Breast Hamartoma With Invasive Ductal Carcinoma
Report of Two Cases and Review of the Literature

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SUMMARY
Two cases of well-defined masses also containing clinical and radiographical abnormalities suggestive of malignancy, subsequently found to be invasive ductal carcinomas in breast hamartomas are described. The patients were 53 and 78 years old. Both presented with a generally soft palpable breast lump, containing a firm area which in one case invaded and ulcerated the skin. Mammography demonstrated two typical hamartomas: one containing a spiculated opacity, the other irregular opacities with suspicious calcifications, suggesting the presence of carcinomas in these benign lesions. The cut surface of these well-circumscribed masses measured 5cm and 7cm. The microscopic appearance was characteristic of breast hamartoma (sharp circumscribed “pseudocapsule” surrounding breast fibrocystic changes with variable amounts of adipose tissue) with the firm area in each case corresponding to invasive ductal carcinoma. In one case the invasive ductal carcinoma was confined to the hamartoma, whereas in the other malignant tumor, cells extended beyond the surrounding breast tissue and infiltrated the skin. These findings raise the question of secondary involvement of a hamartoma by invasive carcinoma. Breast hamartomas are probably underrecognized lesions. In our view, these findings do not justify a more aggressive approach towards the management of breast hamartomas.

Introduction
Breast hamartoma is an uncommon benign lesion which is frequently found on mammography. Macroscopically it is seen as a well-circumscribed tumor. Microscopically, it is composed of a variable mixture of epithelial, fat and fibrous elements. It is not entirely unexpected that the epithelial component may undergo malignant changes. However, only two cases of in situ malignant transformation in hamartoma have been reported. The incidence of breast hamartoma is not known. Many hamartomas probably remain undiagnosed, however we might expect that the widespread use of screening mammography would lead to an increase in the number of cases recognized. As in fibroadenomas with a reported incidence of 0.1% of malignant change, it is likely that carcinoma arising in hamartoma is a coincidental finding.

Results
Case One
A 78 year-old woman was admitted with the diagnosis of a right breast tumor. Mammography demonstrated a typical mostly fatty hamartoma, containing an area of irregular glandular tissue with very suspicious calcifications (Fig. 1). On examination a soft well-circumscribed partially indurated mass was
Table 1. Gross pathologic findings

<table>
<thead>
<tr>
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<th>Case one</th>
<th>Case two</th>
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<tbody>
<tr>
<td>Hamartoma (size)</td>
<td>7 cm</td>
<td>5 cm</td>
</tr>
<tr>
<td>Hamartoma (color)</td>
<td>yellow</td>
<td>off white</td>
</tr>
<tr>
<td>Hamartoma (texture)</td>
<td>soft</td>
<td>rubbery</td>
</tr>
<tr>
<td>Cancer area (size)</td>
<td>3 cm</td>
<td>2 cm</td>
</tr>
<tr>
<td>Cancer area (texture)</td>
<td>firm nodule</td>
<td>firm subcapsular nodule</td>
</tr>
</tbody>
</table>

Pathology

Both lesions were well defined masses with smooth glistening surface (Fig. 2a, 2b and 2c). The gross pathological findings are summarized in Table 1. In case one the large firm area disrupted the capsule of the hamartoma invading the surrounding tissue and the skin. Microscopically the main masses were surrounded by a thin layer of "normal compressed tissue." In the masses some lobules were normal although the majority presented fibrocystic changes with variable amounts of adipose tissue (Fig. 3a, 3b and 3c). The firm area observed on macroscopic examination corresponded to an invasive ductal carcinoma within the hamartomas (Fig. 4a, 4b, 4c, 4d and 4e). Tumor cells infiltrated the stroma almost reaching the surface of the hamartoma in case two. In case one the surrounding breast tissue and skin were infiltrated. Tumor cells were large and arranged in solid clusters. Nuclei were pleomorphic and nucleoli were prominent in some cells. Ductal in situ carcinoma (DCIS) within the hamartoma was identified at the periphery of the invasive area of case one (Fig. 5a and 5b). According to the recently proposed classification, features (solid growth pattern with central luminal necrosis, pleomorphism of the nuclei) were consistent with poorly differentiated DCIS. We have not observed any DCIS features in the breast tissue far from the hamartoma. Immunohistochemistry showed that tumor cells were negative for estrogen and progesterone receptors. There were no lymph node metastasis in the axillary dissections.

Discussion

Breast hamartoma is a slow growing tumor which occurs at all ages after puberty. It is a rare benign breast lump, and clinical diagnosis may be difficult as on palpation the lesion has a similar consistency to breast tissue. Since the definition of the histological criteria of breast hamartoma in 1971 and the description of the radiological signs in 1978, a total of 216 cases, including our cases, have been reported. All patients were female. In one case the hamartoma occurred in an ectopic breast in the inguinal region. This certainly widely underestimates the frequency.
Fig. 2. a) Case one: the hamartoma is in the center of the sample. A part of carcinoma area is seen in the upper zone (arrow). - b) Case two: gross appearance of the hamartoma. The surface is smooth. The cut surface (c) is white. A subcapsular area of carcinoma is observed (arrows).
Fig. 3. a) Case one: breast hamartoma consisting largely of mature fat. Isolated lobules present fibrocystic changes. H.E. × 90. - b) Case two: peripheral portion of the breast hamartoma. Note the sharp delimitation from the surrounding tissue. H.E. × 28. - c) Same case: glandular tissue shows fibrocystic changes. H.E. × 125.
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of this lesion as a review of our records reveals more than 60 cases. The microscopic findings in breast hamartoma are no different to those of fibrocystic changes of the breast. However, the presence at the periphery of "normal compressed tissue" is the clue to the diagnosis. It is impossible to give a histological diagnosis of hamartoma if the surgical specimen is received in pieces. The macroscopic appearance depends on the quantity of adipose tissue. It can constitute in rare cases more than 50% of the whole mass. In the cases we have described there was a noticeable difference in the proportion of fatty tissue.

Few cases of breast hamartomas with epithelial hyperplasia with or without atypia have been re-

Fig. 4. a–b) Case one: low power view showing the circum­scriptio­n of the lesion. The area corresponding to an invasive ductal carcinoma is clearly seen and is illustrated at high magnification (b). H.E. × 27; × 320. – c–d) Case two: low power view. Dark area corresponds to an invasive ductal carcinoma illustrated at high magnification (d). H.E. × 8.9; × 213.
ported and only one case associating atypical lobular hyperplasia and cancer have been described. We cannot explain why epithelial hyperplasia is rare in breast hamartomas. However, it is interesting to note that in fibroadenomas where atypical epithelial hyperplasia can occur, at least 225 carcinomas have been reported.

Amongst the 214 previous breast hamartomas reported in the literature only two have been described containing carcinoma. Interestingly both cases presented in situ lesions: respectively, a lobular carcinoma in situ and a lobular carcinoma in situ with foci of microinvasive lobular carcinoma. To our knowledge invasive ductal carcinoma has never been previously described in breast hamartoma. Its occurrence seems to be a coincidental finding, as is also observed in fibroadenoma. In our case two the invasive ductal carcinoma is confined to the hamartoma with histologically confirmed cancer-free margins. The patient is alive with no evidence of recurrent disease at a follow-up period of seven years. No focal or suspicious lesion was identified in the last mammographic control (June 1995). In case one carcinoma extended beyond the hamartoma to invade the adipose tissue and the skin. It is not possible to exclude secondary involvement of the hamartoma by invasive ductal carcinoma, though the presence of a ductal in situ carcinoma at the periphery of the invasive part within this hamartoma and the absence of DCIS in the normal breast tissue away from the hamartoma is in favor of the invasive ductal carcinoma arising in the hamartoma. Since a hamartoma can be considered a "breast in the breast," it could conceivably contain any breast pathology. In our cases, these carcinomas were macroscopically evident, whereas in the two previously reported cases, the carcinomatous foci (lobular carcinoma in situ and lobular carcinoma in situ with foci of microinvasive lobular carcinoma) were microscopic findings. This stresses the need for adequate macroscopic examination of benign breast lesion and for adequate sampling for histology. As breast hamartomas have such distinctive appearances on mammography as compared with other breast lesions, it has been proposed that no surgical therapy is required. However, if the diagnosis is uncertain or the patient complains of discomfort, then surgery is indicated. We do not believe that because of our cases a more aggressive approach towards the management of breast hamartomas is required.

Material and Methods

In both cases the specimens were photographed and fixed in 4% buffered formalin solution. Multiple samples of specimen one and the whole mass of specimen two were embedded in paraffin and stained with hematoxilin and eosin. For hormonal receptors assessment additional paraffin-embedded sections were also studied with monoclonal antibodies (estradiol and progesterone) using methods previously described.

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References

Fig. 5. a) Case one: low power view of intraductal carcinoma adjacent to invasive part (out of the field). Note the solid growth pattern with central luminal necrosis on the left. H.E. x 41. - b) The high power shows marked nuclear pleomorphism and autophagocytosis. H.E. x 297.

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