Author's response to reviews

Title: Metachronous isolated breast metastasis from pulmonary adenocarcinoma with micropapillary component causing diagnostic challenges

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Author's response to reviews: see over
Dear Editors and Reviewers

Thank you for your attention to our report and sincere comments. I tried to give you a point-by-point response to the concerns and I revised my manuscript in accordance to your comments.

I believe that this report provides additional information on metastasis to the breast from pulmonary adenocarcinoma with a micropapillary component. Please review my revised manuscripts again and do not hesitate to contact us if there is any problem.

Thank you, and with best regards.

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1. It is better to describe the detailed molecular mutation of EGFR on this metastasis.

⇒ Thank you for your comment. We analyzed the mutation of EGFR in the metastatic breast tumor specimen and there was a heterozygote mutation in Exon 19 of EGFR gene. The mutation analysis revealed a 9-bp deletion in exon 19, namely, c.2239_2247del9, which resulted in a deletion of three amino acids, namely p.L747_E749del. I described the results of molecular mutation of EGFR on this metastasis in the manuscript. (Page 5~6)

2. Wondering if there was any molecular analysis on the original lung adenocarcinoma specimen. If available, would like to compare the results to those from current specimen.

⇒ Thank you for your comment. We also analyzed the mutation of EGFR in the original lung adenocarcinoma specimen and there was same heterozygote mutation in Exon 19 of EGFR gene as in the metastatic breast tumor specimen. I compared the findings between two specimens and described the results in the manuscript with additional figures. (Page 5~6, Figure 5)
I think the biggest contribution this paper will have for clinical practice is mention or discussion of how one might recognize this situation and avoid inadvertently diagnosing a metastasis as a primary breast tumor.

Therefore, please add a couple paragraphs that discuss in better detail how such a lesion might be suspected if it arises--not only by the pathologist but by radiologists, surgeons, and other oncologists. There is brief mention about careful history, which is important. But to me, the most common clue is the combination of an ER/PR negative breast tumor without an in situ component. Especially high grade tumors without an in situ component (sometimes ER/PR positive GYNE tumors can show up in the breast).

So the recommendation would be for a surgeon or radiologist who receives such a diagnosis (ER/PR negative tumor without mention of an in situ component)--they can ask the pathologist about in situ disease, they can look for previously diagnosed tumor history (and request pathology comparison), etc.

⇒ Thank you for your comment. I added a couple paragraphs that discuss in better detail how such a lesion might be suspected if it arises. (Page 7~8)