**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 77209

**Manuscript Type:** LETTER TO THE EDITOR

**Imaging of fibroadenoma: Be careful with imaging follow-up**

Ece B *et al*. Be careful with imaging follow-up fibroadenoma

Bunyamin Ece, Sonay Aydın

**Bunyamin Ece,** Department of Radiology, Kastamonu University, Kastamonu 37150, Turkey

**Sonay Aydın,** Department of Radiology, Erzincan University, Erzincan 24142, Turkey

**Author contributions:** Aydın S was responsible for conception and supervision; Ece B was responsible for design; Ece B and Aydın S conducted the literature search and reviewed the manuscript critically, were responsible for materials, and wrote the manuscript; All authors have read and approved the final manuscript.

**Corresponding author: Bunyamin Ece, MD, Associate Professor, Doctor,** Department of Radiology, Kastamonu University, Kuzeykent 57, Alay Street No. 4, Kastamonu 37150, Turkey. bunyaminece@hotmail.com

**Received:** April 19, 2022

**Revised:** June 10, 2022

**Accepted:** July 29, 2022

**Published online:**

**Abstract**

The present letter to the editor is related to the study titled, “Preoperational diagnosis and management of breast ductal carcinoma in situ arising within fibroadenoma: Two case reports.” Fibroadenoma is the most common benign mass lesion in young females. Based on this study showing that malignancy can develop on fibroadenomas, we want to emphasize that careful sonographic follow-up of fibroadenomas should be done and that each lesion should be followed carefully and separately in cases with multiple fibroadenomas. Additionally, we want to emphasize the critical role of sonographic examination in diagnosing fibroadenoma, the importance of correctly defining benign and malignant sonographic findings, and which lesions should be followed up sonographically and which lesions should be evaluated histopathologically.

**Key Words:** Breast; Fibroadenoma; Malignity; Follow-up; Ultrasound

Ece B, Aydın S. Imaging of fibroadenoma: Be careful with imaging follow-up. *World J Clin Cases* 2022; In press

**Core Tip:** We read with interest the case report of two cases presented as examples of malignancies developing from fibroadenoma followed as benign. With this letter to the editor, we wanted to emphasize the importance of sonographic evaluation of single and multiple fibroadenoma cases, which we frequently encounter in daily practice, as well as which lesions should be referred for sonographic follow-up and which lesions should be referred for histopathological examination. Additionally, based on the first case in this case report, we want to emphasize the importance of carefully following each lesion in cases with multiple fibroadenomas.

**TO THE EDITOR**

We read the article titled, “Nonoperational diagnosis and management of breast ducal carcinoma in situ arising within adenocarcinoma: Two case reports”[1] with interest and appreciate the authors’ comprehensive case report. The article provides remarkable and useful information regarding malignant entities that arise on adenocarcinoma, which is the most frequent benign breast disease. One of the important features of this article is that it shows imaging findings about malignancy developing on adenocarcinoma that were followed as benign for a while. Another important point is to detect the malignancy by excision made on suspicion of one of the lesions in a case with multiple adenocarcinoma. According to this case results, we conclude that as radiologists, we need to be more careful when evaluating single or multiple adenocarcinoma cases, which we frequently see in daily practice, and when referring them for ultrasonically follow-up.

At this point, we believe it is necessary to emphasize the importance of phonographic examination in diagnosing adenocarcinoma, the importance of accurately defining benign and malignant phonographic findings, and the distinction between which lesions should be referred for phonographic follow-up and which lesions should be evaluated anthropologically. Additionally, although the risk of developing malignancy from adenocarcinoma is low, we want to emphasize once again, based on the first case in this article, that each lesion should be evaluated separately when following up on cases with multiple adenocarcinoma.

Various clinical dilemmas arise when a lesion suspicious of adenocarcinoma is detected in a patient. It is well known that adenocarcinoma are the most common benign mass lesion in young females[2], and currently, an immediate intervention procedure is not usually performed on a lesion with a misdiagnosis of fibroadenoma. Histopathological examination of every fibroadenoma prediagnosed lesion was abandoned a long time ago. While all fibroadenoma prediagnosed lesions were excised until the mid-1980s[3], research published in the 1990s recommended that fibroadenomas with no suspicion of malignancy based on fine needle aspiration biopsy results be followed up[4]. Later studies suggested that young patients with benign sonographic findings could be safely followed without biopsy[5]. Additionally, it was stated that a quality sonographic scan has a high negative predictive value and that short-term imaging follow-up would be a good alternative to biopsy[6]. Today, when a fibroadenoma prediagnosed lesion is first seen, according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS)[7] BI-RADS 3 classification and evaluating probably in the benign category is a common practice, and a short-term imaging follow-up of 6 mo is recommended[8]. However, in the presence of various suspicious sonographic findings, lesions are classified as BI-RADS 4 and histopathological correlation is recommended[9]. Although malignant transformation of fibroadenomas is rare, it is seen between 0.002% and 0.125%[10]. Therefore, it is important to emphasize fibroadenoma imaging and suspicious findings.

The following sonographic findings indicate that the lesion is not a typical fibroadenoma: taller than wide orientation, deterioration of orientation parallel to the skin, deterioration in the thin echogenic ring around the lesion, thickening and irregular border feature, angulation at the edges, hypoechoic shadowing, heterogeneous internal structure, containing cystic areas and microcalcifications, microlobulation and spicule contour feature and echogenicity changes in surrounding tissue[5,11,12]. On magnetic resonance imaging (MRI), fibroadenomas are often isointense or hypointense in comparison to adjacent breast tissue on T1 weighted image and hypointense or hyperintense on T2 weighted image. It usually presents as a type 1 dynamic curve pattern in contrast-enhanced dynamic series, which is characterized by a slow enhancement and a persistent enhancement in the delayed phase. It may also contain non-enhancing internal septations. Contrary to malignant lesions, they are characterized by high apparent diffusion coefficient (ADC) values in diffusion-weighted imaging (DWI).

Histopathological examination can be performed in the following situations respectively; In the presence of suspicious findings on sonographic examination, an increase in size during sonographic follow-up, an immobile and poorly circumscribed lesion, advanced age (> 35 years), a family history of cancer, and a lesion greater than 2.5 cm in diameter[13–15].

Novel radiologic studies continue to emphasize the critical distinction between fibroadenomas and malignant tumors. Radiomics—a diagnostic tool based on artificial intelligence—has been evaluated for the aforementioned purpose using sonographic and magnetic resonance images; it is stated that the radiomics signature may be a useful predictive parameter for the differentiation of fibroadenomas from malignant lesions and phyllodes tumors[16,17]. Additionally, novel MRI approaches have been developed to distinguish fibradenomas from malignant lesions, one of which is three-dimensional amide proton transfer weighted magnetic resonance imaging. It is said that this unique technique performed similarly to dynamic contrast enhanced MRI in differentiating fibroadenomas from malignant breast tumors and better than DWI and added additional information on tumor cell activity to DWI images[18].

In the literature, the use of contrast-enhanced ultrasonography to differentiate fibroadenomas from ductal carcinoma *in situ* (DCIS) has been shown to be helpful. In contrast-enhanced ultrasonography examinations utilizing microbubble agents, DCIS is more likely than fibroadenoma to exhibit an earlier wash-in time, hyperintense enhancement, blood perfusion defects, an enlarged enhancement scope and penetrating vessels[19]. In addition, there are studies reporting that the use of digital breast tomosynthesis (DBT) in patients with dense breast tissue will increase sensitivity and specificity in the diagnosis of malignancy, as well as in the diagnosis and follow-up of benign lesions such as fibroadenoma. Tomosynthesis is able to detect more invasive tumors than two-dimensional mammography alone, and DBT will also find more benign lesions. Lesion shape and margins are generally well depicted by DBT[20]. In addition, noninvasive functional MRI examination can potentially be utilized to assess breast lesions. Using DWI and MR spectroscopy, the lesion is evaluated. In comparison to benign lesions, malignant lesions exhibit lower ADC values and restricted diffusion. The proton MR spectroscopy can identify the biochemical characteristics of tissue. Total choline resonance at 3.14–3.34 ppm has been associated to oncogenesis and tumor progression, as well as found in malignant breast tumors due to complicated metabolism[21].

As a result, it is important to keep in mind that malignancy may develop on fibroadenomas, which is the most common benign mass lesion of the breast, albeit rarely. Additionally, caution should be exercised during the diagnosis and sonographic follow-up of patients with multiple fibroadenomas, with each lesion being documented separately and each lesion being carefully evaluated during the follow-up.

**REFERENCES**

1 **Wu J**, Sun KW, Mo QP, Yang ZR, Chen Y, Zhong MC. Preoperational diagnosis and management of breast ductal carcinoma *in situ* arising within fibroadenoma: Two case reports. *World J Clin Cases* 2022; **10**: 3496-3504 [PMID: 35611194 DOI: 10.12998/wjcc.v10.i11.3496]

2 **Santen RJ**, Mansel R. Benign breast disorders. *N Engl J Med* 2005; **353**: 275-285 [PMID: 16034013 DOI: 10.1056/NEJMra035692]

3 **Wilkinson S**, Forrest AP. Fibro-adenoma of the breast. *Br J Surg* 1985; **72**: 838-840 [PMID: 4041718 DOI: 10.1002/bjs.1800721021]

4 **Wilkinson S**, Anderson TJ, Rifkind E, Chetty U, Forrest AP. Fibroadenoma of the breast: a follow-up of conservative management. *Br J Surg* 1989; **76**: 390-391 [PMID: 2720350 DOI: 10.1002/bjs.1800760424]

5 **Smith GE**, Burrows P. Ultrasound diagnosis of fibroadenoma - is biopsy always necessary? *Clin Radiol* 2008; **63**: 511-5; discussion 516-7 [PMID: 18374713 DOI: 10.1016/j.crad.2007.10.015]

6 **Park YM**, Kim EK, Lee JH, Ryu JH, Han SS, Choi SJ, Lee SJ, Yoon HK. Palpable breast masses with probably benign morphology at sonography: can biopsy be deferred? *Acta Radiol* 2008; **49**: 1104-1111 [PMID: 18855166 DOI: 10.1080/02841850802438504]

7 **Morris E,** Comstock C, Lee C. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. *Am Col Radio* 2013 [DOI: 10.1016/j.ejrad.2006.08.030]

8 **Graf O**, Helbich TH, Hopf G, Graf C, Sickles EA. Probably benign breast masses at US: is follow-up an acceptable alternative to biopsy? *Radiology* 2007; **244**: 87-93 [PMID: 17581897 DOI: 10.1148/radiol.2441060258]

9 **Clauser P**, Bazzocchi M, Marcon M, Londero V, Zuiani C. Results of Short-Term Follow-Up in BI-RADS 3 and 4a Breast Lesions with a Histological Diagnosis of Fibroadenoma at Percutaneous Needle Biopsy. *Breast Care (Basel)* 2017; **12**: 238-242 [PMID: 29070987 DOI: 10.1159/000477536]

10 **Wu YT**, Chen ST, Chen CJ, Kuo YL, Tseng LM, Chen DR, Kuo SJ, Lai HW. Breast cancer arising within fibroadenoma: collective analysis of case reports in the literature and hints on treatment policy. *World J Surg Oncol* 2014; **12**: 335 [PMID: 25382741 DOI: 10.1186/1477-7819-12-335]

11 **Stavros AT**, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995; **196**: 123-134 [PMID: 7784555 DOI: 10.1148/radiology.196.1.7784555]

12 **Skaane P**, Engedal K. Analysis of sonographic features in the differentiation of fibroadenoma and invasive ductal carcinoma. *AJR Am J Roentgenol* 1998; **170**: 109-114 [PMID: 9423610 DOI: 10.2214/ajr.170.1.9423610]

13 **Salati SA**. Breast fibroadenomas: a review in the light of current literature. *Pol Przegl Chir* 2020; **93**: 40-48 [PMID: 33729177 DOI: 10.5604/01.3001.0014.5676]

14 **Hubbard JL**, Cagle K, Davis JW, Kaups KL, Kodama M. Criteria for excision of suspected fibroadenomas of the breast. *Am J Surg* 2015; **209**: 297-301 [PMID: 25682095 DOI: 10.1016/j.amjsurg.2013.12.037]

15 **Peng Y**, Xie F, Zhao Y, Wang S; Chinese Society of Breast Surgery. Clinical practice guideline for breast fibroadenoma: Chinese Society of Breast Surgery (CSBrS) practice guideline 2021. *Chin Med J (Engl)* 2021; **134**: 1014-1016 [PMID: 33859107 DOI: 10.1097/CM9.0000000000001462]

16 **Tsuchiya M**, Masui T, Terauchi K, Yamada T, Katyayama M, Ichikawa S, Noda Y, Goshima S. MRI-based radiomics analysis for differentiating phyllodes tumors of the breast from fibroadenomas. *Eur Radiol* 2022; **32**: 4090-4100 [PMID: 35044510 DOI: 10.1007/s00330-021-08510-8]

17 **Du Y**, Zha HL, Wang H, Liu XP, Pan JZ, Du LW, Cai MJ, Zong M, Li CY. Ultrasound-based radiomics nomogram for differentiation of triple-negative breast cancer from fibroadenoma. *Br J Radiol* 2022; **95**: 20210598 [PMID: 35138938 DOI: 10.1259/bjr.20210598]

18 **Zhang N**, Kang J, Wang H, Liu A, Miao Y, Ma X, Song Q, Zhang L, Wang J, Shen Z, Xu X. Differentiation of fibroadenomas *vs* malignant breast tumors utilizing three-dimensional amide proton transfer weighted magnetic resonance imaging. *Clin Imaging* 2022; **81**: 15-23 [PMID: 34597999 DOI: 10.1016/j.clinimag.2021.09.002]

19 **Li W**, Zhou Q, Xia S, Wu Y, Fei X, Wang Y, Tao L, Fan J, Zhou W. Application of Contrast-Enhanced Ultrasound in the Diagnosis of Ductal Carcinoma In Situ: Analysis of 127 Cases. *J Ultrasound Med* 2020; **39**: 39-50 [PMID: 31206200 DOI: 10.1002/jum.15069]

20 **Hooley RJ**, Durand MA, Philpotts LE. Advances in Digital Breast Tomosynthesis. *AJR Am J Roentgenol* 2017; **208**: 256-266 [PMID: 27786548 DOI: 10.2214/AJR.16.17127]

21 **Bayoumi D**, Sakrana A, Abdelhalim E. Role of multi-parametric MRI in the differentiation between mucinous breast carcinoma and fibroadenoma. *Egypt J Radiol Nucl Med* 2021; **52:** 260 [DOI: 10.1186/s43055-021-00622-x]

**Footnotes**

**Conflict-of-interest statement:** All theauthors report no relevant conflicts of interest for this article.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Unsolicited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** April 19, 2022

**First decision:** May 30, 2022

**Article in press:**

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** Turkey

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C

Grade D (Fair): D

Grade E (Poor): 0

**P-Reviewer:** Chen Q, China; Yang H, China **S-Editor:** Fan JR **L-Editor:** Filipodia **P-Editor:** Fan JR