, coalesce in the subareolar region into lactiferous sinuses approximately 5–8 mm in