

## Peer Review File

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### Reviewer A

**Comment 1:** Negative brain imaging findings are mentioned in the title, but this is not an adequate expression. Originally, images of meningeal carcinomatosis often show contrast-enhanced findings of meningitis due to vasodilatation as an inflammatory finding around the brain surface of the cerebrum, cerebellar sulcus, and brainstem. Other findings include enlarged ventricles due to impaired cerebrospinal fluid absorption and contrast-enhanced findings of the internal auditory canal and trigeminal nerve that suggest cranial nerve damage. Furthermore, within the spinal cavity, there are inflammatory findings such as contrast-enhanced findings on the spinal cord surface called rail way signs and dissemination of nodules. Each of these is a non-specific finding that is observed not only in cancer but also in infectious diseases.

**Reply 1:** We really appreciate the reviewer's comments. We consulted the radiologist in our hospital – Dr. Dong, who is expert in the imaging of nervous system. The patient underwent right breast-conserving surgery with homolateral axillary lymph node dissection on September 7, 2022. She did not undergo an MRI of the brain during neo-adjuvant chemotherapy, which might because the patient did not have any neurological symptoms. After operation (September 7), she showed some slightly neurological manifestations including headache, dizziness, nausea, vomiting and neck pain. Since then, she had received three enhanced brain MRI examinations on September 12 (to explore the cause of headache), October 6 (malignant cell was found in the CSF), and October 26 (with whole brain radiotherapy completed), 2022, respectively. According to the reviewer's suggestions and guidance, we revisited these results of MRI under the help of radiologist. At the time of the patient's first MRI, cerebellar sulcus, brainstem, internal auditory canal and trigeminal nerve didn't show obviously typical high signal intensity. At the time of the patient's second MRI, with the interference of artifacts, radiologist still found that cerebellar sulcus and brainstem showed atypical enhancement. Given the lumbar puncture with CSF analysis, doctors made the diagnosis of LM from breast cancer. At the time of third MRI, contrast-enhanced findings were faintly visible in cerebellar sulcus, brainstem, internal auditory canal and trigeminal nerve,

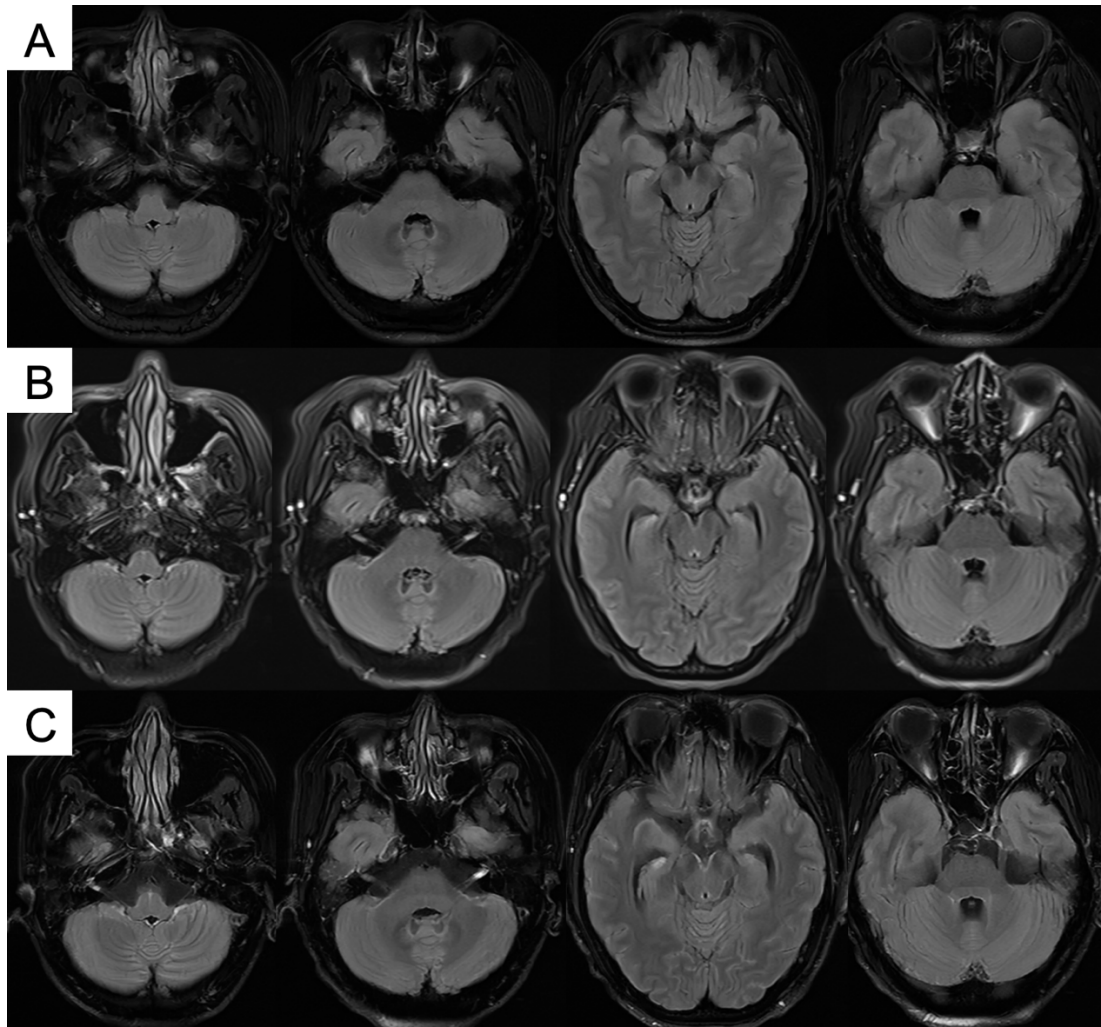
although these non-specific imaging findings can also be observed not only in cancer but also in infectious diseases.

**Changes in the text:** According to the reviewer's comments, the related manuscript content has been revised in Page 7, line 92-97 and Page 9, line 135-142. We also add a figure (Figure 5) as advised.

**Comment 2:** Since the imaging findings are negative, all contrast-enhanced brain MRI and spinal MRI should demonstrate the absence of the above findings. It may be necessary to present images around the brainstem, internal auditory canal, and basal cistern level. It is also necessary to state that the patient does not have hydrocephalus.

**Reply 2:** We really appreciate the reviewer's comments. We checked the results of patient's brain MRI under the guidance. The images around the basal cistern level, internal auditory canal, brainstem and trigeminal nerve are shown in Figure 4. At the time of the patient's first MRI, these brain structures didn't show typical high signal intensity. At the time of third MRI on October 26, contrast-enhanced findings were faintly visible in these structures. After discussion, all the author and the radiologists from our hospital determined that the patient did not have hydrocephalus.

**Changes in the text:** According to the reviewer's comments, the related manuscript content has been revised in Page 7, line 92-97 and Page 9, line 135-142. We also add a figure (Figure 4) as advised.



**Figure 4 T2-flair, post-contrast brain MRI of the patient at the time when :**

(A) Patient received first enhanced MRI on September 12, 2022 to explore the cause of headache. (B) Malignant cell was found in the cerebrospinal fluid on October 6, 2022. (C) Patient was treated with whole brain radiation therapy with 30 Gy over 10 fractions completed on October 26, 2022. The structures shown are the basal cistern level, internal auditory canal, brainstem and trigeminal nerve in order from left to right. The patient's second MRI image had artifacts.

**Comment 3:** By emphasizing that the time from breast cancer to brain metastasis in triple-negative breast cancer is extremely quick compared to other subtypes, we should emphasize that the progression of symptoms is important. In particular, it should be emphasized that cranial nerve damage is a symptom highly suggestive of meningeal carcinomatosis, which is unlikely to occur due to intraparenchymal metastasis.

**Reply 3:** We sincerely appreciate the reviewer's constructive comments. The comments with the reviewer's professional insights are of great value to us. All the authors agreed to integrate the reviewer's great comments in our manuscript, hoping that all the clinician and readers can benefit from.

**Changes in the text:** We have incorporated additional information into the manuscript as advised (see Page 10, line 92 - Page 11, line 180).

## **Reviewer B**

**Comment 1:** Should address new innovative approaches for treatment PMID: 36468085.

**Reply 1:** We really appreciate this comment. We checked and cited the recent review (PMID: 36468085).

**Changes in the text:**

We have supplemented some contents based on your advice (see Page 10, line 160-165).

Ref:

11. Klaas E, Mohamed S, Poe J, et al. Innovative Approaches for Breast Cancer Metastasis to the Brain. Arch Med Case Rep Case Study 2022;6(4):147.

**Comment 2:** Authors should also go through the current standard practice algorithm PMID: 37388704.

**Reply 2:** We thank for the reviewer's suggestion. We checked and cited the recent review (PMID: 37388704).

**Changes in the text:**

We have supplemented some contents based on your advice (see Page 10, line 165-166).

Ref:

12. Klaas E, Sung E, Azizi E, et al. Advanced breast cancer metastasized in the brain: treatment standards and innovations. J Cancer Metastasis Treat 2023;9:23.