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CASE REPORT

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Change from triple negative type to triple positive type; A case report of discordance of re-biopsy from primary breast cancer

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Abstract

The patient was a 60-year-old woman who had visited a clinic with the chief complaint of a mass in the right breast prior to being referred to our hospital. Breast examination revealed the presence of a 3-cm hard elastic mass in the C region of the right breast. Computed tomography (CT) further indicated metastases to the liver and lungs. Upon needle biopsy of the primary tumor, the patient was diagnosed with triple-negative (ER (-), PgR (-), HER2 (-)) invasive lobular carcinoma. Chemotherapy was successful in achieving a transient partial response (PR); however, the tumor later advanced to a progressive disease (PD) after five cycles of oral fluoropyrimidine derivative therapy (S-1). Re-biopsy of the primary tumor revealed that the tumor was triple-positive (ER (+), PgR (+), HER2 (+)). The patient was subsequently treated with anti-HER2 therapy and has since achieved complete response (CR). Although biological changes sometimes occur from the primary to the metastatic tumor, changes in the primary tumor itself during the course of treatment is a rare event. Furthermore, the transition from triple-negative to triple-positive status is very uncommon. Re-biopsy rarely changes the biological characteristics of a tumor; however, biological changes can have a significant impact on treatment if they do occur. Thus, it is important to perform a re-biopsy if the current treatment results in PD.

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Keywords: *anti-HER2 therapy; computed tomography; oral fluoropyrimidine derivative therapy*

Introduction

The incidence of breast cancer is increasing worldwide, with the number of patients having more than doubled from 800,000 in 1990 to 1,680,000 in 2016 [1]. Metastatic and recurrent breast cancer, excluding local recurrence, is difficult to treat. The 10-year survival after chemotherapy is approximately 5%, and only 2-3% maintain CR after 20 years [2]. Thus, available treatments aim to prolong survival and maintain/improve quality of life. Advancements in treatment strategies, particularly those with multiple novel therapeutics that have emerged since the 2010s, have gradually prolonged the survival of patients after recurrence [3-5].

Systemic therapy, or pharmacotherapy, is generally required for metastatic and recurrent breast cancer. There are several subtypes of breast cancer, and patients are assessed based on the expression of predictive factors (ER, PgR, HER2) prior to the start of treatment to ensure that the treatment is effective [6]. Treatment planning varies greatly depending on receptor expression, and treatment strategies that are tailored to each subtype have contributed to the overall improved outcomes of breast cancer treatment. In a subset of cases, the underlying biology of the metastatic tumor can differ from that of the primary tumor [7]. Thus, it is ideal to perform a re-biopsy while patients undergo treatment for metastatic and recurrent breast cancer. In the present study, we describe the case of a patient with metastatic and recurrent breast cancer. Re-biopsy of the primary tumor revealed that the tumor had undergone biological changes during the course of treatment, and CR was achieved once the treatment regimen was changed based on the findings of re-biopsy.

Case study

Case: 60-year-old woman
Past history: None
Family history: None
Initial assessment: A 3-cm hard elastic mass in the C region of the right breast.
Mammography: A high signal intensity region with a micro-serrated margin in the U region of the right breast.
Ultrasound: An irregular, 4.8-cm hypoechoic mass in the C region of the right breast.
CT: A small 7-mm nodule in the right upper lobe (S2), as well as liver metastasis in S8 and the lateral portion of the left lobe of the liver (Figure 1).
Tumor markers: Normal levels of carcinoembryonic antigen (CEA) and cancer antigen 15-3.
Pathological diagnosis based on needle biopsy: ER (-), PgR (-), HER2 (-) invasive lobular carcinoma.

Diagnosis: Right breast cancer (T2N1M1 Stage IV) with liver and lung metastases.

Prior treatment: Pharmacotherapy with 5 cycles of 5-fluorouracil, epidoxorubicin and cyclophosphamide, 4 cycles of nab-paclitaxel, vinorelbine, eribulin and S-1 (Figure 2).

Pathological diagnosis based on re-biopsy: ER (+), PgR (+), HER2 (+) invasive lobular carcinoma

Treatment after re-biopsy: The patient was treated with 4 cycles of pertuzumab, trastuzumab and docetaxel, and has since been treated with physical therapy.

Immunohistochemistry from the initial biopsy and re-biopsy (Figure 3 and Figure 4).

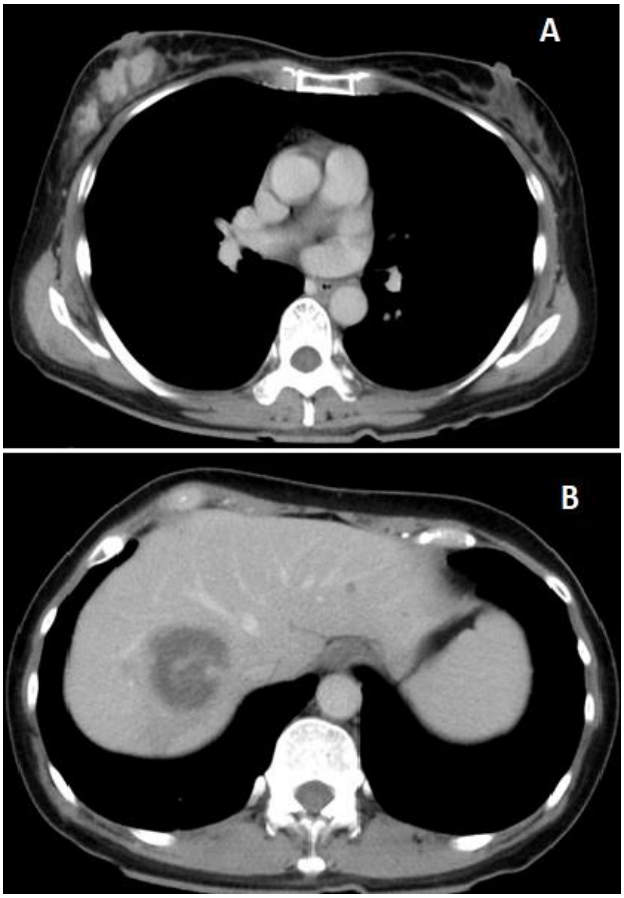
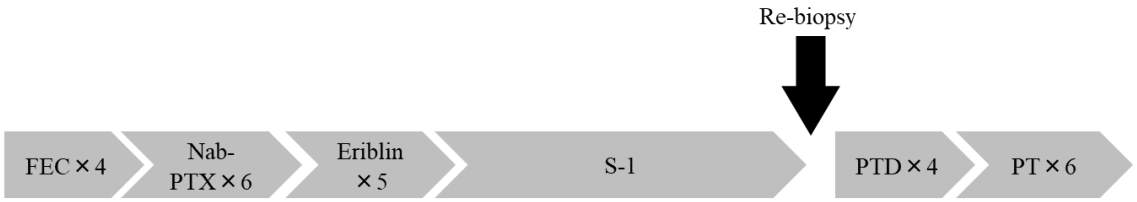


Figure 1. a. CT of primary tumor was performed at first; b. CT of liver metastases were performed at first.



FEC; 5-FU 500mg/m^2 +epirubicin 100mg/m^2 +cyclophosphamide 500mg/m^2

Nab-PTX; 220mg/m^2

Eriblin; 1.4mg/m^2

S-1; 100mg/body/day

PTD; pertuzumab+trasutuzumab+docetaxel ;840mg/m^2,8mg/m^2, 75mg/m^2

PT; pertuzumab 420mg/m^2+trasutuzumab 6mg/m^2

Figure. 2 Chemotherapy regimen of this case.

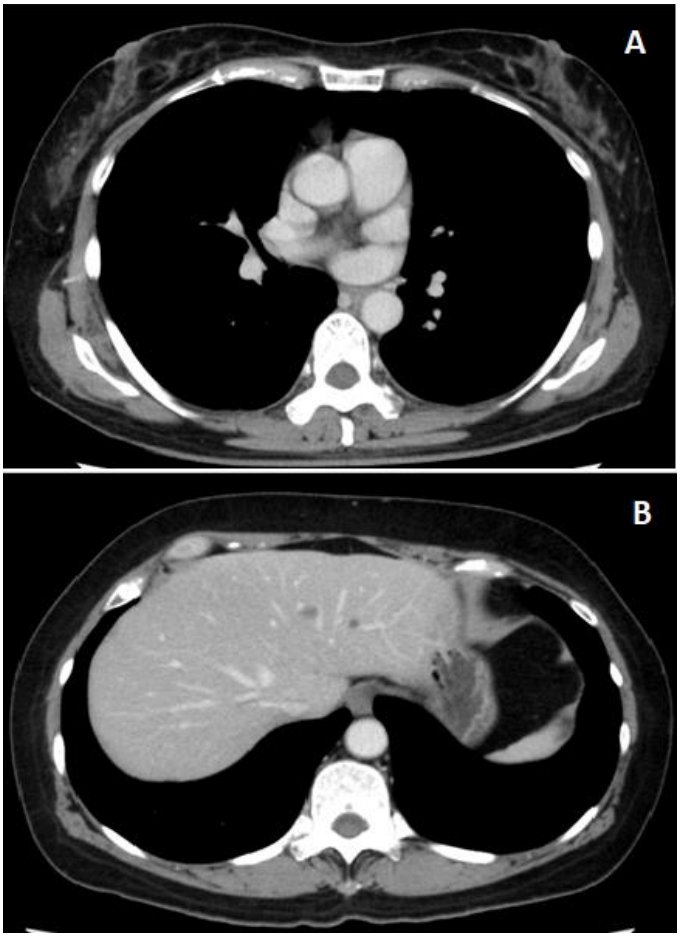
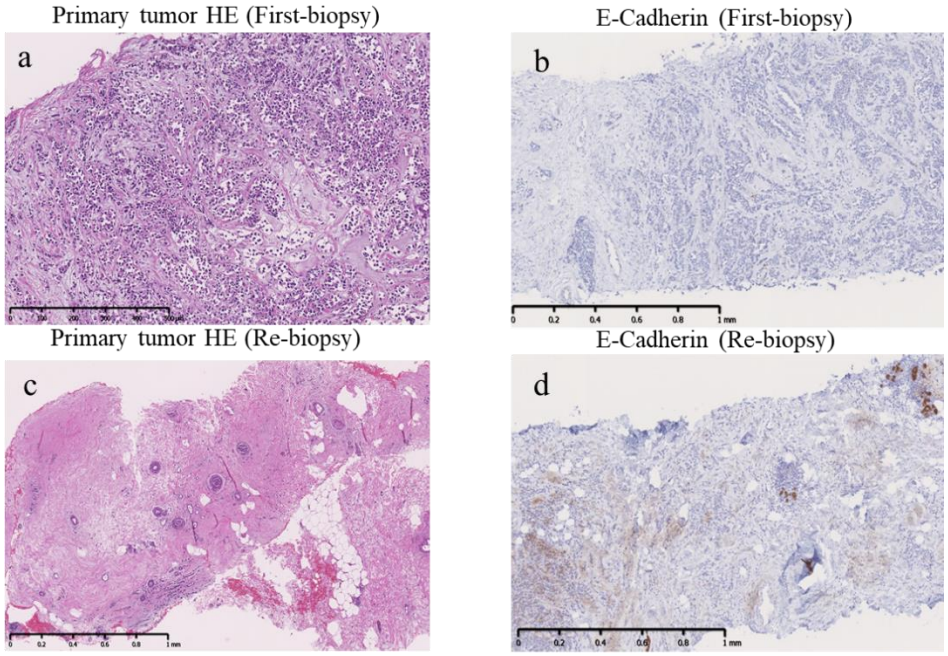


Figure 3: a. CT of primary tumor was performed after chemotherapy; b. CT of liver metastases were performed after chemotherapy.



HE; hematoxylin and eosin stain

E-cadherin staining decreased with re-biopsy.

Figure 4: a. primary tumor of HE staining at first biopsy. (×100)**;** b. primary tumor of E-Cadherin staining at re-biopsy. (×100)**;** c. primary tumor of HE staining at first biopsy. (×100)**;** d. primary tumor of E-Cadherin staining at re-biopsy. (×100).

Discussion and conclusion

Breast cancer typically consists of different clones that vary genetically. Such heterogeneity might contribute to differences in the evaluation of hormone receptor and HER2 expressions. In particular, the results of needle biopsy, which is representative of only a part of a tumor, may vary depending on where the biopsy was taken [6]. In general, discordance in the expression of HER2 and hormone receptors in breast cancer has been reported in primary and metastatic tumors [8-10]. Thus, re-biopsy of the metastatic tumor is recommended in cases in which it is possible. Several retrospective studies have examined the discordance in the expression of HER2 and hormone receptors between the primary tumor and distant metastatic tumor. For example, Ieni et al. [9], used immunohistochemistry and fluorescence in situ hybridization to examine HER2 expression in 148 cases of primary breast tumors and simultaneous axillary lymph node metastases. The authors demonstrated that while HER2 expression of the primary breast tumors and axillary lymph node metastases matched in 95.28% (n=141) cases, there was a mismatch of HER2 expression in 4.72% (n=7) of all cases. They further demonstrated that in metastatic tumors, HER2 expression became negative in 4 cases while it became positive in the remaining 3 cases. Most studies [10-14] to date compared the expression of HER2 and hormone receptors in primary versus metastatic tumors, and evidence comparing biopsy results within the primary tumor itself is limited. We demonstrated a transition from triple-negative to triple-positive phenotype, which is likely a very rare event. It is possible that the initial biopsy was taken from a HER2-negative area of the tumor, or that treatment induced the transition.

We also used various markers for immunohistochemistry evaluation of the initial biopsy and re-biopsy tissues. Specifically, we used the markers of epithelial-mesenchymal transition (EMT), namely E-cadherin and vimentin. We demonstrated that the expression of E-cadherin, which is an epithelial marker, increased after treatment. This suggests that the treatment might have reversed EMT. In fact, eribulin acts to reverse EMT [15,16], and our patient achieved progression-free survival for 33 months with S-1 after undergoing treatment with eribulin. This, in combination with the findings from immunohistochemistry, suggests that eribulin might have had an impact on the transition.

Here, we demonstrated that the biological characteristic of the primary tumor changed from triple-negative to triple-positive over the course of treatment. As a result, the treatment regimen was changed and the patient has maintained PR. Although biological changes due to re-biopsy are uncommon, they can have a significant impact on the treatment if they do occur. Thus, it is important to perform a re-biopsy in cases in which the initial treatment results in PD.

References

1. Sharma R. Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990-2016: evidence from Global Burden of Disease Study 2016. Breast Cancer. 2019; 26: 428-445.
2. Greenberg PA, Hortobagyi GN, Smith TL, Ziegler LD, Frye DK, et al. Long-term follow-up of patients with complete remission following combination chemotherapy for metastatic breast cancer. J Clin Oncol. 1996; 14: 2197-2205.
3. Cortes J, O'Shaughnessy J, Loesch D, Blum JL, Vahdat LT, et al. Eribulin monotherapy versus treatment of physician's choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet. 2011; 12: 914-923.
4. Baselga J, Cortés J, Kim SB, Im SA, Hegg R, et al. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med. 2012; 12: 109-119.
5. 5.Verma S, Miles D, Gianni L, Krop IE, Welslau M, et al. Trastuzumab emtansine for HER2-positive advanced breast cancer. N Engl J Med. 2012; 8: 1783-1791.
6. Cardoso F, Shimon SP, Senkus E, Curigliano G, Aapro MS, et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Ann Oncol. 2020; 31: 1623-1649.
7. Wolff AC, Hammond ME, Hicks DG, Dowsett M, McShane LM, et al. Recommendations for human epidermal growth factor receptor 2 testing in breast cancer : American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. J Clin Oncol. 2013; 31: 3997-4013.
8. Aitken SJ, Thomas JS, Langdon SP, Harrison DJ, Faratian D. Quantitative analysis of changes in ER, PR and HER2 expression in primary breast cancer and paired nodal metastases. Ann Oncol. 2010; 21: 1254-1261.
9. Ieni A, Barresi V, Caltabiano R, Cascone AM, Sordo RD, et al. Discordance rate of HER2 status in primary breast carcinomas versus synchronous axillary lymph node metastases : a multicenter retrospective investigation. Onco Targets Ther. 2014; 7: 1267- 1272.
10. Ataseven B, Gologan D, Gunesch A, Kehl V, Hoegel B, et al. HER2/neu, Topoisomerase 2a, Estrogen and Progesterone Receptors : Discordance between Primary Breast Cancer and Metastatic Axillary Lymph Node in Expression and Amplification Characteristics. Breast Care (Basel). 2012; 7: 465- 470.
11. Aurilio G, Disalvatore D, Pruneri G, Bagnardi V, Viale G, et al. A meta-analysis of oestrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 discordance between primary breast cancer and metastases. Eur J Cancer. 2014; 50: 277-289.
12. Dadioti PA, Valavanis C, Gavressea T, Tzaida O, Trihia H, et al. Discordant expression of hormone receptors and HER2 in breast cancer. A retrospective comparison of primary tumors with paired metachronous recurrences or metastases. J BUON. 2012; 17: 277-283.
13. Moussa O, Purdie C, Vinnicombe S, Thompson AM. Biomarker discordance: prospective and retrospective evidence that biopsy of recurrent disease is of clinical utility.Cancer Biomark. 2012-2013; 12: 231-239.
14. Rossi S, Basso M, Strippoli A, Dadduzio V, Cerchiaro E, et al. Hormone Receptor Status and HER2 Expression in Primary Breast Cancer Compared With Synchronous

Axillary Metastases or Recurrent Metastatic Disease. Clin Breast Cancer. 2015; 15: 307-312.

15. Goto W, Kashiwagi S, Asano Y, Takada K, Takahashi K, et al. The Effects of Eribulin on Breast Cancer Microenvironment Identified Using Eribulin-resistant Breast Cancer Cell Lines. Anticancer Res. 2019; 39: 4031-4041.

16. Kashiwagi S, Asano Y, Goto W, Takada K, Takahashi K, et al. Mesenchymal-epithelial Transition and Tumor Vascular Remodeling in Eribulin Chemotherapy for Breast Cancer. Anticancer Res. 2018; 38: 401-410.

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