Metastatic Invasive Lobular Carcinoma of the Breast Presenting Peritoneal Metastasis with Bilateral Ureteral Obstruction

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Abstract: The most common sites for recurrence of breast cancer are the lungs, liver, and bones. The frequency of peritoneal, gastrointestinal metastasis is significantly lower than those, and bilateral ureteral obstruction caused by peritoneal metastasis is relatively rare. A 66-year-old woman was referred to our hospital because of appetite loss and frequent urination. She was on adjuvant hormonal therapy for local recurrence of right breast cancer. She was diagnosed with bilateral ureteral obstruction due to extramural compression. Exploratory laparoscopy revealed omental cake and peritoneal nodules of which pathological examination showed peritoneal metastasis of invasive lobular carcinoma. Peritoneal metastases from breast cancer are unusual and consequently difficult to identify without non-invasive tools. Exploratory laparoscopy revealed that the cause of hydronephrosis in this case was peritoneal metastasis of invasive lobular carcinoma. Clinical history and histological study play a pivotal role in determining the correct diagnosis.

Keywords: breast cancer, peritoneal metastasis, ureteral obstruction.

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Background

Breast cancer easily metastasizes to the whole body, usually to the lungs, liver, bones, and lymph nodes. Nakamura et al [1, 2], reported that metastasis to the adrenal glands, ovaries and peritoneum was found in 37.9–40%, 24.5–26% and 16–21.5% of autopsy cases, respectively. The condition is rarely diagnosed before death. Mukaiyama et al stated that 31% of autopsy cases had metastases to the gastrointestinal tract and peritoneum, but only 6% could be clinically diagnosed before death [3]. Invasive lobular carcinoma is known to be the second most common histological type of invasive breast cancer, representing 5–15% of cases, following invasive ductal carcinoma, which accounts for 65–75% of all cases [4–6]. In patients with recurrent breast cancer, the rates of metastasis to the peritoneum and retroperitoneum have been reported to be 0.6% and 3.1%. This event tends to be more common in invasive lobular carcinoma than in invasive ductal carcinoma [7]. Hydronephrosis is a rare complication of metastatic breast cancer [8, 9]. We herein report a case of metastatic invasive lobular carcinoma of the breast to the peritoneum presenting with bilateral ure-
teral obstruction without bowel obstruction.

**Case presentation**

A 66-year-old woman was referred to our hospital because of appetite loss and frequent urination during adjuvant hormonal therapy after resection of a local recurrent tumor of an invasive lobular carcinoma of the breast.

She had a past history of hormone receptor positive and human epidermal receptor 2 (HER2) negative invasive lobular carcinoma of the right breast (Figure 1 A to D), and had undergone total mastectomy with axillary lymph node dissection 22 years previously, after which she received hormone therapy with tamoxifen. However, local recurrence was detected and resected 7 years previously.

The recurrent tumor was metastasis of invasive lobular carcinoma. Immunohistochemical staining was positive for estrogen receptor (ER) (95%) and progesterone receptor (PgR) (95%), and the Ki-67 index was <5%. At that time, HER2 showed positive conversion (luminal B HER2-positive type).

She was treated with letrozole, a non-steroidal aromatase inhibitor for adjuvant hormonal therapy, without any evidence of distant metastasis. Her tumor marker values were within normal limits during follow up.

On admission, the patient had an operation scar

![Microscopic findings](image1.png)

**Figure 1. Microscopic findings, and Immunostaining findings.** A: Microscopic findings (Hematoxylin-Eosin (H&E) staining: ×20). Tumor cells with a high a nuclear/cytoplasmic ratio proliferated in a cord among these collagen fibers (Indian filing). B-E: Immunostaining findings (×40). ER-positive (B), PgR-positive (C), Ki-67-labeling index <5% (D), HER2 negative (E). ER: estrogen receptor, PgR: progesterone receptor, HER2: human epidermal receptor2.
Recurrent Breast Cancer Presenting Hydronephrosis

from a Stewart's incision and from local resection on her right chest. There were no positive findings in her neck, axilla, or abdomen. Laboratory data showed renal dysfunction (blood urea nitrogen: 32 mg/dl, creatinine: 4.74 mg/dl), and her tumor marker levels (carcinoembryonic antigen, cancer antigen 15–3) were within the normal limits.

Abdominal ultrasound (US) and computed tomography (CT) revealed a small amount of ascites, omental shrinkage, bilateral hydronephrosis, and extramural compression of the ureters (Figure 2 A and B). Cytology of the urine, cystoscopy and ureteroscopy showed no particular findings other than ureteral obstruction. Gastroduodenoscopy, total colonoscopy and positron emission tomography-computed tomography (PET-CT) did not show any particular lesions.

The patient first underwent ureteral stent placement for renal dysfunction. After the recovery of her renal function, exploratory laparoscopy was performed under a diagnosis of bilateral hydronephrosis with ascites caused by peritoneal metastasis of breast cancer or retroperitoneal fibrosis.

There was a large amount of serous turbid ascites in the abdomen, in the subphrenium and Douglas cavity (Figure 3 A). The omentum was shrunken, which made so-called "omental cake" (Figure 3 B). There were numerous small, whitish nodules on the parietal peritoneum (Figure 3 C and D). The appendix and reproductive organs were intact. The upper urinary tract could not be fully explored, so we collected ascites for cytology, and did an incisional biopsy of the omentum and peritoneal nodule for pathological examinations.

The cytology of the ascites showed no evidence of malignancy. A histopathological examination of the omentum and peritoneal nodule showed a proliferation of atypical cells having round nuclei, and a small amount of eosinophilic cytoplasm in cords among the adipose tissue or embedded in a fibrous connective tissue (Figure 4 A). Immunohistochemically, these atypical epithelial cells were positive for ER: 95%, PgR: 5%, Ki-67 index was less than 5% and HER2(1+), suggesting a type of luminal type B (Figure 4 B, C, D and E). Based on these findings, we made a conclusive diagnosis of peritoneal metastasis of recurrent invasive lobular carcinoma of the breast. After the definite diagnosis was made, the patient was treated with palbociclib (a cyclin-dependent kinase 4/6 inhibitor) and fulvestrant (an ER antagonist).

**Discussion**

Considering the current evidence, we concluded that the bilateral hydronephrosis was caused by peritoneal metastasis of breast cancer. Interestingly, recurrence was observed as a luminal B HER2-positive type. The rates of negative to positive conversion were 21.5% (95% CI=18.1–25.5%), 15.9% (95% CI=11.3–22%), and 9.5% (95% CI=7.4–12.1%), respectively [10]. It is possible that cytokines, such as TNF-α, elevated reactive oxygen species, hypoxia due to angiopathy,
DNA damage, and heat shock protein are induced to increase the inherent properties of cancer cells [11, 12].

Late recurrence of breast cancer more than 5 years after surgery is estimated to be about 10% [13], which is not rare compared to other organ cancers. Breast cancer often metastasizes to other parenchymal organs, such as bone, lymph node, lung and liver [3]. Intraabdominal metastasis of breast cancer is usually found in the liver. Extrahepatic metastasis of breast cancer has been reported, but it is extremely rare. Caskey et al reported stomach metastasis of breast cancer [14], and Tabei et al reported a few cases of retroperitoneal and peritoneal metastasis [15].

Ureteral obstruction with hydronephrosis is a rare complication of metastatic breast cancer [8, 9]. Winston et al reported that 11% of patients with metastatic lobular breast cancer with peritoneal metastasis had hydronephrosis caused by metastatic infiltration of the retroperitoneum, and resection was performed in all the cases that involved small or large bowel obstruction [16]. A case of hydronephrosis without bowel obstruction by metastatic lobular breast carcinoma is considered rare.

As shown in our case, it is hard to detect peritoneal metastasis using CT or PET-CT unless the tumor has reached a certain volume [17]. Most cases have bowel obstruction because they are discovered after peritoneal metastasis has progressed.

There are some current reports on patients with peritoneal carcinomatosis of breast cancer who achieved long-term survival with treatment [18, 19], but whether a long-term effect can be expected in all cases is unclear. As the survival rate of breast cancer improves, the number of cases involving peritoneal recurrence at more than 5 years after surgery—as was observed in this case—is expected to increase. It is expected that cases such as this will accumulate and that effective treatments will be discovered.

We should keep in mind the possibility that breast cancer patients may develop peritoneal recurrence without other organ recurrence. Although most cases have some bowel symptoms, it is difficult to detect peritoneal metastasis in the early stage, and there are also rare cases, such as ours, that only present bilateral hydronephrosis. In the present case, a patient with metastatic invasive lobular carcinoma of the breast to the peritoneum presented with bilateral ureteral obstruction that could be diagnosed in exploratory laparoscopy.
Conclusion

We herein described a rare case of recurrent invasive lobular carcinoma of the breast, presenting bilateral ureteral obstruction caused by peritoneal metastasis without bowel obstruction.

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Conflict of Interest

The authors declare no conflicts of interest in association with the present study.

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Figure 4. Resected specimens. A: Microscopic findings (H&E, × 20). B-E: Immunostaining findings (× 40). ER positive (B), PgR positive (C), Ki-67-labeling index <5% (D), HER2 (1+) (E). ER: estrogen receptor, PgR: progesterone, HER2: human epidermal receptor 2.
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