ALL RESPONSES TO THE REVIEWER'S COMMENTS

Manuscript number: 71343

Title: Langerhans Cell Histiocytosis Presenting as an Isolated Brain Tumour: A Case Report and Literature Review

Date: Monday, October 25, 2021

Note:

1. The different colors of each row represent different reviewers.

Reviewer	No.	Content of comment	Our response
Reviewer #1:	**1**	*The authors show the LCH case with multiple lesions defined by PET or MRI. The case is so interesting, however, I have some concerns.* *1. Please describe the novelty of the current case.*	From the current case, we conclude three novelties: 1. There are no previous reports of ^{18}F-FDG PET/CT for assessing the metabolic activity of the brain parenchymal LCH. To our knowledge, the present case is the first case

			with a PET/CT description. Although SUVmax of brain lesion is similar to SUVmax of LCH involving other sites or organs reported in the literature. 2. Because 30% of patients with LCH involve multiple organ systems, the use of a single imaging modality to assess a single site for lesions may be inaccurate or missed. Therefore, a systematic evaluation or targeted examination for involvement of other tissues (bone, soft tissue, central nervous system, lung) is essential. 3. MRI images of this case further validated the findings of Kim et al. The sulcal

			enhancement and the leptomeningeal involvement around the lesion may be the characteristic signs of the brain parenchymal LCH.
Reviewer #1:	**2**	*2.Please enrich the discussion citing following article. Treatment Outcomes of Langerhans Cell Histiocytosis: A Retrospective Study. Hashimoto K, Nishimura S, Sakata N, Inoue M, Sawada A, Akagi M. Medicina (Kaunas). 2021 Apr 7; 57(4):356. doi: 10.3390/medicina57040356.*	Thanks for the reviewer's recommendation. This paper is very good. We've read and quoted it.
Reviewer #2:	**1**	*THe authors present an interesting case of LCH (Langerhans cell histiocytosis) involving the brain parenchyma. It is an*	Thanks for the reviewer's recommendation. The clinical features are not described in sufficient detail, and the clinical symptoms

		interesting read and provides good overview of imaging features of these lesions, while proposing new areas of research in diagnostic evaluation of LCH. Few suggestions/ questions i have for them are: 1) Mention about the clinical features of LC involving the brain parenchyma in the literature.	section has been added. "**The clinical presentation of LCH is non-characteristic and varies depending on the site; mostly non-specific symptoms of mass effect such as headache, seizures, hemiparesis and/or sensory disturbances.**"
Reviewer #2:	**2**	*2) Table 1 is not a part of the submitted manuscript and I have not been able to go through them. The images submitted with the manuscript are great.*	Table 1 has been added after the ***Reference*** and uploaded as a separate **Word file (named 71343-Table File)** to the submission system. Meanwhile, the references are updated.

Reviewer #2:	**3**	*3) This patient also had pulmonary findings and it would be interesting to see if the diagnosis could be confirmed with just lung biopsy? Could the patient have been treated with prednisone and vinblastine without resection? If so, what guided the decision for brain tumor resection.*	Before the pathological diagnosis was confirmed, the possibility of glioblastoma was first considered in a 47-year-old patient with intracranial lesions. Moreover, cases of LCH involving brain parenchyma were extremely rare. There is no previous experience of puncturing lung lesions to confirm the diagnosis of LCH, even if the lung findings suggest the possibility of histiocytosis.
Reviewer #2:	**4**	*4) The conclusions need revision of words. Would suggest rewording post-treatment response, rather than post=\-treatment strategies. Mention suggested treatment plan*	We rewrote the conclusion. "**As a systemic disease, LCH has the potential to involve the brain parenchyma, and making a diagnosis is extremely challenging. The use**

		for intracranial lesions of LCH - do they all need resection?	**of multimodality imaging or whole-body imaging, combined with the manifestation of lesions at other sites, can be helpful in the diagnosis of this disease. Moreover, multimodality imaging is useful in assessing the systemic status of LCH, developing treatment plans, and evaluating post- treatment strategies**." The cases of LCH involving brain parenchyma are very rare, and a unified treatment consensus has not been formed. No more than 30 cases were reviewed. Brain tumors were considered before resection, and the diagnosis was confirmed by pathological

			examination after resection.