Invasive micropapillary carcinoma of the breast in male patients: A case report

Keith Cordner, Ike Uzoaru

ABSTRACT

Introduction: Invasive micropapillary carcinoma (IMPC) of the breast is a rare morphologic variant of invasive ductal carcinoma (IDC) and is often associated with poor patient outcomes. Breast cancer is extremely rare in males accounting for approximately 1% of all breast cancers. The most common histologic types include IDC and IMPC. As tumors with IMPC components can be found in other organs, metastatic invasive mammary carcinoma (IMC) should be considered as a differential diagnosis when IMPC is found in the breast.

Case Report: We report a case of primary IMPC of the breast with regional axillary metastasis in an African American male in his eighth decade. A modified radical mastectomy was performed. Upon pathological examination the tumor was positive for estrogen and negative for human epidermal growth factor receptor 2 (HER2). The patient has responded well postoperatively with tamoxifen as the sole treatment.

Conclusion: Due to the rare nature of the disease and the lack of published literature, additional data is needed to better evaluate the response to treatment and survival in male patients with breast IMPC.

Keywords: Invasive ductal carcinoma, Invasive micropapillary carcinoma, Metastatic IMC

INTRODUCTION

Male breast cancer is a rare occurrence, accounting for less than 1% of all cancers in men [1] and approximately 1% of all breast cancers in general. Invasive micropapillary carcinoma (IMPC) is a rare form of mammary carcinoma which occurs mostly in women and accounts for approximately 3.8–5.9% of all breast cancer cases [2]. Invasive micropapillary carcinoma of the breast is histologically characterized by pseudopapillary and tubuloalveolar cell clusters in retracted clear spaces. It is a rare form of mammary carcinoma linked to increased frequency of lymph node invasion and metastases [2, 3]. Invasive micropapillary carcinoma of the breast is very rare in males with mainly single case reports from multiple different institutions [4–13]. The median age in the reported cases of IMPC is 66 years with an age range of 36–81 years. Herein we report a case of invasive micropapillary carcinoma of the right breast in an 81-year-old male patient with axillary lymph nodal metastases.

CASE REPORT

An African American male patient in his eighth decade, with multiple comorbidities, presented with a self-detected palpable right breast mass immediately medial to the nipple. Initial ultrasound showed a hypoechoic 19 mm breast mass and abnormal axillary lymph nodes. A subsequent ultrasound of the right breast and axilla revealed a 1.9 cm right breast mass...
with two abnormal appearing right axillary lymph nodes. Furthermore, ultrasound-guided core needle biopsy of the mass and axillary lymph nodes revealed an invasive grade 2 of 3 micropapillary carcinoma with lymph node metastasis (Figures 1–3). Immunostains were performed on the tumor with the following antibodies: epithelial membrane antigen (EMA), GATA3, estrogen receptor (ER), progesterone receptor (PR), and HER2/neu (Figures 4 and 5). Epithelial membrane antigen showed reverse polarity positivity on the outside of the malignant nests consistent with IMPC. The patient underwent a right modified radical mastectomy with right axillary lymph node dissection. The tumor was an invasive carcinoma with a predominant micropapillary pattern (approximately 95%) and staged as T1cN1a with metastatic carcinoma involving 3 of 18 axillary lymph nodes. The ER, PR, and HER2/neu were quantitatively scored using Ventana Virtuoso image analysis. The Oncotype DX recurrence score was 6. He received adjuvant radiation therapy utilizing three field technique (two total dose of 50 Gy in 2 Gy per fraction tissue right chest wall) and regional lymphatics. Placed on tamoxifen, the patient has responded well to treatment with no recurrence since diagnosis.

**DISCUSSION**

Invasive micropapillary carcinoma is a rare primary breast carcinoma, histologically illustrated by small, tightly cohesive groups of neoplastic cells within well-delineated clear spaces resembling lymphatic vessels...
These tumors behave aggressively and are characterized by their high incidence of lymphovascular space invasion, lymph node metastasis, local recurrence, and distant metastases [14]. Although IMPC is believed to be a very aggressive type of breast cancer, however, some studies suggest that there are no significant prognostic differences between IMPC and invasive ductal carcinoma (IDC) [3, 15]. In fact, some studies indicate IMPC may have a better long-term survival rate than IDC [16].

In a large review of IMPC of the breast in 624 patients, Chen et al. [2] found that approximately 53% and 4% of patients had lymph node metastasis and distant metastasis, respectively, at presentation. They also noted that patients with 4 or more positive lymph nodes had worse disease-specific (DSS) and overall survival (OS) than patients with negative or 1–3 positive lymph nodes. Moreover, this latter group of patients with 1–3 positive lymph nodes shows similar DSS and OS with the node negative patients. Our patient had 3 positive lymph nodes out of 18 and is doing well with no recurrence albeit with a short follow-up of three years. In a large study and update involving 1993 cases of IMPC with the median age of 50–62 years, Yang et al. [3] found that most of the patients had lymph node metastasis at presentation. They also found that some of the factors predisposing patients with IMPC to early lymph node metastasis include increased tumor infiltrating lymphocytes, high expression of vascular endothelial growth factor by increasing vascular density, and presence of microvilli on the inside out surfaces of the morules of IMPC using electromicroscopy. These surface microvilli may have strong interaction with surrounding lymphatics for easier metastasis.

Interestingly, non-breast IMPC or components of IMPC may be seen in other organs including the urinary bladder, lungs, and salivary glands [17–19], suggesting metastatic IMPC as a secondary tumor should be considered in the differential diagnosis of breast IMPC. However, no evidence of a non-breast IMPC primary tumor was seen in our case, either clinically or by imaging. The tumor in our case showed histological and immunophenotypic features consistent with IMPC-reverse polarity positivity for EMA, positive for GATA3 and ER.

Invasive micropapillary carcinoma is even more uncommon in males. The literature finds case reports from single institutions in predominantly Asian countries, chiefly Japan [4–13]. Consequently, no significant data exists to comprehensively evaluate the behavior, response to treatment, and survival in males carrying the diagnosis of IMPC of the breast. Any discussion on this issue has been extrapolated from the data in females diagnosed with IMPC.

Among the reported cases, mastectomy with axillary lymph node dissection followed by adjuvant therapy is the mainstay of treatment (Table 1). Hormone receptor studies showed positive estrogen receptors in eight cases, including ours [5, 7, 8, 10, 11,13], with most patients receiving adjuvant estrogen modulator treatment with tamoxifen. Three cases of triple positive IMC of the breast in a male patient have been reported [10–12]. One patient

<table>
<thead>
<tr>
<th>Age</th>
<th>IMC (%)</th>
<th>Estrogen receptor</th>
<th>Progesterone</th>
<th>Her2/neu</th>
<th>Ki67 (%)</th>
<th>Nodal status</th>
<th>Treatment</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erhan et al. [4]</td>
<td>66</td>
<td>100</td>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
<td>60</td>
<td>NR</td>
<td>CEF</td>
</tr>
<tr>
<td>El Hadj et al. [5]</td>
<td>36</td>
<td>100</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>2</td>
<td>Doxo, C, Pac</td>
<td></td>
</tr>
<tr>
<td>Shimizu et al. [6]</td>
<td>77</td>
<td>100</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
<td>NR</td>
<td>22</td>
<td>DFUR/TAM</td>
</tr>
<tr>
<td>Minoshima et al. [7]</td>
<td>56</td>
<td>67</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
<td>35</td>
<td>1</td>
<td>FEC-DOC</td>
</tr>
<tr>
<td>Nagai et al. [8]</td>
<td>73</td>
<td>80</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Akamatsu et al. [9]</td>
<td>81</td>
<td>90</td>
<td>Positive</td>
<td>No data</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
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<tr>
<td>Shuja et al. [10]</td>
<td>60</td>
<td>95</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>NR</td>
<td>16</td>
<td>Rad, C, F, Doxo</td>
</tr>
<tr>
<td>Trépant et al. [11]</td>
<td>73</td>
<td>NR</td>
<td>Positive</td>
<td>Positive</td>
<td>positive</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Dong et al. [12]</td>
<td>46</td>
<td>90</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>10</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Tsushima et al. [13]</td>
<td>63</td>
<td>60</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
<td>5</td>
<td>0</td>
<td>TAM</td>
</tr>
<tr>
<td>Present case</td>
<td>81</td>
<td>95</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
<td>NR</td>
<td>3</td>
<td>Rad, TAM</td>
</tr>
</tbody>
</table>

Abbreviations: C: cyclophosphamide; E: epirubicin; F: 5-fluorouracil; Doxo: doxorubicin; Pac: Paclitaxel; DFUR: deoxyfluorouridine; TAM: tamoxifen; DOC: Docetaxel; NR: not reported; Synapt: Synaptophysin.
CONCLUSION

Although IMPC tumors of the breast are extremely rare in males, they are morphologically indistinguishable from those found in females. However, as components of IMC can be seen in other organs, metastatic IMPCs as secondary tumors should be included in the differential diagnosis of breast IMPC. Surgery and adjuvant therapy appear to be adequate treatment in patients with primary IMC of the breast. Due to scarcity of published information, additional studies and data are needed to fully evaluate the behavior of this tumor in male patients.

REFERENCES


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Author Contributions

Keith Cordner – Acquisition of data, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Ike Uzoaru – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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