

Revision of the article

Journal title: World Journal of Clinical Cases

Manuscript NO: 72207

Title: Unusual MRI findings of brain and leptomeningeal metastasis in epidermal growth factor receptor-mutant lung adenocarcinoma: A case report

Authors: Na Li, Yu-Jun WANG, Fang-Mei Zhu and Shui-Tang Deng

Correspondence To: Yu-Jun WANG, Doctor, Chief Doctor, Department of Radiology, Zhejiang Provincial Hospital of Chinese Medicine, 54 Youdian Road, Hangzhou 310012, China. 981861280@qq.com

Revision of the article

This article has been modified as follows:

Reviewer #1: It would be more appropriate to use the term "isolated or focal gyriform appearance" instead of "Unique gyriform appearance" used in the study.

1、 We have used the term "isolated gyriform appearance" and “isolated gyriform lesion” instead of "Unique gyriform appearance" and “unique gyriform lesion” used in the study. And using the term “mass effect” instead of “space occupying effect” .

Reviewer #1: Diseases with leptomeningeal involvement were not discussed sufficiently in the study (For example, leptomeningitis, vasculitis, neurosarcoidosis, inflammatory involvement of rheumatological diseases, etc.).

2、 In the discussion, the diseases with leptomeningeal involvement (primary central nervous system vasculitis and tuberculous meningitis) have been discussed in the study on page 8.

Reviewer #1: Differential diagnoses should be developed in the discussion section. If the patient was detected during the Covid-19 pandemic, Covid-19 must be specified in the differential diagnosis. It should be noted that even if it has been detected before, Covid-19 can still have similar involvement.

3、 The patient was detected in October 2019, which was not during the Covid-19 pandemic. The patient was not infected with Covid-19 during hospitalization.

Reviewer #1: In the radiological discussion, it should be noted that the contrast-enhanced T2-weighted FLAIR sequence can better detect leptomeningeal tumoral or infective-inflammatory involvement. A limitation of this study is that other, smaller areas of metastasis on the leptomeningeal surfaces may have been overlooked because contrast-enhanced T2-weighted FLAIR was not taken. It should also be emphasized in the study that leptomeningeal metastases usually present with more diffuse involvement, and isolated ones can be seen less frequently.

4、 In the radiological discussion, we have noted that “Compared with T1WI enhancement sequence, the contrast-enhanced T2-weighted FLAIR sequence is more sensitive to detect

leptomeningeal tumoral or infective-inflammatory involvement. A limitation of this study is that other, smaller areas of metastasis on the leptomeningeal surfaces may have been overlooked because contrast-enhanced T2-weighted FLAIR was not taken. " on page 6 line 11. And "leptomeningeal metastases usually present with more diffuse involvement, and isolated ones can be seen less frequently" was added on page 5 line 21.

Reviewer #1: In the discussion, the findings of advanced radiological imaging methods (such as perfusion MR) should be explained in more detail in the differential diagnosis of diseases with leptomeningeal involvement.

5、 In the discussion, the findings of advanced radiological imaging methods (perfusion-weighted imaging and MRS of peritumoral edema) have been explained in detail in the differential diagnosis of high-grade gliomas and brain metastasis on page 8.

Reviewer #2: Firstly, the intra-operative image and the macroscopic image of the tumor should be added, as the surgery to remove the tumor was an important part in diagnosis and treatment of the condition.

6、 Unfortunately, the intra-operative image、 video and the macroscopic image of the tumor, which are kept in the operating room for only 1 year, fail to save, because the surgery (in October 2019) is too long away from now. Therefore, these pictures are not added in the study.

Reviewer #2: Secondly, the CSF results should be added, as the author stated leptomeningeal metastasis.

7、 The CSF results have been added in *Laboratory examinations*, and the CSF cytology showed malignant epithelial cells in the CSF.

Reviewer #3: Please try to correct some spelling mistakes try to reduce the abbreviations in the title.

8、 We have reduced the abbreviations in the title: "Unusual MRI findings of brain and leptomeningeal metastasis in EGFR-mutated lung adenocarcinoma: A case report" has been corrected to "Unusual MRI findings of brain and leptomeningeal metastasis in epidermal growth factor receptor-mutant lung adenocarcinoma: A case report"

9、 We have corrected some spelling mistake: ①In the abstract at the level of the CASE SUMMARY, "The brain and leptomeningeal metastases were confirmed by operation and pathological examination" was corrected into "The brain and leptomeningeal metastasis was confirmed by operation and pathological examination". ②In the DISCUSSION (first paragraph of page 6), the word "was" has been corrected into "were" in the sentence "The lesions of left frontal cortex, subcortex and local leptomeninges, forming a isolated gyriform appearance was shown with avid contrast enhancement in our case". ③ In the DISCUSSION (last paragraph of page 7), we have used the term " High-grade glioma" instead of "High-grade gliomas" ,and " High-grade gliomas tend to occur in the subcortical white matter" was corrected into "High-grade glioma tends to occur in the subcortical white matter" .

10、 In the DISCUSSION (on page 5) , the sentences "Patients with non-small-cell lung cancer harboring EGFR mutations were more susceptible to develop into brain or leptomeningeal

metastases when compared to those with EGFR wild-type” has been corrected into “Patients with non-small-cell lung cancer harboring EGFR mutations were more susceptible to develop brain or leptomeningeal metastases when compared with those bearing EGFR wild-type”

11、 In the DISCUSSION (on page 5) , the sentences “Brain metastasis in non-small cell lung cancer patients might behave differently, as it depends on tumor nodules, or more or less cystic and necrotic lesions” has been corrected into “Brain metastasis might vary in non-small cell lung cancer patients, as it depends on tumor nodules, or more or less cystic and necrotic lesions”

12、 In the DISCUSSION (first paragraph of page 6),we have used the sentences “Making a diagnosis of LM is difficult, which is relied on cerebrospinal fluid (CSF), clinical, and radiographic findings “ instead of “Diagnosis of LM is difficult, and relies on cerebrospinal fluid (CSF), clinical, and radiographic findings”. And using “LM was revealed significantly on preoperative T₁WI enhancement in our patient ” instead of “careful observation revealed significant LM on preoperative T₁WI enhancement in our patient”

13、 In the *Further diagnostic work-up*, “ the mass shown to be located in the left frontal lobe” has been corrected into “ the mass shown to be located in the left frontal lobe and adjacent leptomeninges” .

Reviewer #3: In the abstract at the level of the CASE SUMMARY, try to reformulate the sentence, because one risks to understand that the adenocarcinoma of the lung was of metastatic origin

14、 In the abstract at the level of the CASE SUMMARY, we have reformulated the sentence, using “We herein presented a case report of a 76-year-old male with an established diagnosis of cerebral parenchyma and leptomeningeal metastasis of lung adenocarcinoma ” instead of “We herein presented a case report of a 76-year-old male with an established diagnosis of metastatic adenocarcinoma of the lung, wherein the cerebral parenchyma and leptomeningeal metastasis appeared in gyriform” .

15、 Besides, since the first draft of the article was written in 2020, we forgot to correct the patient's examination time in the artical when submitting. We have now corrected it to the specific time: Using "In 2014" instead of "Six years ago"; Using "In January 2019" instead of “Eighteen months ago” ; Using “ In October 2019” instead of “Eight months earlier”.

16、 In the DISCUSSION, the sentences “Cerebral infarction is the most common ischemic disease of CNS, and should be considered seriously” and “Besides, cerebral infarction is mostly manifested as the swelling of brain parenchyma, which does not have an obvious space occupying effect. However, the lesion in our patient had a certain space-occupying effect on MR imaging, and the local brain parenchyma showed no sign of swelling” have been deleted,because of the statement duplication.

17、 In the DISCUSSION (first paragraph of page 6), we have added “And CSF cytology examination also showed malignant tumor cells 2 months later.”

18、 In the **CASE PRESENTATION**, “*Personal and family history*

The patient had no particular individual or family history.” has been added.

19、 In the *Imaging examinations*, “Magnetic resonance angiography (MRA) showed no obvious abnormalities in the intracranial blood vessels.” has been added.

20、 In the DISCUSSION (third paragraph of page 7), we have deleted the word “also” in the sentence “the prognosis of LM in non-small cell lung carcinoma remained poor, and also the median overall survival is only 3 months”.

21、 In the DISCUSSION (fourth paragraph of page 7), the sentence “Cerebral infarction also tends to occur at the junction of gray and white matter, which involves in the cerebral cortex and subcortical white matter, but the lesions are often wedge-shaped or fan-shaped” has been deleted.

22、 In the DISCUSSION (second paragraph of page 7), the sentence “the metastases form pure vasogenic edema, and” has been deleted.

If you have any questions, however, please feel free to contact us via e-mail at: 981861280@qq.com

Best regards,

Yu-Jun Wang