Case Report:

Occult Breast Cancer

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Abstract

Today breast cancer is the most common cancer type in women, in both developed and developing countries. However, occult breast cancer is a highly rare type in all breast cancers. For the first time in history to know, Halsted defined the term “occult breast cancer” with 2 cases of his’ in the journal, Annals of Surgery. We have 2 similar cases who were 52 and 61-years-old patients and presented our clinic with left axillary swelling and pain. On physical examination and with imaging techniques there wasn’t any primary lesion found. Examination of lymph nodes’ biopsy material was compatible with breast cancer metastasis for both of the patients and they were diagnosed with occult breast cancer. They underwent a modified radical mastectomy surgery and axillary curettage. Histopathologic examination of the excised breast material revealed T1 invasive breast cancer.

Keywords: occult, breast, cancer, general surgery

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Introduction

Smith Surgery Papyrus is the first known document to cite breast cancer B.C. 3000-2500. About this cancer type, writer said “there is no treatment”. Over the years with the developments about surgery, it is understood that this cancer type can be treated by resections. For the first time Radical Mastectomy surgery method has been used by Halsted in 1894.¹ Today breast cancer is the most common cancer type in women, in both developed and developing countries. It is thought that in 2013, 464.000 women have died because of the breast cancer worldwide.² Occult breast cancer, is a type of breast cancer which doesn’t have any manifestations in physical exam or in any imaging study and shows itself only by axillary lymphadenopathy. For the first time, it is described by William Halsted with two presented cases in the journal Annals of Surgery, 1907.³ Incidence of this rare cancer type is less than 0,34-0,88% amongst all breast cancers.⁴⁻⁷ In this report, we present two of our cases

who complain of left axillary swelling and pain.

Case Report

Case 1:

Fifty two-year-old woman patient, presented to our hospital with left axillary swelling and pain. There was no pathologic finding on bilateral breast USG. There was also no other clinical findings on physical examination, rather than obvious lymphadenopathies.

Malignant epithelial cell groups were seen in the image guided Fine Needle Aspiration Biopsy (FNAB) of axillary lymph nodes. In immunohistochemically staining, sample seemed to be estrogen receptor and progesterone receptor positive. These findings are judged to be compatible with breast carcinoma. In accordance to pathology results, we started to search for a primary focus in breast.

Dynamic Bilateral Breast MRI showed that, both breast paranchymas are symmetrical and mildly heterogeneously dyed fittingly premenopausal age. There was no sign of any suspicious lesion or focally stained area. Any pathol-

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Fig 1. MRI (T1-postcontrast) showing pa-thological lymph nodes with short axis diameter of 2 cm in left axilla.

ogy of breast were not seen in diffusion MRI rather than axillary lymphadenopathies (**Fig 1**). FDG PET scan showed us hypermetabolic, metastatic lymph nodes; the largest ones measuring 20x12mm and 15x10mm in left axillary fossa. Since imaging studies showed no sign of a primary focus, left axillary lymph node dissection was performed and material was analyzed pathologically and dyed ER, PR, Ki-67, mammaglobin and CA-125 positive; CERB-B2 negative. Nuclear expression with GATA-3 and membranous expression with E-Cadherin were seen. There were also metastasis of tumor in 5 of the 15 lymph nodes dissected. Immune profile of these lymph nodes taken was evaluated for papillary and micro papillary differentiating breast carcinoma (**Fig 2**). Acquired imaging results, clinical picture and having no result from searching for an extra mammary primary focal of tumor lead us to diagnosis of occult breast cancer. PET/CT scan didn't detect any lesion other than the one in the left axilla.

Thereafter the patient underwent left simple mastectomy. In pathologic examination of the dissected material, there wasn't any occupant lesion. However, there was a 6mm radius area with irregular borders. Immunohistochemically evaluation of the dissected material showed estrogen receptor, progesterone receptor, E-cadherin with membranous positive and CERB-B2 negative. Tumor type is reported as invasive breast carcinoma. Histological grade of tumour is determined as 2+2+2=6, Grade 2/3; and nuclear grade 2/3. At the same time no sign of in-situ component, perineural invasion, vascular invasion, lymphatic invasion, multicentricity, necrosis or calcifi-

Fig 2. Malignant epithelial tumour cells with big nucleus and distinct nucleoli

cation was seen. Pathologic stage determined for tumor defined as pT1b N2a M0 L0 V0 R0. (Tumor markers Ca 15.3 and CEA was in normal ranges. Total Blood Count, biochemistry, urine analysis, hormone levels and ELISA studies did not show any specificity.)

At last, post-operative treatment for this case planned as 4 dose of doxorubicin & cyclophosphamide 1 in every 21 day for chemotherapy and after 12 weeks of weekly paclitaxel treatment. Radiotherapy is also planned for after chemotherapy period.

Case 2:

Sixty one-year-old women with positive family history of breast cancer, presented to our hospital with complain of left axillary mass. She reported that her daughters were diagnosed as breast cancer.

Tru-cut biopsy performed and malignant epithelial cells are seen in lymphoid base (**Fig 3**). In immunohistochemistry evaluation, biopsy material seemed to be ER positive and CERB-B2, PR negative. Findings were found to be compatible with breast carcinoma metastasis.

On breast USG evaluation, increase in premammarian and mammarian fatty tissue, lipomatous appearance was observed in both breasts. There was a fibrocystic lobule in periareolar area of left breast and 39x21mm, solid, pathological lymph nodes without fatty hilus were observed in left axilla. On suspicion of occult breast cancer, dynamic bilateral breast MRI with contrast and diffusion MRI evaluation showed no malignant mass, lesion or pathological contrast, but pathological lymphadenopathy in axilla were observed (**Fig4**).

We performed left axillary level 1-2 lymph node dissection in and immunohistochemistry

Fig 3. Atypical, pleomorphic, epithelial cell groups that shows mitosis and lympho-cytes that infiltrate the tumor in tru-cut biopsy material.

Fig 4 MRI (T1-postcontrast) showing a 35x23mm pathological lymph node in left axilla.

showed ER (+) but PR and CERB-B2 (-) cells. There was a focal nuclear staining and membranous expression with E-cadherin. According to these findings, there was carcinoma metastases and extracapsular invasion in three of the eleven lymph nodes. That was compatible with breast cancer metastasis. Complete blood count, biochemistry, urinalysis, hormone levels and ELISA tests were examined and nothing indicative for malignancy was found.

Primary lesion wasn't observed and diagnosis was made in favor of occult breast cancer. After the diagnosis, we performed a mastectomy surgery. Excision material was examined macroscopically and there wasn't any tumor although there were some millimetrically firm areas. Immunohistochemically characteristics were estrogen receptor positive, progesterone receptor and CERB-B2 negative. Tumor type was invasive breast carcinoma, in situ components were ductal and lobular carcinoma. Histological grade of tumor is defined as 3+3+3=9, grade

3/3, and nuclear grade 3/3. Pathologic stage determined for tumor defined as pT1a N1a M0 L1 V0 R0.

At last, post-operative treatment for this case also planned as the first patient which is 4 dose of doxorubicin & cyclophosphamide 1 in every 21 day for chemotherapy and after 12 weeks of weekly paclitaxel treatment. Radiotherapy is also planned for after chemotherapy period.

Discussion

Breast cancer is the most common cancer seen among women and causes many deaths every year. Occult breast cancer is a rare type of it. Even though imaging techniques are improved and owing to that, prevalence of occult breast cancer diagnose is getting decreased. Only 0.34-0.88% of breast cancers are occult breast cancers.^[4-7] This condition doesn't have any specific finding on breast, but it comes out as axillary lymphadenopathy. Sometimes it can be diagnosed by the symptoms which are the results of distant metastasis.

Through the algorithm we use to diagnose occult breast cancer, one must exclude all the other reasons that show itself as an axillary lymphadenopathy (skin lesion, sebaceous cyst, congenital anomalies, infectious lymphadenopathy, inflammatory lymphadenopathy, lymphoma, lung cancer, melanoma, pancreatic cancer, colon cancer etc.). For the patients presented with axillary lymphadenopathy, primary focus of diagnosis should be evaluating the breast. If there aren't any findings on breast USG and MRI, other primary cancer focuses, metastasis and other diagnosis should be explored with further evaluation. On this stage of diagnostic workup, PET/CT can be used.

It is difficult to diagnose occult breast cancer because it doesn't give any finding on breast. When it shows itself as axillary lymphadenopathy, all the other causes must be excluded. On the pathological examination of axillary lymph node biopsy material, especially being positive for estrogen receptor, progesterone receptor and CERB-B2 directs us to the breast cancer diagnose.^{5,8,9} However it is highly important to study other tests to find the right diagnose since any focus can't be found with imaging techniques.

To treat the occult breast cancer, after reaching the diagnosis, surgery is recommended. Modified radical mastectomy, adjuvant chemotherapy

and hormonotherapy give better outcomes by the means of survival.¹⁰ Sometimes the tumor focus can't be found even in the mastectomy material. The two cases we report, presented our clinic with left axillary lymphadenopathy. On physical examination there wasn't any findings on breast. The hematological and biochemical tests we studied to exclude the other diagnosis were in normal range. Also the tumor markers were negative.

For patient 1, it was recommended to make a biopsy owing to the screening the lymph nodes that can be interpreted as breast malignancy. Malign epithelial cell groups were identified by fine needle aspiration biopsy. Immunohistochemically characteristics were estrogen and progesterone positive and that finding was compatible with breast cancer metastasis. To find the primary focus and to make a breast protective surgery, mammography, ultrasonography, MRI and PET/CT were carried out, but no mass was found. Since the primary focus wasn't seen with screening, she was diagnosed as occult breast cancer and undergone a left mastectomy surgery.

Patient 2 presented to our clinic with similar symptoms such as left axillary swelling and pain. We ran some initial tests which didn't give any clue about primary pathology.

So that we decided to evaluate the origin of the lymphadenopathy, tru-cut biopsy was performed and malignant epithelial cell groups with lymphoid rich base was found. It was compatible with breast cancer metastasis. On ultrasound screening a pathologic lymph node was seen in the left axillary area, which was 39x21mm, solid and without fatty hilus. In the next step, the primary focus wasn't found also with breast MRI but pathologic reactive axillary lymphadenopathy was seen. She was undergone an axillary lymph node dissection and there was metastasis on the 3 of 11 lymph nodes that dissected. Screening and other tests to find primary focus didn't give any clue. She was diagnosed with occult breast cancer and left simple mastectomy was applied.

Conclusion

Occult breast cancer is rare and doesn't reveal itself clinically or radiologically in breast. Due to axillary metastasis, it manifests as axillary lymphadenopathy. For all patients, who presented with lymphadenopathy, all benign and malignant causes must be thought, physical examination, blood work-up, tumor markers and biochemical evaluation should be done. Screening tests for whole body should also be performed. According to its findings, differential diagnosis must include also occult breast cancer.

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