CASE REPORT

Ductal carcinoma in situ of the breast arising in encapsulated mammary hamartoma ; A case report

Kansei Komaki[1], Mayumi Funagayama[2], Tomokazu Saitoh[2], Yorio Maeda[2], Toru Hayashi[3], Miyuki Kanematsu[4], and Akira Tangoku[4]

[1]Department of Breast Surgery, JA Tokushima Kouseiren Anan Medical Center, Anan City, Japan [2]Department of Breast Surgery and [3]Department of Pathology, Breastopia Miyazaki Hospital, Miyazaki, Japan and [4]Department of Thoracic, Endocrine Surgery and Oncology, Tokushima Graduated School, Tokushima, Japan

Abstract : Mammary hamartoma is benign lesion and relatively rare. 17 cases of breast cancer associated with a hamartoma had been previously documented in the literature. We describe herein a case of noninvasive ductal carcinoma of the breast arising in hamartoma in a woman of 60's. The discordance of images of the mass between mammogram and ultrasonogram can lead us to detect the carcinoma within the hamartoma in our case. J. Med. Invest. 67 : 368-371, August, 2020

Keywords **:** *Breast cancer, Mammary hamartoma, Ductal carcinoma in situ*

INTRODUCTION

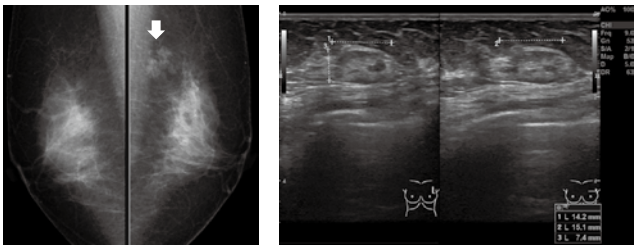
Mammary hamartoma is commonly shown an encapsulated mass containing fat and parenchymal densities in mammogram or ultrasonogram. Hamartoma is a distinct subtype of benign tumor, forming circumscribed or lobulated mass consisting of a mixture of fat tissue and normal parenchyma with fibrous stroma. Hamartomas are essentially disorganized overgrowth of normal mammary tissue, and they are named fibroadenolipoma or adenolipofibroma in other word. Stromal element of hamartoma uncommonly shows myoid change or muscle differentiation (1). Coexistence of breast carcinoma with a mammary hamartoma is extremely rare. Cases with hamartoma associated carcinoma had been reported in the literature (2-6). We describe a case of hamartoma from which ductal carcinoma in situ had arisen. In our case, ductal carcinoma in situ had developed within hamartoma and had limited to the region of hamartoma. The discordance between mammogram or ultrasonogram and CT image of the lesion had led us to do core needle biopsy of the lesion, and we were finally able to detect breast cancer in hamartoma. The report emphasizes the importance of adequate imaging analyses or tissue sampling of mammary hamartoma.

CASE REPORT

A woman of 60's had jointed to mass screening for breast cancer every other year. She is healthy except undergoing medication for hypertension. Her family history of breast pathology or hereditary disease is absent. As she was pointed out an abnormal shadow in her left mammography, she visited to the outpatient clinic for further examination. Ultrasonography and mammography were routinely done. Mammogram revealed an irregular and lobulated dense shadow in the upper-outer quadrant of left breast (Fig. 1a). Ultrasonogram revealed an oval tumor with heterogeneous internal echoes, representing the hamartoma (Fig. 1b). A physical finding revealed a firm, ill-defined, mobile, oval tumor with a smooth surface measuring 3 × 2 cm at the upper-outer quadrant of the left breast and no swelling of axillary lymph nodes. As the images of the lesion are quietly different between ultrasonogram and mammogram, the patient was examined MRI.

A T2-weighted MRI image revealed no emphasized mass. A T1-weighted dynamic MRI revealed irregular and lobular mass, measuring 15 mm and being shaped like mammographic image (Fig. 1c). Dynamic curve of MRI imaging showed steep and constant pattern. From MRI image the lesion was thought to be malignancy, such as scirrhous type of ductal carcinoma or noninvasive carcinoma.

Core needle biopsy using ultrasonography was performed. Two specimens were collected. Microscopically, cancer cells which were medium-sized to large nuclei filled many ducts and proliferated in flat, solid and comedo pattern (Fig. 2a and 2b). Diagnosis of the lesion was ductal carcinoma in situ of the breast. Preoperative CT study showed the lesion in her left breast, be emphasized lobular shadow within an oval mass (Fig. 1d). It



1a 1b

Fig 1a. Mammogram revealed an irregular and lobulated dense shadow (arrow) in the upper-outer quadrant of left breast.
Fig 1b. Ultrasonogram revealed an oval tumor with heterogeneous internal echoes, which was 15.1×14.2×7.4 mm in size, representing the hamartoma.

Abbreviations
CT : Computed Tomography, MRI : Magnetic Resonance Image

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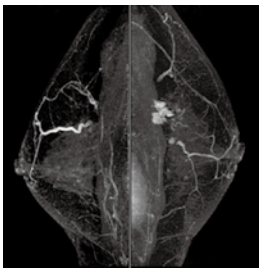
Address correspondence and reprint requests to Kansei Komaki, Department of Breast Surgery, JA Tokushima Kouseiren Anan Medical Center, Kawahara 6-1, Takarada-cho, Anan City, Tokushima, 774-0045, Japan.



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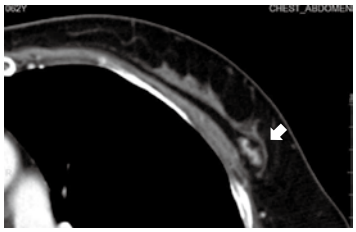
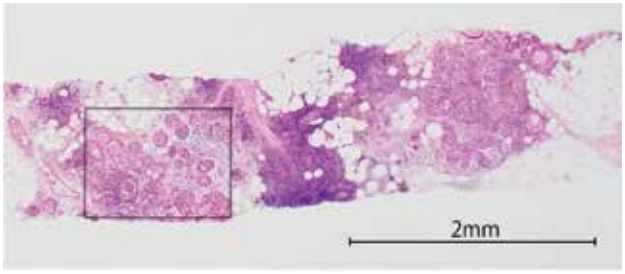
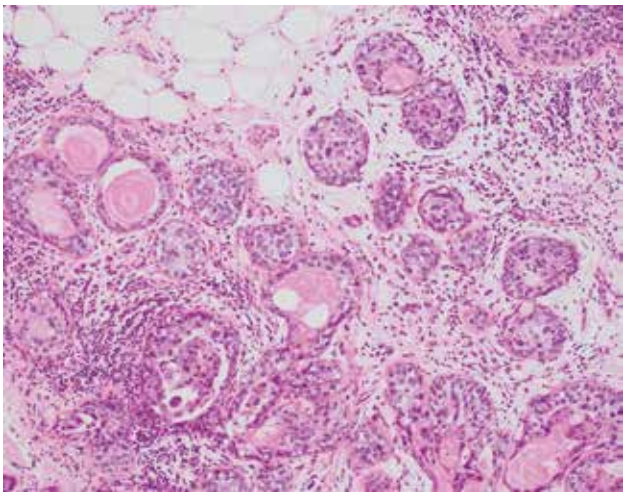


1d

Fig 1c. T1-weighted dynamic MRI revealed irregular and lobular mass, measuring 15mm and being shaped like mammographic image.
Fig 1d. Preoperative CT study showed the lesion in her left breast, be emphasized lobular shadow within an oval mass (arrow).



2a



2b

Fig 2a. CNB specimen (low power field) : Cancer cells filled many ducts showing solid and partially comedo pattern.
Fig 2b. High power field of boxed area of Figure 2a.

might be thought that lobular-shaped malignant lesion had extended within the circumscribed mass.

The patient underwent a partial glandectomy and also sentinel nodes biopsy. No metastasis to a sentinel lymph node was proven by OSNA (One-step nucleic acid amplification) assay for intra-operative detection of lymph node metastasis. The lesion was resected with surrounding normal tissue. The specimen of the breast was fixed in buffered formalin, and it cut into eleven slices having 6 mm width. In the 7th slice, capsuled yellowish mass in which grey and slightly firm area was observed in the mass was collected (Fig. 3). Postoperatively, the patient has been doing well for several months.

Pathology

Microscopically, Hamartoma composed of mature fat tissue with scattered mammary ducts and lobules with clear encapsulation by delicate fibrous tissue included ductal carcinoma in situ inside (Fig. 4a). The cancer cells have high grade nuclei with central necrosis (Fig. 4b). The spreading of cancer cell was 13 × 4 mm, and hamartoma was 22 × 7 mm in size.

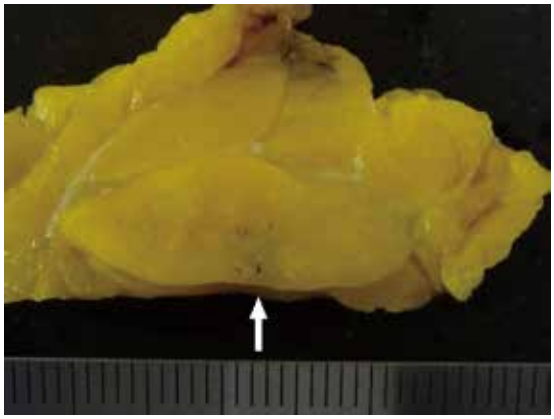
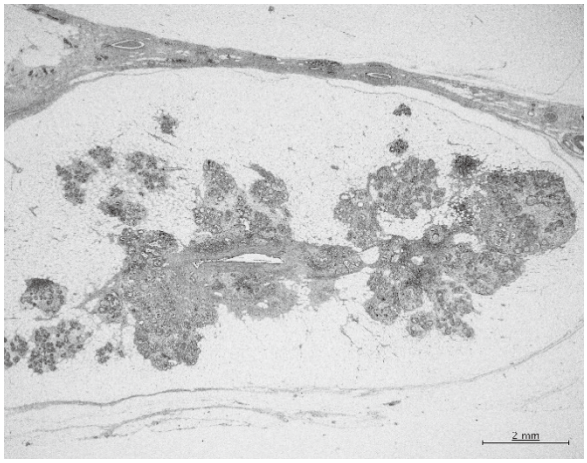
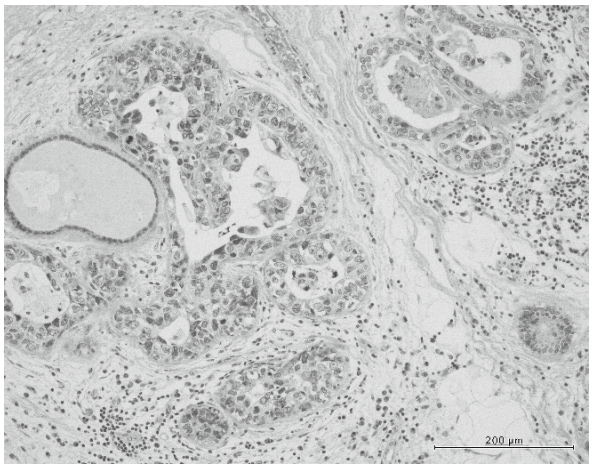


Fig 3. Cutsurface of the tumor : In the 7th slice, capsuled mass was collected in which grey and slightly firm area (arrow) was observed.



4a



4b

Fig 4a. Low power magnification : Mass including ductal carcinoma in situ inside was encapsulated by delicate fibrous tissue.
Fig 4b. High power magnification : Cancer cells have high grade nuclei with central necrosis.

Immunohistochemistry

Immunohistochemically, the cancer cells were both negative for estrogen and progesterone receptors, and human epidermal growth factor receptor type 2 (HER2/neu) protein expression was also negative. Some parts of cancer cells show immunoreactivity for epidermal growth factor receptor (EGFR) with cell membrane staining pattern, and they were negative for CK5/6. The carcinoma was considered as basal cell type carcinoma.

DISCUSSION

The first description of mammary hamartoma had been written by Hogeman and Ostberg in their report in 1968 (7). Mammary hamartoma is circumscribed lesion composed of disorganized overgrowth of normal breast tissues, and showing various composition of ductal and lobular epithelium and stromal elements. Hamartoma is often named as fibroadenolipoma or adenolipofibroma. The pathogenesis of the development of mammary hamartoma is not fully clear. Sevim and Kocaasy et al. reported a clinicopathologic analysis of 27 cases of hamartoma including one myoid hamartom, and mentioned the mean age and tumor size of them was 41.8 years and 3.9 cm, respectively, and described that breast hamartoma approximately accounts for 5% of all benign breast lesion (8). Mammary hamartomas have a typical area of radiolucent and smooth edges in mammography where fat and various amounts of fibrous and adenomatous tissues were shown. Although radiologic feature is characteristic, Helvie et al. reported that 29% of the tumors in their study could not be detected on mammography (9). Typical ultasonogram of hamartoma showed sonolucent fat and a heterogenous internal echoes. Images of several diagnostic procedure of hamartoma are reflected their pathologic structures. Although pathologic diagnosis and treatment are completely able to make by excisional biopsy of the lesion, pathologic diagnosis cannot be always done by ultrasonograpy-guided core needle biopsy because of above mentioned internal texture of hamartoma. Herbert et al. reported immunohistochemical studies of 24 breast hamartoma cases, in which all cases showed estrogen and progesterone receptors positivity in epithelial cells as well as in the stromal cells and no HER2/neu positivity were noted in these cases (10). Breast cancer associated with hamartoma is rare. Mendoiola et al. had described the first case report of a malignant lesion associated with hamartoma in 1982 (2). Nami et al. had reported 15 cases with coexistence of breast cancer and hamartoma (11) , and after the report Kai and Fukai were described a new case of carcinoma arising in mammary hamartoma in 2012 (12) and 2018 (13), respectively. Among the 17 cases past, 13 cases had carcinomas inside of the hamartoma. Cases involving both the hamartoma and adjacent normal breast tissue are difficult to judge whether carcinoma arose in hamartoma or carcinoma invaded to hamartoma. Our case was believed that carcinoma had arisen in hamartoma because carcinoma in situ completely had located within the encapsulated hamartoma. Among the past 17 cases, types of carcinoma associated with hamartoma are 1 combination of lobular and ductal, 1 mucinous, 4 lobular and 11 ductal, and cases with noninvasive carcinoma associated are only 3 cases. And among them, molecular subtype of cancer was indicated in only two cases, that is, one (12) showed both negative for estrogen and progesterone receptors, and HER2/neu negative same as our case, and the other (13) showed estrogen receptor weakly positive, progesterone receptor negative, and HER2/neu positive. Early detection of a minimal malignant change in the hamartoma is an important point. Nami et al. descried that cluster of microcalcifications, pleomorphic microcacifications and spiculated masses were typical sign for coexistence of breast cancer in hamartoma (11). Sclerosing adenosis often shows architectural distortion and is recently well known as the lesion of developing breast cancer (14) . Fukai et al. reported a case in which ductal carcinoma in situ arose in sclerosing adenosis encapsulated by a hamartoma (13). It is important to perform periodical observation even if the prior diagnosis was benign hamartoma, and revelation the discordance of the lesion in each image, such as mammography, ultrasonography or MRI is also important to discover malignancies. In our case, image of lesion by mammography or MRI was differ from that by ultrasonography. Cowden syndrome is a disorder condition characterized by multiple noncancerous, tumor-like growths called hamartomas and an increased risk of developing breast cancer, thyroid cancer or GI tract cancers and it thought to related mutations in the PTEN gene (15). Although genetic analysis was not done in our case, breast cancer occurred in the case revealed basal cell like cancer. Although there are no reports discussed the genetic mechanism of mammary hamartoma, it may exist a certain mechanism of carcinogenesis related gene abnormality with occurring carcinoma in hamartoma. Genetic abnormalities of carcinomas in hamartoma should be analyzed in future.

CONSENT FOR PUBLICATION

All presentations in current manuscript were granted consent to publication from the patient by the documentation.

AUTHORS' CONTRIBUTION

KK, FM, YM, MK and TS analyzed and interpreted the patient's data and examination findings. FM is surgeon who performed treatments for this patient. TH contributed pathologic study in the case. The manuscript was prepared by KK under the supervision of AT and TH. All authors read and approved the final manuscript.

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