Extracts from Pertinent Current Literature

Expression of the BRCA1 Complex Member BRE Predicts Disease free survival in Breast Cancer

Noordermeer SM, Wennemers M, Bergevoet SM, van der Heijden A, Tönnissen E, Sweep FC, Jansen JH, Span PN, van der Reijden BA.

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Breast cancer is the second commonest tumor in women. Despite great improvements in diagnostic imaging techniques and treatment, breast cancer still remains one of the leading causes of cancer mortality in women. According to the author of this article, recent advances in gene expression profiling have shown breast cancer to be a heterogeneous disease and the current prognostication using clinico-pathological features, such as age, tumour size, histological grade, and lymph node metastases is not sufficient to fully predict therapy response and disease outcome. So in this retrospective cohort study of 229 non-familial breast cancer patients, author studied the expression levels of Brain and Reproductive organ-Expressed (*BRE)*, which encodes a member of the BRCA1 DNA damage repair complex, to demonstrate its usefulness in predicting the disease-free survival (DFS) in non-familial breast cancer patients. The predictive value of *BRE* expression depended on whether the patients had received radiotherapy as a part of their primary treatment or not. In radiotherapy-treated patients, high *BRE* expression predicted a favorable DFS (hazard ratio (HR) = 0.47, 95 % confidence interval (CI) = 0.28–0.78, $p = 0.004$), while in non-treated patients, high *BRE* expression predicted an adverse prognosis (HR = 2.59, 95 % CI = 1.00–6.75, $p = 0.05$). Moreover, among radiotherapy-treated patients, the prognostic impact of *BRE* expression was confined to patients with smaller tumors (HR = 0.23, 95 % CI = 0.068–0.75, $p = 0.015$) and it remained an independent factor after correction for the other prognostic factors such as age, tumor size, lymph node involvement, and histological grade (HR = 0.50, CI = 0.27–0.90,$p = 0.021$). In addition, high *BRE* expression predicted a favorable relapse-free survival in a publicly available dataset of 2,324 breast cancer patients (HR = 0.59, CI = 0.51–0.68, $p < 0.001$). Based upon this data, authors concluded that BRE is a promising candidate for future functional studies aimed at developing targeted therapies.

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Breast Cancer Metastasising to the Pelvis and Abdomen: What the Gynaecologist Needs to know

EK Moore, R Roylance, AN Rosenthal. BJOG 2012; 119: 788–794.

Breast cancer is the most common cancer in women, accounting for 23% of all female cancers worldwide, with1.38 million new diagnoses in 2008. Typical sites of distant metastatic spread include the lungs, liver and bone, but some women also develop intraperitoneal breast cancer. Intraperitoneal breast cancer is a spectrum of disease ranging from microscopic ovarian disease, found incidentally at the time of surgery for other indications, to widespread intraperitoneal carcinomatosis. It has been hypothesised that breast cancer may have a predilection for developing ovarian metastases, because of a favourable local hormonal environment. It is one of the most common non-genital cancers to metastasise to the ovary. Several risk factors predispose women to developing both breast and ovarian cancer, including: increased age, low parity, estrogen exposure and, most importantly, family history and BRCA1 and BRCA2 gene mutations. These data indicate that the majority of women with intraperitoneal breast cancer are premenopausal, and present subsequent to treatment for their primary tumour. This contrasts with ovarian cancer in which the median age at presentation is 63 years. It is therefore interesting to note that although the risk of BRCA1 and BRCA2 mutations in the general breast cancer population is thought to be under 2%, data from two studies suggests higher rates of mutations in women with intraperitoneal breast cancer (10% actual and 9% estimated, respectively). The predominant morphological subtype of primary breast cancer in the general population is invasive ductal carcinoma followed by invasive lobular carcinoma. The lobular carcinoma subtype has a particular predilection for intraperitoneal metastasis. A total of 79.5% women are found to be estrogen receptor (ER)-positive in intraperitoneal breast cancers. Pelvic masses are frequently detected or investigated with ultrasound, having bilateral and solid masses more frequently. The spectrum of symptomatic presentation of intraperitoneal breast cancer appears similar to the primary presentation of ovarian cancer, with the most common symptoms being abdominal distension followed by gastrointestinal symptoms.

Median survival following surgery in the five studies published since 2003 ranged from 10 to 54 months, with 5-year survival rates of 24–40% in the two studies that reported this parameter. This appears to be higher than the equivalent survival data for women with breast cancer and distant disease, and is not dissimilar to women with stage-III ovarian cancer. As with ovarian cancer, the best survival rates occur when women are optimally debulked. In fact, median survival in 'optimally' debulked women (definitions varied from 1 to 2 cm maximum residual disease diameter) ranged from 24 to 36 months, compared with 4–20 months for women who were sub-optimally

debulked, with 5-year survival rates of 16 and 3%, respectively. In contrast the only study looking at women not undergoing surgical resection (n = 44) observed a median survival of 1.6 months from diagnosis of intraperitoneal breast cancer. Given that the only study of survival in women with intraperitoneal breast cancer not undergoing surgery found a median survival of under 2 months, and debulking surgery for intraperitoneal breast cancer has been reported to yield survival rates similar to those seen in women presenting with stage-III ovarian cancer. Hence it is possible that carefully selected women who undergo surgery may have a better prognosis. This hypothesis is supported by a recent systematic review of hepatic breast cancer metastectomy, which concluded that surgical therapy may benefit a subset of women. It is important to note that there is currently no published data on quality of life (QoL), or even disease-free survival, in these women. However, we speculate that debulking surgery for intraperitoneal breast cancer might delay or prevent the onset of local complications (e.g. bowel obstruction), thereby potentially improving QoL.

Until more extensive data becomes available, it is recommended that breast oncology multidisciplinary teams (MDTs) should consider referring women with intraperitoneal breast cancer to a gynaecological oncology MDT, as it is possible that pelvic surgery may be of benefit.

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"A recent issue of the journal of Obstetrics and Gynecology highlighted a fact that 5,000 cases of breast cancer, 54,000 cases of hypertension and nearly 14,000 cases of heart attacks, can be staved off annually, if the mothers adhered to the practice of breast feading of each child for at least one year".

Reference: The Express Tribune, June 9, 2013.