Case Report
Granular cell tumor of the male breast: a case report and review of literature

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Abstract: Granular cell tumor of the breast is an extremely rare tumor which occurs in men. We reported a rare case of a male breast granular cell tumor and a review of the literature. A 43-year-old Asian man presented with a painless mass in his left breast two weeks ago. Clinically, this single, painless and immobile mass was resembled breast carcinoma. The patient underwent lumpectomy of left breast mass. Histopathologic staining best differentiates breast granular cell tumor from other breast tumors with their positive staining for S-100, vimentin, inhibin-α and CD68 and negative for cytokeratin (CK), CD34 and smooth-muscle actin (SMA).

Keywords: Granular cell tumor, breast carcinoma, immunohistochemistry

Introduction
Granular cell tumor (GCT) is a relatively rare soft tissue tumor with neurogenic origin which mostly occurs in tongue, head and neck. It can also occur in any sites of the body, such as skin, subcutaneous tissue, respiratory tract, gastrointestinal tract and genital tract [1, 2]. Granular cell tumor of the breast (GCTB) only accounts for 5% to 15% of GCT and [3]. The majority of GCTB were seen in African-American women which range from 30 to 50 years old [4]; however, 6.6% of GCTB occur in men [5]. As GCT often appeared to be a single, painless and immobile mass, which resembled breast cancer through clinical and imaging examinations, the diagnosis of GCT is really a challenge for clinicians. Up to the present, pathological examinations are the most frequently used and definite method for the final diagnosis of GCT. Herein, we reported a rare case of male benign GCTB which mimicked breast cancer by clinical examinations and imaging findings.

Case report
A 43-year-old Asian man presented with a painless mass in his left breast two weeks ago. Breast examination showed a palpable firm mass with poor mobility in the upper inner quadrant of the left breast. The mass measured pigeon-egg in size and protruded above surrounding surface of the skin. No color and temperature change in breast. No abnormal in opposite breast and both axillary lymph nodes. The patient had no history of malignant or other diseases including hypertension. Also, he had no family history of any malignancy. The patient underwent lumpectomy of left breast mass. The case was finally diagnosed as benign GCT by pathological examinations. Grossly, the solid tumor was 1.1×0.9×0.8 cm, with poor envelope and white in cut surface. No necrosis was found within the tumor. Hematoxylin and eosin (H&E) staining showed that the tumor located within the breast tissue and it had incomplete envelope and the margin was unclear. The tumor cells infiltrated into the surrounding fat tissues (Figure 1C), without invading into the nerve tissue or vascellum. The tumor cells were polygo-
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Figure 1. Hematoxylin and eosin (H&E) staining findings. A. At low magnification, the tumor had incomplete envelope and the margin was unclear. The tumor cells grew in an infiltrative pattern without necrosis. ×12.5. B. The nest-like large and eosinophilic granular tumor cells exhibited an infiltrative growth pattern and the breast ducts were involved centrally. ×100. C. The tumor cells infiltrated into the surrounding fat tissues. ×100. D. The tumor cells were polygonal or oval in shape with clear border. They presented small nucleoli and abundant eosinophilic granular in cytoplasm. Mitotic figures were very rare. ×100.

Discussion

GCT was firstly alluded by Weber in 1854 and fully described by Abrikossoff et al. in 1926 [6]. Abrikossoff proposed GCT was origin from striated skeletal muscle cells and he termed it as myoblastoma. Subsequently, some authors showed evidence that GCT was origin from smooth muscle cells. Currently, most scholars accept that GCT is origin from Schwann cells because of positive S-100 and ultrastructural features of the tumor cells [7].

The current evidence of prevalence of GCTB suggests 1:617 in screened population and 6.7:1000 among total clinical population [3]. The case we reported here was a benign GCTB occurred in a male patient which was extremely rare. To our knowledge, cases of male GCTB in English-language literatures which could be obtained enough data were demonstrated in Table 1 [8-42].

GCTB typically presents as a firm, painless, slow growing mass, ranging from regular well defined to irregular poor defined [3]. GCTB may cause retraction or ulceration of the overlying skin or may be fixed to the pectoralis major muscle [3]. Men suffer GCTB are extremely rare, the majority of these patients are pre-menopausal women. And a hypothesis that hormones had relationship with the pathogenesis of GCTB, however no relative receptors have been found on the tumor [31]. GCTB can occur in any sites of the breast and the predominant quadrant is upper inner quadrant of the breast, as in our case, where parallels the distribution...
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of cutaneous sensory branches of the supraclavicular nerve [31]. Compared with breast cancer, the most common quadrant is outer upper quadrant. GCTB is difficult to differentiate with breast malignancies through both breast ultrasound and mammography because of heterogeneity, irregularity, spiculation, poor boundary and so on [3]. Up to the present, pathological examinations including H&E and IHC stains are the most accurate diagnostic techniques.

Microscopically, tumor cells are usually described as large, polygonal cells with nests, cords or clusters-like patterns. They contain characteristic abundant granular eosinophilic cytoplasm and uniform small, round or oval nuclei [32]. GCT does not display mitoses, nuclear multiplicity, atypia and pleomorphism [32]. Immunohistochemically, S-100 is a sensitive marker for GCT, however it is not specific as 10% of breast malignancies display S-100 positive [33]. CD68 is a distinctive feature for GCT and associates with abundant phagolysomes existed in cytoplasm [33]. Moreover, vimentin, inhibin-α and are reported to be positive in some cases [34-37]. Periodic acid-Schiff stain (PAS) is often positive [15]. Cytokeratin, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), estrogen receptor (ER), progesterone (PR) and gross cystic disease fluid protein (GCDFP-15) are generally negative [3, 4, 34].

Malignant granular cell tumor (MGCT) only accounts for 1-2% of all GCTs [3]. The widely accepted clinical features of MGCT of breast are large, rapid growing mass, which are associated with lymphadenopathy, aggressive local invasion and poor border [3]. Six histological criteria of MGCT was established by Fanburg-Smith et al. (FS criteria) [38], including necrosis, spindling of the tumor cells, vesicular nuclei with large nucleoli, increased mitotic rate (>2

Figure 2. Immunohistochemical staining findings. A. The tumor cells were strong positive for S-100. ×200. B. The tumor cells were moderate to strong positive for Vimentin. ×200. C. The tumor cells were moderate positive for Inhibin-α. ×200. D. The tumor cells were weak positive for CD68. ×200.
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Table 1. Cases of Male Granular cell tumor of the breast

<table>
<thead>
<tr>
<th>No.</th>
<th>First Author Year</th>
<th>Age (yo)</th>
<th>Side and quadrant</th>
<th>Size (cm)</th>
<th>Benign/ malignant</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Taglietti, 2011 [10]</td>
<td>2011</td>
<td>R, outer quadrant</td>
<td>2.5</td>
<td>Benign</td>
<td>Wide local excision</td>
</tr>
<tr>
<td>6</td>
<td>Irshad [12]</td>
<td>2008</td>
<td>R, inner quadrant</td>
<td>1.9</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>8</td>
<td>Adeniran [4]</td>
<td>2004</td>
<td>R</td>
<td>0.8</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>9</td>
<td>Adeniran [4]</td>
<td>2004</td>
<td>L</td>
<td>1.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>10</td>
<td>Adeniran [4]</td>
<td>2004</td>
<td>L</td>
<td>2.5</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>12</td>
<td>McCluggage [15]</td>
<td>1999</td>
<td>R</td>
<td>1.4</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>13</td>
<td>Calò [16]</td>
<td>1990</td>
<td>L, outer quadrant</td>
<td>1.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>14</td>
<td>Chachlani [17]</td>
<td>1997</td>
<td>R</td>
<td>1.3</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>15</td>
<td>Okuda [18]</td>
<td>1996</td>
<td>outer upper quadrant</td>
<td>2.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>16</td>
<td>Reale [20]</td>
<td>1995</td>
<td>outer upper quadrant</td>
<td>2.7</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>17</td>
<td>Mariscal [21]</td>
<td>1995</td>
<td>R, outer quadrant</td>
<td>1.7</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>18</td>
<td>Placidi [22]</td>
<td>1995</td>
<td>L, upper quadrant</td>
<td>1.5</td>
<td>Benign</td>
<td>Wide local excision</td>
</tr>
<tr>
<td>19</td>
<td>Rogall [23]</td>
<td>1995</td>
<td>R, upper and outer upper quadrant</td>
<td>1.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>20</td>
<td>Damiiani [25]</td>
<td>1992</td>
<td>L</td>
<td>2.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>21</td>
<td>Baeten [26]</td>
<td>1989</td>
<td>R, subareolar</td>
<td>2.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>22</td>
<td>Khansur [41]</td>
<td>1987</td>
<td>NA</td>
<td>&gt;2.5</td>
<td>Malignant</td>
<td>Local excision and systemic chemotherapy</td>
</tr>
<tr>
<td>23</td>
<td>DeMay</td>
<td>1984</td>
<td>R, outer upper quadrant</td>
<td>1.5</td>
<td>Benign</td>
<td>NA</td>
</tr>
<tr>
<td>24</td>
<td>Sussman [42]</td>
<td>1973</td>
<td>L, outer upper quadrant</td>
<td>1.8</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>25</td>
<td>Hart [27]</td>
<td>1973</td>
<td>L, subareola</td>
<td>3.0</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>26</td>
<td>Umansky [28]</td>
<td>1968</td>
<td>L, subareola</td>
<td>NA</td>
<td>Malignant</td>
<td>Radical mastectomy</td>
</tr>
<tr>
<td>27</td>
<td>Mulcaire [19]</td>
<td>1968</td>
<td>R, outer upper quadrant</td>
<td>2.1</td>
<td>Benign</td>
<td>wide local excision</td>
</tr>
<tr>
<td>28</td>
<td>Peison [29]</td>
<td>1964</td>
<td>L, subareola</td>
<td>1.8</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
<tr>
<td>29</td>
<td>Simon [30]</td>
<td>1947</td>
<td>R, upper quadrant</td>
<td>2.5</td>
<td>Benign</td>
<td>Local excision</td>
</tr>
</tbody>
</table>

Abbreviations: L, left; R, right; mo, months; NA, not available; yo, years old.

With the aim of preventing inappropriate and unnecessary treatments, GCTB should be considered more during the differential diagnosis, including scirrhous malignancies, granulomatous mastitis, metastatic clear cell malignancies, histiocytoid-myoblastomatoid breast carcinoma (HMBC) and so on [3].

In conclusion, GCTB is a very rare benign disease occurred in male which mimics breast...
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malignancy clinically and radiologically. The definitive diagnosis is through histopathological and immunohistochemical findings. Clinicians and pathologists should keep in mind this rare benign tumor occur in men in order to avoid over-treating.

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Disclosure of conflict of interest

None.

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