Introduction

Breast cancer is the most prevalent cancer in the female population; there are more than 1 million cases worldwide annually. Treatment of breast cancer is guided by assessment of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor 2 (HER2). Expression of ER in breast cancer warrants therapy with tamoxifen and portends a better prognosis. Cases with over expression of HER2 warrant therapy with trastuzumab and have a worse prognosis.

There is limited research on comparison of these receptors in primary tumors versus their lymph node metastases. If receptor expression were different, it could guide changes in therapy. Our aim is to determine if there is a significant change in receptor expression in lymph node metastases compared to primary tumors.

Materials and Methods

Patients

All patients having breast cancer with lymph node metastases at our institution between January 2008 and June 2011 were identified.

Lymph node metastases receptor analysis

Tissue microarrays (TMAs) of lymph node metastases were constructed when possible. If there were >5 mm of metastasis present in a single tissue block or if there were not enough cases, all remaining cases were stained individually. Immunohistochemistry (IHC) was performed to score ER, PR, and HER2. HER2 IHC was scored from 0 to 3+. HER2 FISH was performed on both the primary tumor and the lymph node metastases. HER2 IHC was scored from 0 to +3. HER2 FISH was positive if the ratio was >2.2, negative if the ratio was ≤1.8, and equivocal if the ratio was between 1.8 and 2.2. The individual cases were stained with ER, PR, and HER2 IHC.

Results

Cases

122 cases of breast cancer with lymph node metastases were obtained (Table 1). The types of breast cancer represented were invasive ductal carcinoma (102 cases), invasive lobular carcinoma (15 cases), combined ductal and lobular carcinoma (1 case), tubular carcinoma (2 cases), and medullary carcinoma (2 cases).

Receptor changes observed [Table 1]

6 cases showed changes in ER expression, 6 cases showed changes in PR expression (Figure 2A-B) and 1 case showed a gain in HER2 expression. 20 cases showed changes in PR expression, 16 cases showed loss of PR expression (Figure 2C-D) and 4 cases showed a gain in PR expression. 10 cases showed changes in HER2 expression. 1 case showed loss of HER2 expression (Figure 2E-F). 6 cases went from HER2 negative to equivocal, 2 cases went from HER2 equivocal to negative, and 2 cases changed from HER2 equivocal to positive expression.

Conclusions

Changes in receptor expression in lymph node metastases compared to primary tumors do occur. The percentage of cases with changes in prognostic receptor expression warrants attention. Changes in prognostic receptor expression may indicate that repeat testing for ER, PR, and HER2 in lymph node metastases is indicated. Retesting of prognostic receptors in lymph node metastases would guide treatment changes, especially if gain of expression of ER or HER2 were observed. Retesting of prognostic receptors may explain therapy failure in patients with metastatic disease, especially if there is loss of expression of ER or HER2 in the lymph node metastases.