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KLİNİK ARAŞTIRMA *Göğüs Hastalıkları*

Evaluation of thoracic manifestations of breast cancer

İpek ÖZMEN (*), Tülay TÖRÜN (*), Güliz ATAÇ (*), Emine AKSOY (*), Gülbanu HORZUM (*), Yasemin BÖLÜKBAŞI (**), Haluk ÇALIŞIR (*), Kemal TAHAOĞLU (***)

SUMMARY

Objectives: *Clinical and radiological features of 36 patients with breast cancer were investigated retrospectively.*

Materials and methods: *Patients with breast cancer who had pulmonary complaints and radiologic abnormalities observed during oncology follow-ups were hospitalized, and investigated in clinics of chest disease. Pulmonary lesions were classified into 2 groups; Group I: malignant lesions due to metastasis of breast cancer, and Group II: nonmalignant lesions.*

Results: *The mean age of the patients was 52.4±14.8 (28-93) years. Thirty-four patients were previously diagnosed with unilateral and 2 patients with bilateral ductal breast carcinoma. Twenty seven percent (n=10) of the patients were smokers (mean 10.7±6.81 pack-years). The mean time between the detection of breast cancer and the manifestations of pulmonary symptoms was 57.02±53.83 (3-180) months). The most common radiological abnormality was pleural effusion (n=23;63.9 %). Twenty-seven (75 %) patients had malignant (Group I), and 9 (25 %) patients had nonmalignant (Group II) pulmonary lesions. Malignant histopathology (n=27) was established by pleural fluid cytology in 13 (48.1 %), fiber optic bronchoscopy in 8 (29.6 %), pleural biopsy in 4 (14.8 %), CT guided transthoracic needle aspiration biopsy in 1 (3.7 %) and thoracotomy in 1 (3.7 %) patient, respectively. Mean time interval between the diagnosis of breast cancer and the detection of malignant pleural effusion was 69.91±64.21 (3-180) months. Nine (25 %) patients had nonmalignant pulmonary lesions including pneumonia in 3 (33.3 %), pulmonary thromboembolism and DVT in 3 (33,3 %), tuberculosis in 2 (22.2 %) and pulmonary fibrosis in 1 (11,1 %) patient.*

Conclusion: *Pulmonary manifestations of breast cancer are most commonly related to metastases and can be observed in long time after the diagnosis of breast cancer. Besides, these nonmalignant reasons should be kept in mind and histopathologic confirmation should me made.*

Key words: *breast cancer, pleural effusion, malignant effusion, pulmonary metastases*

ÖZET

Meme kanserli olguların akciğer bulgularının değerlendirilmesi

Giriş: *Hastanemizde iki göğüs hastalıkları kliniğinde tetkik edilen 36 meme kanserli hastanın klinik ve radyolojik özellikleri retrospektif olarak değerlendirildi.*

Gereç ve Yöntem: *Onkoloji takipleri sırasında solunumsal yakınmaları olan ve radyolojik bulgular saptanan, hastaneye yatırılarak tetkik edilmiş olan meme kanserli hastalar değerlendirildi. Hastaların pulmoner lezyonları 2 grupta değerlendirildi; Grup I: meme kanseri metastazına bağlı malign lezyonlar, Grup II: malignite dışı lezyonlar.*

Bulgular: *Hastaların yaş ortalaması 52,4±14,8 (28-93) yıl olarak saptandı. Otuz dört hastada tek taraflı, 2 olguda çift taraflı duktal meme kanseri öyküsü mevcuttu. Hastaların % 27'si (n=10) sigara kullanmaktaydı, (ortalama 10,7±6,81 paketyıl). Meme kanseri saptanması ve solunumsal yakınmaların başlaması arasında geçen ortalama süre 57,02±53,83 (3-180) ay, en sık rastlanan radyolojik bulgu plevral efüzyon olarak saptandı (n=23). Pulmoner lezyonlar hastaların 27'inde (% 75) malign (Grup I), 9 (% 25) hastada ise malignite dışı (Grup II) nedenlere bağlı saptandı. Malign histopatoloji saptanan hastalarda (n=27) tanı yöntemleri sırasıyla; plevral sıvı sitolojisi 13 (% 48.1), plevra biyopsisi 4 (% 14.8), Fiberoptik bronkoskopi 8 (% 29.6), transtorakal biyopsi 1 (% 3.7), torakotomi 1 (% 3.7). Malign plevral efüzyon saptanan hastalarda meme kanseri tanısı ile malign efüzyon saptanması arasında geçen süre 69,91±64,21 (3-180) ay olarak saptandı. Dokuz (% 25) hastada pulmoner lezyonlar malignite dışı nedenlere bağlı olarak değerlendirildi: pnömoni 3 (% 33.3), pulmoner emboli ve derin ven trombozu 3 (% 33.3), tüberküloz 2 (% 2.22), pulmoner fibrozis 1 (% 11.1).*

Sonuç: *Meme kanserli hastalarda pulmoner bulgular sıklıkla metastazlar nedeniyle ortaya çıkmaktadır ve meme kanseri tanısından uzun süre sonra ortaya çıkabilirler diğer taraftan malignite dışı pulmoner nedenler de unutulmamalı, histopatolojik doğrulama yapılmalıdır.*

Anahtar kelimeler: *meme kanseri, plevral efüzyon, malign efüzyon, pulmonar metastaz*

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*Süreyyapaşa Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları, **Ereğli Anadolu Hastanesi, Göğüs Hastalıkları, ***Anadolu Sağlık Merkezi, Göğüs Hastalıkları

Abbreviations:
CT : Computed tomography
FOB: Fiber optic bronchoscopy
EFB: Endobronchial forceps biopsy
BNA : Bronchial needle aspiration
TBB : Transbronchial biopsy
DVT: Deep vein thrombosis

Lung is a common site of metastasis from breast cancer. Metastasis can occur both by hematogenous and lymphatic spread. However pulmonary problems may result not only from metastasis but also from treatment, including chemo-radiotherapy related complications, infections or second primary malignancy [1].

In this study we retrospectively investigated clinical and radiological features and pulmonary findings of 36 female patients with breast cancer who admitted to two chest disease clinics with pulmonary complaints or who were referred because of their oncology follow-up revealed new radiological findings.

MATERIALS and METHODS

Patients with breast cancer who had pulmonary complaints and radiological abnormalities observed during oncology follow-up, and had indications for hospitalization were admitted and investigated in two chest disease clinics in our hospital between January 2003, and June 2010.

Pulmonary lesions were classified in 2 groups:

Group I : malignant lesions due to metastasis of breast cancer

Group II: nonmalignant lesions

RESULTS

Thirty-six patients with breast cancer including 32 (88.9 %) cases with pulmonary complaints and 4 (11.1 %) with radiological abnormalities were evaluated. The mean age of the patients was 52.04±14.8 (28-93) years. Thirty-three patients were previously diagnosed with unilateral and 2 patients with bilateral ductal breast carcinoma. Breast cancer was on the left side in 18 (50 %), on the right side in 16 (44.4 %) and bilateral in 2 (5.6 %) patients. One patient was diagnosed as breast cancer while she was being investigated for pleural effusion in our clinic. This patient received chemotherapy, and the other 34 patients had a history of surgical therapy (mastectomy/mastectomy and axillary curretation) and adjuvant chemo-radiotherapy and one patient had received only chemotherapy. Ten (27 %) patients were smokers (mean pack-years). The mean time interval between the detection of breast cancer and the manifestations of pulmonary symptoms was 57.02±53.83 (3-180) months.

The patients' complaints often arise in the first five years (Figure 1).

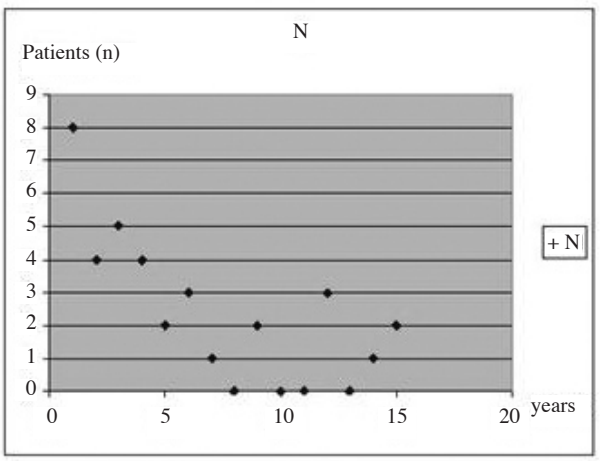

Figure 1. The distribution of number of patients according to the mean time prior to thoracic manifestations and detection of breast cancer.

Tablo 1. Frequency of pulmonary symptoms of the cases with breast cancer.

Symptom	N	%
Dyspnea	21	58,3
Cough	20	55,6
Chest pain	13	36,1
Sputum production	9	25,0
Fever	3	8,3
Weigth loss	3	8,3
Hemoptysis	2	5,6

The most common symptoms are dyspnea, cough and chest pain (58.3, 55.6, and 36.1 %, respectively). Frequency of pulmonary symptoms is shown in Table 1.

In 17 (47.2 %) patients pulmonary lesions were on the same side with breast cancer, in 9 (25 %) cases it was bilateral, in 9 (25 %) patients pulmonary lesions were on the contralateral side of the breast cancer, and 1 (2.8 %) patient had a normal chest X-ray.

In all patients one or more radiological abnormalities were detected either on chest X-ray or on thorax CT (computed tomography) as shown in Table 2.

Tablo 2. Radiological patterns of thoracic involvements of patients with breast cancer.

Radiological patterns	N	%
Pleural effusion	23	63,9
Solitary/multiple pulmonary nodules	8	22,2
Consolidation	8	22,2
Mediastinal Lymphadenopathy	6	16,7
Mass	3	8,3
Ground glass opacity	3	8,3
Reticulonoduler /fibrosis	1	2,8
Ateleclasis	1	2,8
Normal	1	2,8

The most common radiological abnormality was pleural effusion (n=23; 63.9 %) which is on the same side with breast cancer in 11 (47.8 %), on the opposite side in 6 (26.1 %) and bilateral in 6 (26.1 %) patients.

In 27 (75 %) patients metastatic, and and in 9 (25 %) patients nonmalignant pulmonary lesions (Group II) were detected. Pulmonary diagnosis of the patients is shown in Table 3.

Tablo 3. Pulmonary diagnosis of patients with breast cancer.

Group	N	%
Group I Malignant (pulmonary or pleural)	27	75
GroupII nonmalignant	9	25
• pneumonia	3	33,3
• Pulmonary thromboembolism	3	33,3
• tuberculosis	2	22,2
• Fibrosis	1	11,1

Diagnostic procedures of the malignant lesions are shown in Table 4.

Tablo 4. Diagnostic procedures of the malignant lesions.

Diagnostic procedures	N	%
Pleural cytology	13	48,1
Bronchoscopic biopsy	8	29,6
Pleural biopsy	4	14,8
TTNA*	1	3,7
Thoracotomy	1	3,7
Total	27	

**TTNA: Transthoracic needle aspiration biopsy*

Malignant histopathology (n=27) was established by pleural fluid cytology in 13 (48.1 %), pleural biopsy in 4 (14.8 %), fiber optic bronchoscopy in 8 (29.6 %), CT guided transthoracic needle aspiration biopsy in 1 (3.7 %) and thoracotomy in 1 (3.7 %) patient, respectively.

Pleural effusion was observed in 23 (63.9 %) patients. Thoracentesis was performed in 20 patients, however in 3 patients with small amount of pleural effusion thoracentesis was not performed. Pleural etiology was related to nonmalignant factors in 3 (%) patients. Seventeen (73.9 %) patients had malignant histopathology established by pleural fluid cytology in 13, pleural biopsy in 4, and fiber optic bronchoscopic (FOB) examination of endobronchial lesions in 3 patients, respectively.

Among 17 patients with malignant effusions, 10 (58,8 %) patients had effusion on the same side with breast cancer while 4 (23,5 %) had effusion on the opposite side and 3 (17,7 %) patients had bilateral malignant pleural effusions. The mean time interval between the diagnosis of breast cancer and the detection of malignant pleural effusion was 69.91±64.21 (3-180) months.

Fiber optic bronchoscopy was performed in 12 (33,3 %) patients. During bronchoscopic examination endobronchial pathology was detected in 5 (41.7 %), stenosis in 2 (40 %), submucosal infiltration in 2 (40 %), and extrinsic compression on the 1/3 distal part of trachea in 1 (8.3 %) patient. respectively. In these 5 cases (41.7 %) with endobronchial lesions, malignant histopathological diagnosis was obtained by EFB (endobronchial forceps biopsy) or BNA

(bronchial needle aspiration). In seven (58.3 %) patients without endobrochial pathology, malignant histopathology was revealed during transbronchial biopsy in 3 (42.9 %) patients. CT guided transthoracic needle aspiration biopsy in 1 (14.3 %) patient detected mass lesions, and thoracotomy demonstrated malignant histopathology in 1 (14.3 %) patient with solitary pulmonary nodule and pneumonia was diagnosed in 2 (28.6 %) patients.

Nine (25 %) patients had nonmalignasnt pulmonary lesions. Pneumonia was detected in 3 (33.3 %), pulmonary thromboembolism and DVT in 3 (33.3 %), and pulmonary fibrosis in 1 (11.1 %) patient, respectively. Antituberculostatic chemotherapy was administered to 1 patient with thick-walled cavitary lesion on the right upper lobe who had positive sputum culture for M.tuberculosis on Lowenstein-Jensen medium, and the other patient with histopathologically demonstrated tuberculous pleurisy.

In November 2012, data of 19 (52.8 %) out of 36 patients whom we had a phone contact. Fifteen patients had died and 4 patients were alive. Among 15 patients who had died 12 patients had malignant pulmonary lesions (9 malignant pleural effusions) and 3 patients had nonmalignant lesions (pneumonia, fibrosis). The mean survival time of these patients since the detection of malignant pleural effusions was 19.6±14.63 months. Four patients with malignant pulmonary lesions (2 malignant effusions) were still alive.

DISCUSSION

Breast cancer takes the first place among cancers with metastatic spread to lung and pleura. Interestingly, pulmonary metastasis can occur a long time after the diagnosis of breast cancer. Moreover, nonmalignant pulmonary pathology and chemoradiotherapy related problems can also occur. Consequently, in these patients the most important point is the clear descriptions of the pulmonary problems.

In this study 88.9 % (n=32) of the cases were admitted to two clinics in our hospital with pulmonary symptoms. Four (11.1 %) of these patients without pulmonary symptoms were found to have radiographic abnormalities that were recognized during oncology follow-ups. At this point, the importance of periodic radiological controls of patients with breast cancer is evident. These periodic radiographic controls would provide not only early recognition of pulmonary lesions but also information about the change in size of any pulmonary nodules/mass which were present on previous radiographs. Dyspnea, cough and chest pain were the most common (58.3 %, 55.6 %, 36.1 %, respectively) pulmonary symptoms related to pleural effusion are also the most common radiological pattern . Breast cancer is the second most common cause of malignant pleural effusion after lung cancer [1-2]. It is commonly accepted that the primary cancer spreads from the ipsilateral internal mammarian lymph nodes by lymphatic communications to pleura, lung, mediastinal lymph nodes and pericardium to form ipsilateral pleural effusion. Moreover, contralateral or bilateral effusions can occur by lymphatic spread through hepatic and chest wall lymphatics [3].

In several studies, the mean time interval between the diagnosis of primary breast cancer and detection of pleural effusion has been reported as 24-240 months [4,5]. In our study mean time interval between the diagnosis of primary breast cancer and detection of pleural effusion was 69.91±64.21 (8-180) months.

In several studies it is reported that malignant pleural effusion is most commonly unilateral and spred by lymphatic route to the same side of the breast cancer [6]. However, in our study malignant effusion was on the same side with breast cancer in 10 (58.8 %) patients, and on the opposite side in 4 (23,5 %) and bilateral in 3 (17.7 %) patients. In another studies malignant effusion was reported as on the same side with breast cancer in (50 %, 70 %), on the opposite side in 40 % and bilateral in 10 % of the cases [7].

In the study by McDonald M et al. [8] the median

tumor-free interval after primary breast cancer operation was reported as 2.2 years (range 7 days to 20.6 years) and they reported that 31 of the 60 patients (51.6 %) had solitary pulmonary metastases. There are several studies reporting pulmonary metastasis long time after the treatment of breast cancer [9]. In our study the mean time between the diagnosis of breast cancer and detection of malignant pulmonary pathology was 4.8±4.2 (0.3-15.0) years. The rate of isolated nodular metastasis has been reported as 15-25 % [10,11]. However there are studies reporting that presence of pulmonary nodules in a patient who had breast cancer did not always indicate metastasis. These nodules can be nonmalignant. In various studies benign cause of pulmonary lesions is reported as 7 and 18 % [12].

Kamby et al. [13] described metastatic pulmonary nodules as round, variable in size, commonly localized in the lower-mid lung zones and more often localized peripherically rather than centrally. In our study solitary nodules some with accompanying consolidation, but commonly multiple nodules were present in 8 (22.2 %) patients, all of them had malignant histopathology.

Endobronchial metastasis from breast cancer is more commonly seen than the other tumors [14-16]. In several reports breast cancer accounts for 63 % of all endobronchial metastasis [17]. In our study we performed fiber optic bronchoscopy in 12 (33.3 %) patients and endobronchial metastasis was observed in 41.7 % (n=5) of these patients. Endobronchial lesions included mucosal infiltration (n=2), stenosis (n=2), and extrinsic compression (n=2). In 3 patients with ground glass opacification, bilateral pleural effusion and multiple nodules with malignant histopathology was established by transbronchial biopsy. Accompanying radiological patterns of endobronchial lesions were mass lesions in 2 cases, pleural effusion in 3, consolidation and multiple nodules in 1, and mediastinal lymphadenopathy in 1 patient with extrinsic compression. The most common symptoms of these patients were dyspnea, cough and chest pain (58.3, 55.6, 36.1 %, respectively), while in our study the most common radiological pattern was pleural effusion. Cough and hemoptysis are the most common pulmonary symptoms reported in other studies [15].

There are several studies reporting the increased rate of pulmonary metastases among smokers [18,19]. In our study 27 % (n=10) of the patients were smokers (mean duration of smoking, 10.7±6.81 pack-years).

In this study in 25 % (n=9) of the patients nonmalignant pulmonary lesions (Group II) were also observed. These lesions were pneumonia in 3 (33.3 %), pulmonary thromboembolism in 3 (33.3 %), and tuberculosis in 2 patients (22.2 %) of which 1 had tuberculous pleurisy and the other case had cavitation. These 2 patients with tuberculosis can be evaluated as coincidental cases. In 3 patients with pulmonary thromboembolism, breast cancer can be determined as a risk factor. Patients with breast cancer are at risk of venous thromboembolism like all patients with cancer. Microscopic tumor emboli are not also rare in these patients [3].

Radiation therapy to the chest may cause acute or chronic radiation pneumonitis and fibrosis. Between four, and twelve weeks after radiation therapy, patchy consolidations that coalesce on the treatment portals can occur. These lesions may resolve in 6-24 months but usually remain unchanged after 2 years. In this study, radiological changes inside the treatment portals that did not resolve during radiological follow up of 20 months were evaluated as radiation related fibrosis in one patient (11.1 %). Chronic eosinophilic pneumonia after radiation therapy and bronchiolitis obliterans organizing pneumonia syndrome primed by radiation therapy to the breast cancer is also reported in various studies [20-22]. Chemotherapy related complications are also reported as pneumonitis, cardiotoxicity and various infections [6,23].

In conclusion, pulmonary lesions of the patients with breast cancer are most commonly related to metastases, and can be observed long after the diag-

nosis of breast cancer. Besides these nonmalignant etiological factors should be kept in mind, and histopatological confirmation should be performed.

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