Case Report
Secretory breast carcinoma: a report of two cases misdiagnosed on frozen section

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Abstract: Secretory breast carcinoma (SBC) is an extremely rare but distinctive subtype of malignant breast tumor. Herein, we represent two cases of SBC. The morphologic characters of the two cases showed three distinctive histological characters: granular eosinophilic cytoplasm, intracellular/extracellular secretions and prominent fibrous septa among tumor nest. They were misdiagnosed as benign hyperplasia or neoplasm by intraoperative frozen section analysis. Appearance of coagulative necrosis in frozen section could contribute to the diagnosis for malignant tumor. Careful radiological and histopathological examination is also required to arrive at an accurate diagnosis. Total tumor removal can usually be achieved with an appropriate surgical technique.

Keywords: Secretory breast carcinoma, intraoperative frozen section examination, immunohistochemistry, molybdenum-target X-ray photography

Introduction

Secretory breast carcinoma (SBC) is an extremely rare but distinctive subtype of malignant breast tumor [1]. It accounts for less than 0.1% of all cases of invasive breast cancer [2, 3]. Unlike most of the carcinomas which are prone to occur at old ages, SBC has a wide range of age of onset from 3 to 87 years [4]. It was originally described in children and termed as ‘juvenile breast carcinoma’ [5]. The histopathologic character of this tumor is that it consisted of large amounts of intracellular and extracellular secretory material and it is not limited to juvenile, so it was re-termed secretory breast carcinoma [6].

It has been reported that secretory breast carcinoma harbor the balanced t(12;15)(p13;q25) translocation which leads to the expression of the ETV6-NTRK3 fusion gene [7, 8]. The histopathologic character, together with this distinctive fusion gene, indicates that SBC is a unique breast adenocarcinoma.

We report two cases of SBC with both coagulative necrosis and prominent fibrous bands except the distinctive character of secretory and eosinophilic cytoplasm. Coagulative necrosis has not been mentioned in the previous literatures.

Case report

Case one

A 58-year-old female presented with a lump in the left breast which was found six years ago and grew gradually from 1 cm to about 6 cm in diameters. Molybdenum-target X-ray photography showed two 5.3×6.7 cm and 5.8×6.0 cm well-circumscribed subareolar nodes in left breast. Breast ultrasonography revealed a 7.7×5.2 cm, well-circumscribed, irregularly-shaped, cystic and solid mixed echo nodule in the left breast.

Core needle biopsy was performed and the specimen was sent for pathology inspection. Microscopically, the normal breast structure was destroyed and displaced by fibrocollagenous tissue with numerous acute and chronic mixed inflammatory cell infiltrating. Coagulative necrosis and hemosiderin could easily be...
Secretory breast carcinoma was diagnosed as inflammatory fibrinous hyperplasia with local necrosis. The surgeon considered that malignancy can’t be totally excluded and performed a lumpectomy. It was diagnosed by intraoperative frozen section evaluation as benign lesion while the final diagnosis was SBC by routine histological analysis because of the appearance of extracellular and intracellular secretory material. Currently, the patients are disease free after a follow-up period of 17 months.

Case two

A 56 year old woman presented with a painless lump in the left breast in 2009. Physical examination showed a 2 cm in diameters, 2 cm from the nipple, well-circumscribed, mobile mass on the upper outer quadrant. An axillary lymph node approximately 1.5 cm was palpable. No discharge was found from the nipple. Molybdenum-target X-ray photogtaphy showed a large irregular, high-density mass with indistinct margin in the areola area of left breast, which size is about 8.3 cm×6.3 cm, but without calcification. Some imaging features were seen, such as trabecular thickening, nipple retraction, skin thickening and axillary adenopathy. Lumpectomy was performed under local anesthesia. A 2 cm, firm lump with irregular borderline was excised and sent for frozen section examination. It was diagnosed as benign neoplasm. SBC was diagnosed by routine histological analysis because of the appearance of extracellular and intracellular secretory material. Modified radical mastectomy with axillary and sentinel lymph node dissection was further performed. Currently, the patients are disease free after a follow-up period of 8 years.

Pathological findings

The morphologic characters of the two cases are similar. Tumor cells are arranged in solid, microcyst and macrocyst pattern (Figure 1A, 1B). There are abundant eosinophilic secretory material seen. It was diagnosed as inflammatory fibrous hyperplasia with local necrosis. The surgeon considered that malignancy can’t be totally excluded and performed a lumpectomy. It was diagnosed by intraoperative frozen section evaluation as benign lesion while the final diagnosis was SBC by routine histological analysis because of the appearance of extracellular and intracellular secretory material. Currently, the patients are disease free after a follow-up period of 17 months.

Figure 1. Histopathological images of case one (H&E stain). A. Low power view of the primary tumor (original magnification ×100). B. Low power view of the primary tumor (original magnification ×100). C. Patchy coagulative necrosis can be seen (Blue arrow) (original magnification ×100). D. Hemosiderin is locally scattered (Blue arrow) (original magnification ×100).

Figure 2. Histopathological images of case two (H&E stain). A. Low power view of the primary tumor (original magnification ×200). B. High power view of the primary tumor (original magnification ×400). C. The macrocysts with red secretions look like thyroid follicles, even absorption vacuoles were also seen (original magnification ×400). D. Patchy coagulative necrosis can be seen (Blue arrow) (original magnification ×100).
Secretory breast carcinoma

Table 1. Main clinical parameters of 12 cases of SBC reported

<table>
<thead>
<tr>
<th>Author</th>
<th>Age/Sex</th>
<th>Duration symptoms</th>
<th>Size (mm)</th>
<th>Axillary status</th>
<th>Morphological</th>
<th>Treatment</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montalvo [14]</td>
<td>79/F</td>
<td>3 months</td>
<td>17×15</td>
<td>ND</td>
<td>Tubular/solid/microcystic</td>
<td>LE</td>
<td>NED 6 years</td>
</tr>
<tr>
<td>Ding [15]</td>
<td>24/M</td>
<td>4 months</td>
<td>25×20</td>
<td>+(1/26)</td>
<td>Microcystic</td>
<td>MRM+CT</td>
<td>ND</td>
</tr>
<tr>
<td>Li [16]</td>
<td>41/M</td>
<td>40 years</td>
<td>60</td>
<td>-(0/29)</td>
<td>Microcystic</td>
<td>RM+CT</td>
<td>NED 58 months</td>
</tr>
<tr>
<td>Lombardi [17]</td>
<td>50/F</td>
<td>ND</td>
<td>15</td>
<td>ND</td>
<td>Cystic/microcalcification</td>
<td>LE+RT</td>
<td>ND</td>
</tr>
<tr>
<td>Cabello [18]</td>
<td>13/M</td>
<td>4 years</td>
<td>15×6</td>
<td>+(1/28)</td>
<td>Glanulda/cribriform/microcystic</td>
<td>SM+AC+CT</td>
<td>NED 10 years</td>
</tr>
<tr>
<td>Tixier [19]</td>
<td>14/F</td>
<td>7 years</td>
<td>26×18</td>
<td>+(1/11)</td>
<td>ND</td>
<td>LE</td>
<td>RC+LM 15 years</td>
</tr>
<tr>
<td>Yorozuya [20]</td>
<td>9/F</td>
<td>2 years</td>
<td>15×13</td>
<td>-(0/4)</td>
<td>ND</td>
<td>SM+SLND</td>
<td>NED 1 year</td>
</tr>
<tr>
<td>Vieni [10]</td>
<td>33/F</td>
<td>4 months</td>
<td>15</td>
<td>+(1/19)</td>
<td>Solid/tubular/fibrous bundles</td>
<td>UQOE+AC+CT+RT</td>
<td>NED 7 years</td>
</tr>
<tr>
<td>Yaqoo [21]</td>
<td>60/F</td>
<td>2 years</td>
<td>100×80</td>
<td>+(1/1)</td>
<td>Glanulda/Solid</td>
<td>SM</td>
<td>ND</td>
</tr>
<tr>
<td>Arce [22]</td>
<td>52/M</td>
<td>10 years</td>
<td>70×50</td>
<td>+(2/24)</td>
<td>Microcystic</td>
<td>LE</td>
<td>RC+LM 15 months</td>
</tr>
<tr>
<td>Our case 1</td>
<td>58/F</td>
<td>6 years</td>
<td>67×53</td>
<td>-(0/28)</td>
<td>Solid/microcystic/macrocyts/fibrous bundles/necrosis</td>
<td>MRM+AC+CT</td>
<td>NED 17 months</td>
</tr>
<tr>
<td>Our case 2</td>
<td>56/6</td>
<td>ND</td>
<td>20</td>
<td>-(0/16)</td>
<td></td>
<td>MRM+AC+CT</td>
<td>NED 8 years</td>
</tr>
</tbody>
</table>

Abbreviation: F, indicates female; M, male; ND, not described; LE, Lumpectomy; MRM, modified radical mastectomy; RM, radical mastectomy; SM, simple mastectomy; AC, axillary clearance; SLND, sentential lymph node dissection; CT, chemotherapy; RT, radiotherapy; NED, no evidence of disease; RC, recurrence; LM, lung metastasis.

Discussion

The main clinical symptoms of SBC include slowly growing and painless mass in the breast or bloody nipple discharge with or without a palpable mass. The tumor can localize at any part of breast, usually subareolar or near the nipple. Ultrasonography of breast shows hypoechoic or isoechoic mass with a mixed cystic-solid pattern. Grossly, SBC is usually a firm, lobulated, well-circumscribed, gray white to tan brown mass [9]. Although rare, it has been reported that about 15% of the patients have nodal involvement at presentation [10, 11]. We summarized 10 cases of SBC published from the year 2004 to 2016, together with the 2 cases we report in Table 1 [10, 14-22]. The age range from 9 to 79 years with the median age of 41 years. We can infer that SBC is an iner near carcinoma, 7 patients (58%) had symptoms duration more than 2 years, one of whom reached 40 years before operation. Some of these cases were disease free after long time follow-up even the patients had lymph node metastasis at the time of operation. Only 2 cases recurrenced and had lung metastasis.

Histologically, SBC has three distinctive histological characters: granular eosinophilic cytoplasm, intracellular/extracellular secretions and prominent fibrous septa among tumor nest. Prominent fibrous septa can be seen in our two cases and 6/8 cases reported by Din et al. [9]. Other case reports also mentioned this character in SBC [4, 12]. The existence of fibrous bands may be due to low invasive potential of SBC, suggesting its indolent biologi cal behavior. However, granular eosinophilic cytoplasm and secretions are not obvious in frozen section. So SBC is prone to be misdiag nosed by intraoperative frozen section analysis. Detection of coagulative necrosis in frozen section could contribute to the diagnosis for malignant tumor.

Immunohistochemically, most cases reported are triple (ER, PR, Her-2) negative but express basal cell markers as CK14, CK5/6 and EGFR. The tumor usually shows strong reactivity for S-100. Little cases are positive for ER/PR, consistent with the cases described in our study [13]. The secretions showed positive staining for PAS, D-PAS and Alcian blue.
Focal infiltrate margin and absent of myoepithelial can distinguish SBC from benign conditions as lactation adenoma, juvenile papillomatosis with apocrine metaplasia, and lactating lobules. SBC should also be differentiated with acinic cell carcinoma, apocrine carcinoma and cystic hypersecretory carcinoma. In a few extreme conditions, SBC may be confused with thyroid carcinoma. Ganesh et al. report a case of SBC in a middle aged woman who had undergone treatment for papillary carcinoma of thyroid 10 years ago [13]. In this condition, the marker TG may be helpful to distinguish SBC with metastasis thyroid carcinoma. Certainly, if the ETV6-NTRK infusion gene is detected, it will be easy to differentiated SBC with its mimics.

In conclusion, SBC are rare in the breast, so this diagnosis is usually misdiagnosed by intraoperative frozen section analysis. Careful radiological and histopathological examination is required to arrive at an accurate diagnosis. Total tumor removal can usually be achieved with an appropriate surgical technique.

Disclosure of conflict of interest

None.

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