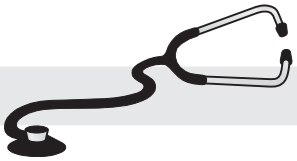

Expect the Unexpected: Peritoneal Spread – Late Relapse Presentation of Breast Cancer

Daniela Katz MD[1], Tamar Peretz MD[1], Bella Maly MD[2], Inna Ospovat MD[1], Nidal Salim MD[1], Nili Ramu MD[1], Nechushtan Hovav MD[1] and Beatrice Uziely MD[1]

[1]Department of Oncology, Sharett Institute of Oncology and [2]Department of Pathology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Key words: breast cancer, peritoneal carcinomatosis, infiltrating ductal carcinoma

IMAJ 2008;10:310–311

Peritoneal carcinomatosis represents dissemination and implantation of tumor cells of variable origin throughout the peritoneal cavity. These tumor cells may arise from intraabdominal primary tumors such as mesothelioma, intraabdominal viscera such as colon adenocarcinoma, ovarian carcinoma and even cholangiocarcinoma [1], or they may spread from extraabdominal malignancies such as breast cancer and melanoma. Establishing the diagnosis of peritoneal carcinomatosis can be difficult and usually requires, in addition to good clinical skills, evidence on imaging modalities that have limited sensitivity and specificity. However, even with a firm diagnosis of peritoneal carcinomatosis, optimal treatment planning for some patients cannot be accomplished without a diagnostic biopsy. This is particularly important for patients with a past history of breast cancer, since these patients have an increased risk of developing new primary ovarian cancer as well as late peritoneal relapse of their breast cancer. Furthermore, the subgroup of patients who are carriers of a mutated copy of either BRCA1 or BRCA2 have a significant increased lifetime risk of developing breast and/or ovarian cancer (risk for breast and ovarian cancer is approximately 80% and 54%, respectively for BRCA1 carriers and 80% and up to 23% for BRCA2 carriers) [2]. Either tumor, when advanced, can present as peritoneal carcinomatosis.

Given the variety of potential metastatic sources of peritoneal carcinomatosis, especially in woman with a past history of breast cancer, a definitive tissue diagnosis should be considered mandatory before commencing therapy. We describe four patients with late relapse of infiltrating ductal carcinoma who presented with single-site peritoneal metastases from breast cancer.

Patient Descriptions

Four patients with a past history of breast cancer were diagnosed with peritoneal carcinomatosis of breast cancer origin. Histological diagnosis was established utilizing both morphological features and immunohistochemical markers. Morphological characteristics of the relapse specimens were correlated with prior breast pathology, and staining with IHC markers such as CK7, CK20, ER, PR, Ca125, Ca15-3, BCA-225 and GCDFP-15 were used to confirm breast cancer.

Serous papillary morphology was not seen in any of the cases, nor was staining for Ca-125, suggesting a diagnosis other than primary peritoneal carcinomatosis (cases 1, 3, 4). Morphological features of mucinous carcinoma in the relapse specimen (case 2) correlated with the original mucinous carcinoma in the breast, and positive staining for estrogen receptor ruled out a gastrointestinal origin. Data on family history, BRCA carrier status, primary breast cancer features and adjuvant therapy and details regarding relapse including time to relapse, patient complaints and evaluation as well as pathological characteristics are summarized in Table 1.

IHC = immunohistochemical

Comment

The cases were diagnosed with single-site late relapse (7–25 years post-breast cancer diagnosis) of breast cancer to the peritoneum. The patients shared some common features, e.g., most of them had negative or low estrogen receptor and progesterone receptor expression despite early-stage primary tumors with no lymph node involvement. Three of the patients had a family history of breast cancer; two of them were BRCA1 carriers of whom one underwent oophorectomy 7 years prior to relapse (case 4). This procedure is known to decrease the risk for carcinomatosis to about 1%–5% but does not eliminate it completely. Diagnosing peritoneal carcinomatosis is not always straightforward. Varied presentations – from asymptomatic patients with only increased tumor markers to patients with acute bowel obstruction that requires an urgent laparotomy (as in three of the patients) – are among the challenges confronting the oncologist. After diagnosing peritoneal carcinomatosis, establishing a histopathological diagnosis is an essential step for tailoring the best treatment. IHC markers such as CK7, CK20, ER, PR, CA 125, CA15-3, BCA-225 and GCDFP-15 are used routinely to confirm breast cancer. However, when diagnostic difficulty arises, other IHC markers such as WT-1 and CEA

Table 1. Patient characteristics at primary diagnosis and at relapse

Case	Age at diagnosis and at relapse (yrs)	TNM staging histology and grade at presentation	ER PR HER-2 at presentation	ER PR HER-2 at relapse	Family ca history/BRCA carrier status/ oophoretomy at presentation	Adjuvant therapy	Presentation at relapse/ diagnostic procedure	Serum CEA (ng/ml) CA125 (u/ml) CA15-3 (u/ml) at relapse	IHC staining of peritoneal specimen/ histology	Remarks
1	55/62	T2.9 cm N0/21 IDC/II	1 Neg NA	2 Neg Neg	Mother: colon ca/ BRCA1/no –	CMFx6 adj. irradiation	Bowel obstruction/ exploratory laparotomy	0.81 55 21.9	Positive BCA-225 GCDFP-15 CK7. Negative Ca -125 CK20	Rectal ca 2 yrs prior to peritoneal relapse
2	72/80	T3 cm N0/14 IDC/I	NA NA Neg	3 1 Neg	Daughter: breast ca/ neg/ no	No adjuvant	Weight loss and ascites. Increased CA125 level/ peri-umbilical lymph node biopsy	4.4 259 15	Mucinous ca.	Local rec. 8 m prior to diagnosis of peritoneal relapse
3	36/61	T(mf) N0/13 IDC/NA	Neg NA NA	Neg Neg Neg	No family history/ NA/ no	No adjuvant	Abdominal pain and constipation/ laparotomy	0.93 264 19.7	Positive CK7 BCA-225 GCDFP-15. Negative Ca -125 CK20	Local rec. 16 years prior to diagnosis of peritoneal relapse
4	43/65	T1N0 IDC/NA	NA NA NA	Neg Neg Neg	Mother and Sister – breast ca/ BRCA1/ yes	No adjuvant	Increasing CA125 level/ laparotomy	0.4 175 42	Positive CK7 GCDFP-15. Negative Ca-125 CK20 Calretinin	4 local rec. treated with radiation and CMF. Pneumonectomy for lung metastases followed by tamoxifen

IDC = invasive ductal carcinoma, IHC = immunohistochemical, neg = negative, NA = not available, ca = carcinoma, CMF = cyclophosfamide, methotrexate, 5-FU, mf = multifocal

(carcinoembrionic antigen) may aid in determining tumor origin [3].

Peritoneal breast cancer metastases were previously reported in the literature as almost a distinct characteristic of infiltrating lobular carcinoma (14% in ILC and 1% in IDC) [4]. In the present report, all four patients suffered single-site late relapse of IDC to the peritoneum. A possible explanation is that the prevalence of IDC is five to six times higher than ILC.

Establishing a diagnosis of peritoneal carcinomatosis is tricky, and even when the diagnosis is reached the origin remains obscure. We suggest that tissue diagnosis is a critical step for correctly individualizing chemotherapeutic protocols for these patients. Certain patient characteristics may be associated with an increased risk of peritoneal spread, including a strong family history of breast cancer and poor estrogen and progesterone receptor expression in the primary tumor.

ILC = infiltrating lobular carcinoma
IDC = infiltrating ductal carcinoma

References

1. Shovman O, Levi Y, Tal S, Shoenfeld Y. Omental cake in a male. IMAJ 2003;5:73–4.
2. King MC, Marks JH, Mandell JB. Breast and ovarian cancer risk due to inherited mutations in BRCA1 and BRCA2. *Science* 2003;302:643–6.
3. Recine MA, Deavers MT, Middleton LP, Silva EG, Malpica A. Serous carcinoma of the ovary and peritoneum with metastases to the breast and axillary lymph nodes a potential pitfall. *Am J Surg Pathol* 2004;28:1646–51.
4. Dixon AR, Ellis IO, Elston CW, Blamey RW. A comparison of the clinical metastatic patterns of invasive lobular and ductal carcinomas of the breast. *Br J Cancer* 1991;63:634–5.

Correspondence: Dr. D. Katz, Dept. of Oncology, Sharett Institute of Oncology, Hadassah- Hebrew University Medical Center, P.O. Box 12000, Jerusalem 12000, Israel.
Phone. (972-50) 857-3864
Fax: (972-2) 643-5089
email: danielakatz@hadassah.org.il