Peer Review File

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Reviewer A

It is apparently a good idea. However, there is a lack of innovation in the study. It is not uncommon for biomarker phenotype conversion in a patient with a locoregional recurrence of breast cancer. The patient's current treatment was not successful, and there was a lack of prior treatment and follow-up. In addition, the author is careless in marking the time in Figure 4.

Comment 1: Lack of innovation in the study
Reply 1: This was a fascinating case that prompted a significant review of the literature on biomarker status change. This case report will add to the growing body of literature accounting for biomarker phenotype conversion in a patient with locoregional recurrence of breast cancer. Though it may not have been a completely novel discovery providing a wow factor, the educational component of this rare phenomena nonetheless instigates insightful discussion. Publication of this case report will contribute to the paucity of similar accounts and encourage future research in the possible form of meta-analyses. Patient follow up and management is ongoing.
Changes in the text: N/A see response above

Comment 2: The author is careless in marking the time in Figure 4
Reply 2: We have updated Figure 4 to reflect the correct timeline
Changes in the text: Figure 4, text changed from April 2021 to April 2020 in accordance with timeline of events.

Reviewer B

In this case report, the authors described an interesting case of locoregional recurrence of breast cancer with biomarker phenotype conversion from TNBC to HER2 positive cancer in a patient who had achieved pathologic complete response after nipple sparing mastectomy and sentinel lymph node biopsy 4 months prior. It is relatively well-written.

Comment 1: Please provide an image showing H&E and HER2 IHC of the primary breast cancer.
Reply 1: The primary breast cancer evaluation was conducted at an outside hospital. Upon receipt of reviewer comments, we immediately placed a request to obtain the specimen to provide an image showing H&E and HER2 IHC of the primary breast cancer. As of February 14, 2022, we have received the specimen and have promptly begun analyses in order to provide these images for the next updated version of our manuscript. Given the legal and patient information safety protocols in place we were unable to receive the specimen prior to this date despite having promptly placing the request. We aim to have the request image in

the next updated manuscript revision.
Changes in the text: Upcoming in manuscript revision

Comment 2: What was the IHC score of HER2 in the primary and recurrent cancers?
Reply 2: The IHC score of HER2 in the primary breast cancer was negative, a score of 0 was calculated. The IHC score of HER2 in the recurrence was equivocal a score of 2+ was calculated.
Changes in the text: We have modified our text as advised. We added the requested data in lines 118-122. Sentences may also be found immediately below. "The patient in this case displayed tumor phenotype discordance in HER2 expression from primary to recurrent tumor. Her primary tumor was an invasive ductal carcinoma triple ER, PR, and Her2 negative, IHC score of 0. Her chest wall recurrence was an invasive ductal carcinoma that is HER2/neu equivocal by IHC, score of 2+ and positive by FISH, see Figure 3B. These results were verified by 2 observers."

Comment 3: Were the antibody clones for HER2 same in the primary and recurrent cases?
Reply 3: No, the antibody clones for HER2 in the primary and recurrence cases were different. In the primary tumor we observe a 4B5 Rabbit monoclonal pathway from ventara. The antibody clone in the recurrence was Dako Herceptest Dxtm kit (link)/ Dako.
Changes in the text: We have modified our text as advised. Lines 83-85
"Moreover, the antibody clones for HER2 in the primary and recurrence tumors were dissimilar. In the primary tumor, the 4B5 Rabbit monoclonal pathway from Ventana was observed. However, the antibody clone in the recurrence was Dako Herceptest Dxtm kit (link)/ Dako."

Comment 4: It has been reported that ISH is more sensitive on detecting HER2 positivity, especially patient with neoadjuvant treatment. If possible, please perform FISH analysis on the primary cancer case, to confirm the original negative HER2 status.
Reply 4: The primary breast cancer evaluation was conducted at an outside hospital. Upon receipt of reviewer comments, we immediately placed a request to obtain the specimen to begin FISH analyses. As of February 14, 2022, we have received the specimen and have promptly begun analyses to provide these images for the next updated version of our manuscript. Given 3-week time of processing FISH analyses we humbly request that the editorial staff grant us the ability to submit a revised manuscript including the requested FISH analysis on the primary case as soon as the analyses are completed.
Changes in the text: Upcoming in manuscript revision

Comment 5: Was there any DCIS in the neoadjuvant mastectomy case? If it was

present, what was the margin status for DCIS?
Was there any DCIS in the neoadjuvant mastectomy case?
Reply 5: No DCIS was identified.
Changes in the text: We have modified our text as advised. Line 76-77
"Final pathology revealed no residual malignancy, no DCIS, and the margins were negative. One sentinel node was retrieved and was negative for carcinoma, ypT0yN0."

Other minor comments:
Comment 1: Line 78: the staging should be ypT0yN0
Reply 1: Agreed, updated accordingly
Changes in text: line 78 updated "…carcinoma, ypT0yN0."

Comment 2: Line 79: Redundant words "noted noticed"
Reply 2: Agreed, redundant word removed
Change in text: Line 79 "Four months after surgery, she noted a mass in the left upper outer chest wall that was..."

Comment 3: Line 195: It should be HER2 instead of HER
Reply 3: Agreed, updated accordingly
Change in text: Line 197-198 "…of patients with HER2+ metastatic breast cancer who had undergone previous treatment with Kadcyla"

Comment 4: Please keep the spelling of certain terms consistent throughout the manuscript, such as pathological complete response vs pathologic complete response, HER2 vs Her2, Figure vs figure, ER vs Er etc.
Reply 4: We have modified our text as advised
Change in text: Each of the terms pathological complete response have been replaced with pathologic complete response for consistency. All Her2 are now HER2 for consistency. All Figure are figure for consistency as with any Er which are now ER.

Comment 5: Please list the full and abbreviations of a term when it is present the first time in the main text.
Reply 5: We have modified our text as advised
Change in text: We have modified our text as advised throughout.

Comment 6: Figure 3: The arrow is not pointing the atypical mitosis
Reply 6: We have removed the arrow and statement
Change in text: Line 263 "Figure 3. A. Chest wall recurrence. Invasive ductal carcinoma, grade 3 (H&E section, high power."

Comment 7: Abstract: Please rewrite the sentence "We present a rare case of locoregional breast cancer recurrence in a young 38-year-old 29 woman with

biomarker phenotype conversion from triple-negative breast cancer in a patient who had achieved pCR after nipple-sparing mastectomy and sentinel lymph node biopsy to HER2 biomarker positive".

Reply 7: We have modified our text as advised, rewritten accordingly.

Change in text: Line 28-31 "This report presents a rare case of locoregional breast cancer recurrence in a young 38-year-old woman with biomarker phenotype conversion from triple-negative breast cancer who had initially achieved pCR after nipple-sparing mastectomy and sentinel lymph node biopsy to HER2 biomarker positive"