Primary peritoneal serous papillary carcinoma that metastasized to an axillary lymph node in a woman with a history of breast cancer: A case report and diagnostic pitfalls

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Abstract Herein, we will report on a patient with primary peritoneal serous papillary carcinoma that metastasized to an axillary lymph node and who had previously undergone a mastectomy and chemotherapy for carcinoma of the right breast. A 40-year-old Japanese woman underwent partial resection of her left lung for metastatic breast cancer at our hospital. Thirteen years later, she developed a left axillary lymph node swelling, and a biopsy was performed. Histological findings were compatible with metastatic breast carcinoma. Positron emission tomography–computed tomography revealed systemic lymphadenopathy, peritoneal nodules, and a liver mass. The patient was diagnosed with recurrent breast cancer and underwent additional chemotherapy. Six months later, she developed ascites. She was diagnosed with serous adenocarcinoma using conventional and immunocytological examinations of the ascites. She underwent suboptimal debulking surgery, consisting of a total hysterectomy, bilateral oophorectomy, and partial omentectomy. The final pathological diagnosis was primary peritoneal serous papillary carcinoma.

The diagnosis and pitfalls of this case will be presented.

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1. Introduction

Primary peritoneal serous papillary carcinoma (PSPC) is a rare disease. Metastases of PSPC to the axillary lymph nodes (LNs) are uncommon, with only isolated cases reported thus far.

Most patients who develop metastatic disease have a history of advanced-stage PSPC. Breast and/or axillary LN involvement upon initial presentation can occur but is rare. These metastases may represent a diagnostic pitfall for pathologists, because these metastases could mimic those from the primary breast carcinoma. Differentiating between metastatic and primary tumors of the breast is of great importance, because treatment and prognosis differ markedly [1]. In this case report, we will present a patient who had a primary peritoneal serous papillary carcinoma that metastasized to a left axillary LN and who had previously undergone a mastectomy and chemotherapy for
carcinoma of the right breast; we will also discuss potential diagnostic pitfalls.

2. Case report

A 40-year-old Japanese woman with no family history of cancer and an unknown BRCA status was referred to our hospital for treatment of a breast cancer metastasis to the lung. Six years prior to this referral, she had undergone a mastectomy and adjuvant chemotherapy for a right breast carcinoma. The details of that treatment are unknown. Partial resection of segment 6 of the left lung was performed. A histopathological examination of the resected specimen revealed tumor cells that were arranged in clusters and trabeculae, as well as fibrosis. The tumor cell nuclei were moderately pleomorphic. Immunohistochemical staining indicated that the carcinoma cells were estrogen receptor (ER) positive and progesterone receptor (PgR) negative. The HER2 score was 0. These findings were consistent with metastatic breast carcinoma (Fig. 1). The patient received additional chemotherapy with docetaxel. Thirteen years later, the patient felt tightness in the left axillary region. She underwent ultrasound (US)-guided needle biopsy of a swollen left axillary LN. The histopathological findings were characteristic of invasive micropapillary carcinoma (IMPC) (Fig. 2). Immunohistochemical staining indicated that the carcinoma cells were ER positive and PgR negative. The HER2 score was 0. These findings were compatible with metastatic breast carcinoma. Her serum cancer antigen 15-3 (CA15-3) was 494 U/mL (normal, <27 U/mL). Positron emission tomography–computed tomography (PET-CT) performed at the time of biopsy revealed right supraclavicular, bilateral axillary, mediastinal, para-aortic, and pelvic lymphadenopathy, as well as multiple peritoneal nodules and multiple masses in the liver. She was diagnosed with recurrence of her breast carcinoma and underwent additional chemotherapy consisting of eribulin, followed by fluorouracil, epirubicin, and cyclophosphamide. Six months later, the patient noticed abdominal distension. US and CT evaluations revealed massive ascites. A cytological examination of the ascites demonstrated numerous atypical cells, suggesting serous adenocarcinoma or mesothelioma (Fig. 3). Immunohistochemical staining of sections of a cell block prepared from the ascites fluid demonstrated that the tumor cells were positive for calretinin, Wilms’ tumor-1 (WT1) protein, cytokeratin (CK)-7, Ber-EP4, epithelial membrane antigen (EMA), and paired-box-gene-8 protein (PAX8) expression and negative for gross cystic disease protein fluid (GCDFP)-15, CK-20, ER, CK-5/6, and carcinoembryonic antigen expression (Fig. 4). Because of these findings, she was diagnosed with serous adenocarcinoma. Her serum CA-125 was 10,455 U/mL (normal, <35 U/mL). She underwent suboptimal debulking surgery, consisting of a total hysterectomy, bilateral oophorectomy, and partial omentectomy. Intraoperative findings showed multiple omental masses and numerous small peritoneal nodules, as well as an intact uterus and bilateral ovaries. The final pathological diagnosis was primary peritoneal serous papillary carcinoma. Immunohistochemical staining of the paraffin sections of the left
lymph node was performed. An examination found PAX8-positive carcinoma cells, a finding consistent with primary peritoneal serous papillary carcinoma that had metastasized to the axillary LN. After recovery from debulking surgery, the patient underwent chemotherapy consisting of paclitaxel and carboplatin.

3. Discussion

Metastases to contralateral axillary LNs are uncommon following prior treatment for a unilateral breast carcinoma, with a reported occurrence rate ranging from 3.6% to 6% [2]. A contralateral axillary LN metastasis has been considered to be a distant metastasis and stage IV disease. Systemic therapy, either chemical or hormonal, is the usual treatment for these metastases. There are 3 diagnostic possibilities for carcinoma found in an axillary LN of a woman who either was concurrently being or had been previously treated for a contralateral breast carcinoma. First, the malignant focus may represent a metastasis from an occult primary in the ipsilateral breast, as a woman with a history of breast cancer has an increased risk of developing a second breast cancer. Second, this finding may represent a contralateral spread from the original breast carcinoma. Third, this finding may represent a metastasis from an extramammary primary tumor, which includes adenocarcinoma of the uterus, gastrointestinal tract, ovary, thyroid, or kidney; lymphoma; melanoma; squamous cell carcinoma from the head, lung, or skin; a primary tumor of the sweat gland; or a neurogenic tumor [3].

When our patient was found to have a swollen left axillary LN, she underwent imaging that was negative for a tumor in her left breast. In addition, the immunohistochemical findings from the left axillary LN biopsy were consistent with breast carcinoma. Furthermore, PET-CT findings, including multiple LN metastases, suggested systemic disease. Therefore, we initially believed that these findings were consistent with a recurrence of the original right breast carcinoma. However, the histopathological findings from the left axillary lymph node demonstrated the characteristic pattern of IMPC, which was different from the histopathology of the lung specimen. Whenever we see a pattern of IMPC in an axillary lymph node, we usually think of metastases from a breast carcinoma, especially in a patient such as ours, who had undergone surgery for breast carcinoma and did not have a history of PSPC or ovarian cancer.

The differential diagnosis of IMPC of the breast includes metastatic serous ovarian carcinoma and PSPC [4]. Pathologists should consider that metastases to the axillary lymph nodes that have the histological appearance of breast IMPC could potentially have originated from an ovarian or peritoneal serous adenocarcinoma [1,5]. If there were any questions regarding a patient’s clinical history or histological findings, an immunohistochemical examination should be performed to confirm the diagnosis.

Immunohistochemistry is useful for differentiating PSPC from IMPC; however, there is some overlap between the patterns of immunoreactivity. Both PSPC and IMPC are
typically positive for CK-7 and ER and negative for CK-20 expression [6,7]. Other markers (e.g., GCDFP-15, mammaglobin, WT1, PAX8, and PAX2) might be useful and are under investigation [8,9]. GCDFP-15 is expressed by 38% of IMPCs and 0% of serous papillary adenocarcinomas [10]. Mammaglobin is expressed by 56% of IMPCs and 0% of ovarian serous papillary carcinomas [11]. These markers might be useful for the differential diagnosis of PSPC versus IMPC. However, the availability of these markers is limited because their rates of expression are low in IMPCs. WT1 and PAX8 appear to have the greatest utility for differentiating primary breast carcinoma from metastatic PSPC because they have a high sensitivity and low potential for aberrant expression [12]. WT1 is detected in 94.7% of serous ovarian carcinomas, 100% of peritoneal serous carcinomas, and 2–3% of IMPCs [6]. Lee et al. reported that the nuclear expression of WT1 was found in 24% of IMPCs, typically in less than 10% of cells, and that cytoplasmic staining has been seen 59% of IMPCs [13]. Moritani et al. showed that the WT1 positivity rate in serous papillary adenocarcinomas was 78%, and the corresponding rate in IMPCs was 3% [10]. Thus, the presence of diffuse nuclear expression of WT1 strongly favors metastatic serous papillary ovarian or peritoneal carcinoma. PAX8, a transcription factor expressed in tumors of renal and thyroid origin and Mullerian tumors, is present in 99% of serous ovarian carcinoma versus metastatic breast cancer to the ovary. Am J Surg Pathol 2005;29:1482-9.

In conclusion, we presented a patient who had a primary peritoneal serous papillary carcinoma that metastasized to an axillary LN and who had previously undergone a mastectomy and chemotherapy for carcinoma of the breast. Pathologists should consider that PSPC might metastasize to axillary LNs. While the clinical history and morphology of the metastasis could help distinguish between primary and metastatic breast carcinomas, an immunohistochemical analysis is essential if the diagnosis remains unclear. PAX8 seems to be the most useful marker for distinguishing ovarian carcinoma or PSPC from breast carcinoma including IMPC.

References