Nerve Invasion by Epithelial Cells in Benign Breast Diseases

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Nerve invasion by glandular epithelial cells in a lesion is usually regarded as invasive carcinoma. However, some benign conditions in the pancreas, prostate, breast and other organs may show involvement of nerve bundles by benign epithelial cells. We report an 18-year-old female with nerve invasion in benign breast disease. The lesion in her right breast revealed fibrocystic changes with ductal hyperplasia and stromal sclerosis. Perineural and intraneural involvement by bland-looking small ducts lined by 2 layers of cells including an outer layer of myoepithelial cells were found, suggestive of benign nerve invasion. There was no evidence of malignant cells in any of the sections. The patient remains well after 31 months of follow-up. About 44 cases of nerve invasion in benign breast diseases have been reported in the literature. It is necessary to carefully evaluate nerve involvement in breast lesions to avoid over-diagnosis and inappropriate operation. [J Chin Med Assoc 2009;72(3):150–152]

Key Words: benign breast diseases, nerve invasion

Introduction

The neoplastic cells of invasive carcinomas in most organs may invade to adjacent lymph nodes, blood vessels and nerves. Epithelial cells in nerves are usually considered malignant. However, epithelial cells may be found in the nerve bundles in some benign conditions in a variety of organs including the pancreas,¹ prostate,² gallbladder,³⁴ skin,⁵⁶ and breast.⁷⁻¹⁴ We report a case showing fibrocystic changes with epithelial hyperplasia, stromal sclerosis and benign nerve invasion by epithelial cells in the right breast of an 18-year-old female.

Case Report

The patient was an 18-year-old female who visited our outpatient department with the chief complaint of painless nodular lesions in bilateral breasts. She had a past history of left breast fibroadenoma removed 17 months before this admission. After admission, excision of the nodules from bilateral breasts was performed. Sections of the lesion from the left breast showed a well-defined fibroadenoma with morphology similar to the previous tumor in the patient’s left breast. Two pieces of tissue from her right breast were submitted fresh for intraoperative frozen section, and 5 subsequent pieces were received in formalin for pathology examination. The breast tissue was firm, with no tumor mass identified grossly. Histology of the lesion from the right breast revealed fibrocystic changes with ductal epithelial hyperplasia and stromal sclerosis (Figure 1). Most impressive of all was the presence of perineural and intraneural invasion by small groups or ductules lined by 2 layers of bland-looking epithelial cells (Figures 2 and 3).

Both layers of cells were cytokeratin (AE1/AE3)-positive. The outer layer of cells was smooth muscle actin- and p63-positive myoepithelial cells (Figure 4), which represented benign ductal proliferation. No diagnostic malignant cells were found in the tissue sections. After excision of bilateral breast lesions, the patient was well after 31 months of follow-up.

Discussion

Nerve invasion by epithelial cells in a lesion usually represents invasion of malignant cells to the nerve
bundles adjacent to carcinomas. In some cancers, nerve invasion is one of the prognostic factors. Occasionaly, a variety of benign conditions in different organs may show nerve invasion, such as chronic pancreatitis, benign prostate, hyperplastic or metaplastic glands of gallbladder, cellular capillary hemangiomas and reactive lesions of the skin and benign diseases of the breast.

The first reported case of nerve invasion in a benign breast lesion was by Ackerman in 1957. Ten years later, Taylor and Norris reported 20 cases out of 1,000 consecutive breast biopsies showing epithelial invasion of nerves in benign diseases of the breast. Seventeen patients received only biopsy and 3 had radical mastectomy. All patients were alive and well, with a median follow-up interval of 7 years. Since then, about 23 cases have been reported in the literature (Table 1). The breast lesions in these 23 cases were cysts, adenosis, papillomatosis, oncocytic metaplasia, periductal inflammation, radial scars, atypical ductal hyperplasia, florid hyperplasia and ductal adenoma with epithelial cells involving nerve bundles. The percentage of nerve invasion in these reports ranged from 0.14% to 3.2%.

The etiology of nerve invasion in benign diseases is uncertain. A small number of cases had previous trauma or excision at the same site. The association of ductal hyperplasia and papillomatosis suggests active growth of benign epithelium around or into the nerve bundles.
The presence of nerve invasion by bland-looking glands in breast diseases does not necessarily indicate invasive carcinoma. Further immunostaining is helpful to identify the 2 types of epithelial cells, including myoepithelial cells within the nerve, to confirm the benign nature of the lesion. Beside benign breast diseases, 4 cases of ductal carcinoma in situ (DCIS) associated with neural invasion were also reported (Table 1).12,16 The epithelial cells surrounding or in the nerve bundles were similar to adjacent DCIS with myoepithelial cells at the edge. These neural-invasive DCIS did not represent invasive carcinoma.

In conclusion, nerve invasion by bland epithelial cells in breast lesions without diagnostic malignant cells should be evaluated carefully to avoid over-diagnosis and inappropriate operation.

References


### Table 1. Number of cases with nerve invasion in benign breast diseases and ductal carcinoma in situ reported in the literature

<table>
<thead>
<tr>
<th>Authors, Year [Ref]</th>
<th>Benign disease</th>
<th>DCIS</th>
<th>Cases reviewed</th>
<th>Percent</th>
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<tr>
<td>Ackerman, 1957 [7]</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Taylor &amp; Norris, 1967 [8]</td>
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<tr>
<td>Davies, 1973 [9]</td>
<td>4</td>
<td>316</td>
<td>1.3</td>
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<td>Tsang &amp; Chan, 1992 [16]</td>
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<td>Gobbi et al, 2001 [12]</td>
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<td>3</td>
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<td>Fellegara &amp; Kuhn, 2007 [14]</td>
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<td>Total</td>
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