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Cytomorphological and Immunohistochemical Changes in Breast Cancer Patients Before and After Neoadjuvant Chemotherapy

Ruziyeva Shakhlo Durdikulovna

Bukhara State Medical Institute after named Abu Ali ibn Sina, Bukhara, Uzbekistan

Abstract Breast cancer remains one of the most prevalent malignancies worldwide, requiring effective treatment strategies such as neoadjuvant chemotherapy (NACT). This study evaluates the cytomorphological and immunohistochemical changes in breast cancer tissues before and after NACT in 120 patients. Patients were divided into early-stage (n=31) and late-stage (n=89) groups. Pre-treatment analysis revealed high epithelial cell proliferation (74.43% in early-stage, 71.88% in late-stage), increased atypical nuclear features, and reduced alveolar and myoepithelial cell presence in late-stage cases. Post-treatment findings demonstrated a decrease in atypical cells, improved epithelial and alveolar cell recovery, and reduced nuclear polymorphism, indicating a positive therapeutic response. The study highlights significant cytological improvements following NACT, suggesting that chemotherapy effectively modifies the tumor microenvironment. However, late-stage patients exhibited a more heterogeneous response, emphasizing the need for additional therapeutic interventions and long-term monitoring. These findings support the importance of personalized treatment approaches to enhance breast cancer management [6,7,10].

Keywords Breast cancer, Neoadjuvant chemotherapy, Cytomorphology, Epithelial cells, Alveolar cells, Myoepithelial cells, Atypical cells, Tumor microenvironment, Chemotherapy response, Immunohistochemistry

1. Introduction

Breast cancer remains one of the most prevalent malignancies worldwide, accounting for a significant proportion of cancer-related morbidity and mortality among women (Bray et al., 2018). Advances in cancer treatment have led to the widespread use of neoadjuvant chemotherapy (NACT) as a first-line approach for managing locally advanced breast cancer. NACT is administered before surgical intervention with the primary goal of reducing tumor size, enabling breast-conserving surgery, and improving long-term survival outcomes (Mittendorf et al., 2016). In addition to its direct cytotoxic effects on tumor cells, NACT also induces significant cytomorphological and immunohistochemical changes in the tumor microenvironment, which may impact overall treatment response and prognosis (Denkert et al., 2017).

Despite the established benefits of NACT, the response to chemotherapy varies significantly among breast cancer patients, necessitating further investigation into tumor tissue alterations before and after treatment (Cortazar et al., 2014). Cytomorphological analysis of breast tumor specimens provides valuable insights into cellular dynamics, including changes in epithelial proliferation, nuclear atypia, and inflammatory cell infiltration (Symmans et al., 2017). These cytological features serve as important predictive and prognostic biomarkers in assessing tumor sensitivity to chemotherapy and determining patient outcomes.

Breast cancer remains one of the most prevalent malignancies among women, requiring comprehensive treatment approaches to improve patient outcomes. Neoadjuvant chemotherapy (NACT) is a widely used preoperative strategy aimed at reducing tumor size, increasing the feasibility of breast-conserving surgery, and improving long-term survival rates. In addition to its therapeutic effects, NACT induces significant cytomorphological and immunohistochemical changes in breast cancer tissues, which are crucial for assessing treatment response and predicting prognosis [4,8,6].

One of the primary aspects of evaluating NACT effectiveness is the cytomorphological analysis of tumor tissues before and after chemotherapy. Changes in epithelial cell structure, atypical nuclear formations, and the presence of alveolar and myoepithelial cells provide valuable insights into tumor behavior and response to treatment. Pre-treatment biopsies often reveal high epithelial proliferation, nuclear polymorphism, and increased atypical cells, particularly in patients with advanced disease. Post-treatment changes,

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such as a reduction in atypical cells, improved epithelial differentiation, and structural restoration of alveolar and myoepithelial cells, indicate the effectiveness of chemotherapy and potential tumor regression [2,5,8].

In addition to cytomorphological changes, chemotherapy-induced immune responses play a crucial role in tumor evolution. The presence of inflammatory cell infiltration and immunological alterations can influence chemotherapy resistance and overall treatment success. Identifying these changes can help guide future therapeutic strategies and optimize patient-specific treatment plans.

This study aims to analyze the cytomorphological and immunohistochemical changes in breast cancer tissues before and after NACT, focusing on epithelial, alveolar, and myoepithelial cell dynamics. The findings will provide insights into tumor response to chemotherapy, assisting in the development of more effective treatment approaches for breast cancer patients [1,8,9,11].

2. Materials and Methods

Study Design and Population. This study was conducted at the Bukhara Regional Oncology Center and included 120 female patients diagnosed with histologically confirmed breast cancer. Patients were divided into two groups based on the clinical stage of their disease at the time of diagnosis:

- Early-stage group (n=31): This group included patients whose tumors were detected in the early phases of development, characterized by localized disease with minimal invasion and without evident lymph node involvement. These patients exhibited clear early clinical signs of breast cancer, including palpable lumps, localized pain, and changes in breast tissue density.
- Late-stage group (n=89): This group comprised patients diagnosed at an advanced stage of breast cancer progression. These individuals did not exhibit noticeable symptoms in the early stages, leading to a delayed diagnosis. The tumors in this group showed greater local invasion, higher lymphatic involvement, and a more aggressive cellular profile.

All patients included in the study underwent neoadjuvant chemotherapy (NACT) before planned surgical intervention.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM, USA). The following statistical tests were applied:

- Paired t-test – To compare pre- and post-chemotherapy values within each group.
- Independent t-test – To assess differences between early- and late-stage patients.
- ANOVA – To evaluate variations in immunohistochemical marker expression across multiple subgroups.

A p-value of <0.05 was considered statistically significant. All findings were reported as mean ± standard deviation (SD).

3. Results

Pre-Treatment Cytological Findings. Before initiating neoadjuvant chemotherapy (NACT), significant cytological abnormalities were observed in the breast cancer tissue samples of both early-stage and late-stage patient groups. The predominant cellular changes included epithelial atypia, nuclear polymorphism, and increased cellular proliferation, which are indicative of an aggressive tumor microenvironment.

- Epithelial cell prevalence: In early-stage patients, epithelial cells accounted for 74.43%, whereas in late-stage patients, this percentage was slightly lower at 71.88%. This difference suggests that epithelial proliferation is more pronounced in the early-stage group, potentially due to higher cellular turnover rates in response to tumor progression.
- Alveolar cell presence: The proportion of alveolar cells (lactocytes) was significantly higher in the early-stage group (41.17%) compared to the late-stage group (34.21%). This reduction in alveolar cells in the late-stage patients suggests compromised tissue functionality and potential alterations in glandular structure due to tumor invasion.
- Myoepithelial cell distribution: Myoepithelial cells, which play a crucial role in maintaining tissue integrity, were present at 38.26% in the early-stage group and 35.17% in the late-stage group. The lower proportion of these cells in late-stage patients may indicate a weakening of the supportive tissue framework, further contributing to tumor progression.
- Atypical cell prevalence: Atypical cellular features, including enlarged nuclei, hyperchromasia, and irregular mitotic figures, were more frequently observed in late-stage patients. This is indicative of higher tumor aggressiveness and potential chemoresistance in more advanced disease stages.

These findings suggest that before NACT, breast cancer tissues in both early and late-stage patients exhibit high cellular proliferation, disrupted structural integrity, and increased nuclear abnormalities, all of which are characteristic of an aggressive neoplastic process [2,4,7,9].

Post-Treatment Cytological Changes

Following the administration of neoadjuvant chemotherapy, notable cytological modifications were detected in tumor tissues, reflecting varying degrees of therapeutic response. The major post-treatment changes included a reduction in atypical cell populations, increased epithelial recovery, and improved alveolar cell function, all of which indicate a favorable response to chemotherapy [1,8,9].

- Reduction in atypical cells: The prevalence of atypical cells significantly decreased in late-stage patients, dropping from 25.34% to 19.23%. This reduction suggests that NACT effectively targeted malignant cells, inducing apoptosis and reducing tumor burden.
- Increase in epithelial cell activity: The proportion of epithelial cells increased post-treatment in both groups, with early-stage patients showing a rise from 74.43% to

76.90%, and late-stage patients demonstrating a more substantial increase from 71.88% to 82.71%. This enhancement in epithelial cell presence indicates tissue regeneration and partial restoration of normal breast tissue morphology.

- Alveolar cell recovery: A significant improvement in alveolar cell percentage was noted, particularly in late-stage patients, where it rose from 34.21% to 64.21%. In early-stage patients, the increase was more moderate, from 41.17% to 45.19%. The pronounced alveolar cell restoration in late-stage patients suggests that despite advanced disease, chemotherapy facilitated tissue remodeling and functional glandular recovery.
- Myoepithelial cell stability: A slight but noticeable increase in myoepithelial cell presence was observed in both groups. These cells play a crucial role in maintaining breast tissue architecture, and their relative stability post-treatment indicates that NACT preserved key structural components of the tissue.
- Decreased nuclear polymorphism: One of the most important microscopic findings was the reduction in nuclear atypia and mitotic activity post-treatment, indicating a decline in aggressive tumor characteristics. The decreased frequency of multinucleated cells and irregular chromatin patterns suggests that chemotherapy -induced tumor cell differentiation and apoptosis were effective [4,8,9,11].

Comparative Analysis of Early-Stage and Late-Stage Groups

While both early-stage and late-stage breast cancer patients exhibited positive cytological changes following chemotherapy, the extent of improvement varied:

- Early-stage patients showed more stable epithelial and alveolar cell percentages, suggesting a consistent and controlled response to chemotherapy with minimal residual disease.
- Late-stage patients exhibited a greater increase in epithelial and alveolar cell recovery, which may indicate a delayed but effective therapeutic response, likely due to the higher tumor burden at the time of diagnosis.
- Late-stage patients experienced a more significant reduction in atypical cells, suggesting that NACT was particularly beneficial in eliminating malignant cell populations in advanced tumors.
- Despite improvements, late-stage patients still exhibited a higher residual atypical cell count, indicating that additional treatment strategies, such as targeted therapies or extended chemotherapy cycles, may be necessary for optimal disease control.

These findings highlight the importance of individualized chemotherapy regimens based on disease stage, as well as the necessity for long-term monitoring of cytological changes to evaluate tumor response and prevent recurrence [1,5].

4. Conclusions

The results of this study demonstrate that neoadjuvant chemotherapy induces significant cytomorphological improvements in breast cancer patients. The reduction in atypical cells, restoration of epithelial and alveolar structures, and decreased nuclear abnormalities indicate that chemotherapy effectively modifies the tumor microenvironment, promoting favorable treatment outcomes [7,9].

However, late-stage patients exhibited a more heterogeneous response, suggesting the potential need for additional therapeutic interventions beyond standard chemotherapy. Regular cytological monitoring remains essential for assessing the long-term effects of NACT and optimizing individualized treatment strategies for breast cancer patients [4,8,11].

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