Paraneoplastic Thrombocytosis in Breast Cancer

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Abstract. *Background: Elevated platelet count at the time of diagnosis has been suggested to identify a subset of patients with cancer (e.g. ovarian and lung adenocarcinoma) and poor prognosis. The evidence on the incidence and prognostic significance of thrombocytosis in breast cancer is, however, incomplete. Patients and Methods: We performed a retrospective analysis of 127 consecutive patients with breast cancer at our Institution. Results: None of the 81 newly- diagnosed patients had an elevated platelet count (mean=252×10^6/l). Out of the 31 patients with metastatic disease, one exhibited mild thrombocytosis (445×10^6/l) but the mean value (239×10^6/l) was similar to that seen in patients with localized disease. Conclusion: We conclude that thrombocytosis in breast cancer is rare and thus, unlike in other types of cancer, and has limited (if any) value in clinical decision making.*

Thrombocytosis can be an early indicator of cancer. In fact, one in three women with ovarian adenocarcinoma have thrombocytosis (average platelet count=558×10^6/l) at the time of diagnosis (1). Importantly, paraneoplastic thrombocytosis in these patients was associated with advanced disease and shortened survival (1). Indeed, in a mouse model of ovarian cancer, the elevated platelet count directly correlated with the tumor size, as well as the burden of metastatic disease, and the use of anti-platelet antibody reduced tumor size and increased survival. By contrast, preoperative thrombocytosis was not a prognostic indicator of survival in colorectal cancer (2).

The literature on thrombocytosis and breast cancer is scant and controversial. High interleukin-6 (IL-6) levels and platelet counts were reported in patients with metastatic breast cancer compared to those with localized disease (3). In a large retrospective study involving 4,300 patients, moderate thrombocytosis (453×10^6/l) was noted in a small (3.7%) subset of patients with breast cancer who tended to be younger and were more likely to present with T2 or T3 disease (4). These patients had shorter overall survival (risk ratio=1.73) (4). By contrast, a recent study suggested that it is the platelet-to-lymphocyte ratio, and not the thrombocyte count *per se*, that predicts survival in patients with breast cancer (5). Of note, in a mouse model of breast cancer, no thrombocytosis was detected in sharp contrast to ovarian and pancreatic cancer models that showed marked thrombocytosis (1).

Our objective was to determine the incidence and prognostic significance of thrombocytosis pre-treatment in patients with newly-diagnosed breast cancer in a community hospital setting.

Patients and Methods

After approval by our Institutional Review Board (IRB Study #13-038), clinicopathological data were retrospectively collected on 127 consecutive patients with breast cancer. This patient cohort included 81 patients with invasive ductal or lobular carcinoma and no metastatic disease, 15 patients with ductal carcinoma *in situ* (DCIS), and 31 patients with advanced disease (metastasis to lymph nodes, bone, liver or brain).

Platelet count at the time of diagnosis was collected from our Laboratory Information System (LIS). Statistical analysis was performed using the ANOVA test.

Results

After reviewing the cases, the invasive-carcinoma group was further divided into invasive ductal carcinoma (IDC, 55 patients), tubular carcinoma (five patients), invasive mucinous carcinoma (three patients), invasive lobular carcinoma (ILC, 16 patients), and invasive papillary carcinoma (two patients). These patients were further classified as luminal A (29 patients), luminal B (42 patients), basal-like (one patient), and HER2/neu (nine patients) based on the breast marker [estrogen and progesterone receptor status by paraffin immunohistochemistry and HER2/neu by fluorescence *in situ* hybridization (FISH)] studies. Estrogen and/or progesterone receptor positivity was defined as 1% or more tumor cells exhibiting nuclear immunoreactivity as per the recent College of American Pathologists (CAP) guidelines.

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The platelet count was within normal limits (150 to 400×10^6/l) in all but two patients, one with thrombocytosis (445×10^6/l) and another with thrombocytopenia (122×10^6/l). Both patients had advanced disease with bone metastasis and the patient with low platelet count was undergoing chemotherapy. We did not note any differences in mean platelet counts between the IDC (246×10^6/l), DCIS (269×10^6/l) and ILC (270×10^6/l) groups. Nor did we see any difference between localized (252×10^6/l) and metastatic disease (239×10^6/l). Patients with basal-like and HER2/neu carcinomas had platelet counts of 255×10^6/l and 244×10^6/l, respectively.

Discussion

Patients with ovarian adenocarcinoma and thrombocytosis were found to have a more advanced disease, higher rate of thromboembolic complications, and shortened overall survival than did patients who had normal platelet counts (1). In these patients, a direct correlation between elevated platelet counts and circulating IL-6 levels were detected (1). Indeed, in a mouse model of ovarian carcinoma suppressing IL-6 production by small interfering RNA restored platelet counts to the normal range and ameliorated tumor progression (1). These findings may open up new avenues in cancer therapy.

Patients with advanced breast cancer also exhibit an increased incidence of thromboembolic complications (6). Furthermore, it was postulated that breast cancer patients with thrombocytosis at the time of diagnosis carry a worse prognosis (4). In our study, none of the 81 patients with newly-diagnosed breast cancer had an elevated platelet count. This finding implies that paraneoplastic thrombocytosis (if it occurs at all in newly-diagnosed early stage breast cancer) is probably too rare to have any practical value in aiding oncologists identify patients who could benefit from more aggressive therapy. We identified one patient with advanced cancer (metastatic disease to bone) who had an elevated platelet count. When a novel therapeutic approach to suppress IL-6 production becomes available, it may be interesting to evaluate it in patients with advanced breast cancer and thrombocytosis.

Competing Interests

The Authors declare that they have no competing interests.

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