



Evaluation of the Relationship Between Axillary Lymph Node Involvement with Frequently Evaluated Prognostic Factors in Breast Cancer

Meme Kanserlerinde Aksiller Lenf Nodu Tutulumunun Sık Değerlendirilen Prognostik Faktörlerle İlişkinin Değerlendirilmesi

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Abstract

Objective: We aimed to evaluate the effect of hormone receptor and immunohistochemistry data on the incidence of primary tumor type and lymph node positivity in breast cancer cases.

Method: Demographic, immunohistochemical data of 62 patients who were biopsied in the institute's interventional radiology clinic and long axis of primary tumor in ultrasonography (USG) were retrospectively evaluated.

Results: The age of the patients, cell type, c-erb B-2 score and axillary lymph node positivity were not significantly correlated with the assessed data, whereas the long axis of primary tumor, estrogen and progesterone receptor severity and prevalence, ki-67 proliferation index affected lymph node involvement ratio.

Conclusion: Evaluation of lymph node involvement with second-line detailed USG before the operation, especially in malignant tumors refer to surgical or interventional radiology departments with negative, high ki-67 PI and C-erb B-2 values in estrogen and progesterone receptors, and the presence of recent axillary USG examination of the cases for breast biopsy regardless of the results, will provide important contribution in the diagnosis and treatment stages.

Keywords: Axillary lymph node, breast cancer, hormone receptors, immunohistochemical data

Öz

Amaç: Meme kanseri olgularında hormon reseptör ve immünohistokimyasal verilerinin, primer tümör tipinin ve büyüklüğünün lenf nodu pozitif olma sıklığına etkisini araştırmayı amaçladık.

Yöntem: Enstitümüz girişimsel radyoloji kliniğinde biyopsi aldığımız 62 olgunun demografik immünohistokimyasal verileri ve ultrasonografide (USG) primer tümör uzun eksenini retrospektif olarak değerlendirilmiştir.

Bulgular: Değerlendirilmeye alınan verilerden hastaların yaşı, hücre tipi, c-erb B-2 skoru, değerlerinin aksiller lenf nodu pozitifliğine anlamlı katkısı bulunamaz iken primer tümörün uzun eksenini, östrojen ve progesteron reseptör şiddeti ve yaygınlığı, ki-67 proliferasyon indeksi lenf nodu tutulumuna etki etmektedir.

Sonuç: Özellikle östrojen ve progesteron reseptörlerine negatif, yüksek ki-67 PI ve C-erb B-2 değerleri elde edilmiş malign tümörlerde, operasyon öncesi ikinci bakı detaylı USG ile lenf nodu tutulumu değerlendirilmesi ve sonuçlar ne olursa olsun meme biyopsisi alınması için cerrahi veya girişimsel radyoloji departmanlarına refere edilen olguların yanlarında son dönemde elde olunmuş aksiller bölge USG incelemesinin bulunmasını sağlamak tanı ve tedavi aşamalarında önemli katkılar sağlayacaktır.

Anahtar kelimeler: Aksiller lenf nodu, hormon reseptörleri, immünohistokimyasal veriler, meme kanseri



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Introduction

Malignant tumors of the breast are the second most common cause of cancer death in women after lung. A woman's risk of death due to breast cancer is 1 in 37 (approximately 2.7%) (1). Although lymph node involvement affects the prognosis, it is not the only indicator. In recent studies, the 5-year survival rate has been determined as 99% only in the presence of breast cancer. This rate decreases to 85% in the spread of local lymph nodes and to 26% in the presence of distant metastases (2). In addition to histopathological examination, staging, immunohistochemical evaluation is frequently performed because it determines the patient's prognosis and contributes to treatment planning. In recent studies, the relationship of immunohistochemical data with prognosis and treatment continues to be evaluated.

Lymph node pathologies are common, and many different entities can affect their size and shape. These may be due to infectious, metabolic, neoplastic or physiological reasons (3). Imaging-guided lymph node biopsies are generally performed using two different methods. These are fine needle biopsy (FNAB) and core needle biopsy (CRI). With CRI, liquid and small particle-containing material is obtained by using a 14-20 G, thicker needle vacuum device (VIB) compared to fine needle. In both methods, local anesthesia can be used if necessary (4).

The aim of the study is to evaluate the relationship between the frequency of sentinel lymph node involvement, histological diagnosis, primary tumor size, cell type, estrogen-progesterone receptor severity-prevalence, c-erb B-2 score and ki-67 proliferation index parameters in cases diagnosed with histopathologically breast cancer.

Materials and Methods

Patients diagnosed with breast cancer histopathologically were included in our study. Age of the patients, long axis of the primary tumor, cell type and immunohistochemical findings were recorded to compare. In the evaluation of hormone receptors, the severity and prevalence of estrogen and progesterone receptors were evaluated together.

Biopsy Procedure

Before the procedure, all patients were questioned about possible contraindications and the presence of anxiety. After sterilization, a topical 10% lidocaine solution (Vemcaine Pump Spray; Nobel Farma medical) was applied to the procedure area. In addition, 5-10 mL of Bupivacaine (Marcaine solution; Pfizer) was applied as a local anesthetic for VIB. 22 G injectors were used for FNAB and 18 G vacuum

biopsy needles were used for vacuum biopsy (Figure 1). USG device was Aplio 500 (Toshiba Medical Systems Europe) and 7.2-14 MHz linear probe was used.

Statistical Analysis

Anova (single factor) was used in the data analysis. The p-value less than 0.05 were considered significant. For statistical evaluation Microsoft Excel pack programme (version 2206) was used.

All procedures performed in studies involving human participants were performed in accordance with institutional and/or national research ethical standards and the 1964 Declaration of Helsinki and its later revisions. The patient data were obtained retrospectively from the archives of our institute and from the patients who underwent true breast and fine-vacuum needle lymph node biopsy in the interventional radiology department. Informed consent was obtained from the patients participating in the study before the procedure.

Ethical approval: All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by our IRB (date: 06.02.2018, no: 825).

Results

A total of 62 female cases participated in our study. The mean age was 48.2 (27-83). Age, cell type, c-erb B-2 score values of the patients were not found to contribute significantly to sentinel lymph node positivity. In addition, it was observed that the long axis of the tumor, estrogen and progesterone receptor severity and extent, and ki-67 proliferation index parameters affected lymph node involvement (Table 1).

FNAB was used in 11 cases and VAP was used in 51 cases. Histopathological results of the cases: Invasive ductal

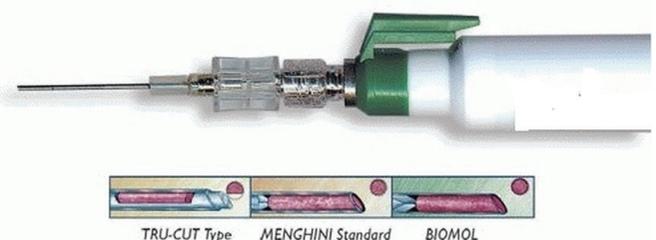


Figure 1. Instrument used for vacuum biopsy

carcinoma in 55 cases and invasive lobular carcinoma in 7 cases (Table 2).

Discussion

USG was used as guide imaging in our study. This modality is the most preferred method because it can clearly show the superficial structures, does not use ionizing radiation, is non-invasive, allows real-time examination, and is inexpensive (5). As the lymph node biopsy technique, VIB was preferred in a significant part of our cases (82.3%). Despite the use of thicker needles, it is a well tolerated method when local anesthesia is used. In our study, no major complications were encountered with this method. Subcutaneous hemorrhage, which can be limited with subcutaneous ice therapy, was observed in only two cases. The only disadvantage of this method is that it is more expensive. In recent years, especially VIB has been replacing excisional surgical techniques. Considering the diagnostic accuracy, sensitivity and specificity, although similar results are obtained, it is a minimally invasive method and is more advantageous in terms of morbidity and cost (6-10). At this point, it should be noted that although micrometastases are present in the sentinel lymph nodes in many cases, residual tumor remains due to false negative results in biopsy, even if it is detected on USG, and it is reported to be an important cause of recurrence (Figure 2).

When the demographic data of the cases were evaluated, it was observed that all cases were female. In the literature, breast cancer is reported to be 100 times more common in women compared to men (11). There was no statistically significant difference between the mean age of the cases with and without axillary lymph node involvement.

In our study, it was observed that tumors with large long axis had more frequent lymph node involvement. Here, the long axis can be defined as the primary tumor burden

indicator in the breast. Malignant tumors reaching larger volumes are more likely to spread to sentinel lymph nodes and other distant tissues.

According to our results, high ki-67 PI increases the possibility of lymph node metastasis. Similarly, in previous studies, high PI was associated with younger patient age, high histological grade, estrogen receptor negativity, and increased risk of metastatic involvement (12-14). A more aggressive course and shorter average survival can be expected in breast cancer cases diagnosed at a young age. Especially the presence of distant metastases (extra-axillary) negatively affects the prognosis.

Presence of estrogen and progesterone receptors in immunohistochemistry studies reduces the possibility of lymph node involvement. Presence of estrogen and progesterone receptors can be defined as a positive prognostic factor in this respect, as it will increase the chance of cure of the tumor with hormone therapy and lymph node involvement will be less expected. Similar to our study, there are many studies in the literature reporting the positive contribution of hormone receptor positivity to clinical course and axillary involvement (15-18).

In our study, although increased C-erb B-2 expression was found to be higher in cases with axillary lymph node involvement, the difference was not statistically significant. The results obtained in the literature on this subject are controversial. There are studies reporting that axillary lymph node involvement is increased in cancers with

Table 2. The distribution of pathologic results and biopsy procedure

		No of nodes	%
Diagnosis	Invasive ductal carcinoma	55	88.7
	Invasive lobular carcinoma	7	11.3
Technic	FNAB	11	17.7
	VAB	51	82.3

FNAB: Fine needle biopsy

Table 1. Relation of immunohistochemical data with axillary lymph node

Findings	Sentinel lymph node negative	Sentinel lymph node positive	p
Long axis of the primary tumor	20.36±11.1 mm	31.4±12.2 mm	<0.01
The mean age of patients	60.23±11.5	58.33±13.12	0.32
Ki-67 PI %	12.42±11	18.16±13.18	0.012
Estrogen receptor x diffusiveness (%)	66.88±30.87	50.66±32.67	0.028
Progesteron receptor x diffusiveness (%)	56.74±35.75	38.33±34.03	0.026
The mean C-erb B-2 score	0.67±1.07	1.17±1.31	0.11
Invasive ductal ca	22	33	0.13
Invasive lobuler ca	3	4	

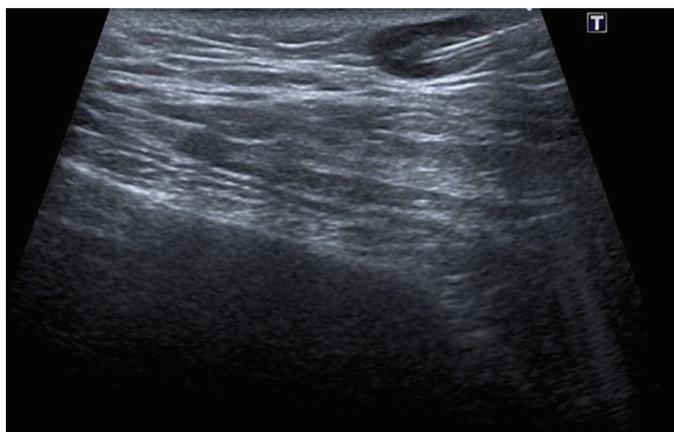


Figure 2. Fifty-three years old female case. Since the axillary lymph node has a benign appearance (oval shaped, fatty hilus intact) radiologically, histopathological examination was not performed. Biopsy was recommended because estrogen and progesterone receptors were negative. Micrometastasis was found as a result of the fine needle biopsy

increased expression (19,20). However, Tweedie et al. (21) stated that it had no reverse effect.

Finally, it was determined that the cell type did not affect the probability of axillary lymph node metastasis. In our study, the diagnosis of most of the cases was invasive ductal carcinoma, in line with the literature. Seven of our cases were diagnosed with invasive lobular carcinoma. Detection of only two cell types in histopathological results may affect the judgment that axillary involvement is not cell type dependent. We might have had a different outcome had our case group had neuro-endocrine carcinomas or micropapillary carcinomas, which were described as potentially more aggressive. Of course, since these entities are rare, a study with a larger series is needed.

Although there are many studies on this subject in the literature, the number of studies in which axillary lymph node involvement, which is an important prognostic indicator, is evaluated in isolation is very few. In most of the studies, the correlation of immunohistochemical data with the survival time of the cases was evaluated. In addition, studies conducted in recent years tend to classify breast cancers according to the results of immunohistochemical data and to predict prognosis according to this classification.

Study Limitations

The first limitation of our study is that not all lymph node biopsies were performed with VIB. Because there are studies indicating that VAP has a higher sensitivity in detecting the presence of axillary lymph node metastasis in breast cancer compared to FNAB (22,23). The second limitation is the

relatively small number of cases. Similar studies in this area with more cases will contribute to the literature.

Conclusion

When the results of our study are evaluated, we recommend that axillary lymph node involvement be evaluated with detailed USG in the second look before biopsy and operation in malignant tumors that do not have estrogen and progesterone receptors and have high ki-67 PI and C-erb B-2 values. However, regardless of the immunohistochemical results, ensuring that the cases referred to surgery or interventional radiology departments for breast biopsy are accompanied by recent axillary region USG examinations will provide important contributions in the diagnosis and treatment stages.

Ethics

Ethics Committee Approval: All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was approved by our IRB (date: 06.02.2018, no: 825).

Informed Consent: Informed consent was obtained from the patients participating in the study before the procedure.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.Ö., M.Ö., Concept: D.Ö., M.Ö., Design: D.Ö., M.Ö., Data Collection or Processing: D.Ö., M.Ö., Analysis or Interpretation: D.Ö., M.Ö., Literature Search: D.Ö., M.Ö., Writing: D.Ö., M.Ö.

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