

May 18, 2020

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 55225- manuscript file.doc).

Title: Anti-N-methyl-D-aspartate-receptor antibody encephalitis combined with syphilis: A case report.

Author: Xi-Yu Li, Zhi-Hong Shi, Ya-Lin Guan, Yong Ji

Name of Journal: *World Journal of Clinical Cases*

ESPS Manuscript NO: 55225

The manuscript has been improved according to the suggestions of reviewers: (1) The title is too long, and it should be no more than 12 words; (2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s). 6 Re-review: Required. 7 Recommendation: Conditional acceptance. (Han Zhang) .

Format has been updated, as follows:

(1) We added the running title of "Xi-Yu Li *et al.* Anti-N-methyl-D-aspartate-receptor antibody encephalitis combined with syphilis".

(2) We revised the author's institution to : " **Zhi-Hong Shi, Ya-Lin Guan, Yong Ji**, Tianjin Key Laboratory of Cerebrovascular and of neurodegenerative diseases, Tianjin dementia institute, Department of neurology, Tianjin Huanhu Hospital, Tianjin, 300350, Tianjin city, China. **Yong Ji**, China National Clinical Research Center for Neurological Diseases,

Department of neurology Beijing Tiantan Hospital, Capital Medical University, Beijing, 100070, Beijing city, China.”

(3) According to the format requirements of the guideline, we have changed the font “supported by” in bold to “ **supported by**”.

(4) We revised the format of address of correspondence author to “**Zhi-Hong Shi, MD, PhD, DSc (Med)**, Tianjin Key Laboratory of Cerebrovascular and of neurodegenerative diseases, Tianjin dementia institute, Department of neurology, Tianjin Huanhu Hospital, NO 6 Ji Zhao St, Jinnan District, Tianjin, 300350, China. shzhh1204@126.com.”.

(5) We added the telephone and fax number and ORCID number in our article, as follows “**Telephone and fax:** +86-022-59065662; **ORCID number:** Xi-Yu Li (0000-0002-2586-1187); Zhi-Hong Shi (0000-0001-5235-6349); Ya-Lin Guan (0000-0002-8892-8422); Yong Ji (0000-0002-2191-6996);”.

(6) We have revised the number of words of the abstract, in which the background part is shortened to 80 words, the case summary part is shortened to 150 words, and the conclusion part is shortened to 19 words. This specific content is changed as follows: “The pathogenesis of the disease are unclear. Syphilis is an infectious disease caused by *Treponema pallidum* that can invade the nervous and immune systems and cause systemic symptoms.” , “ We report a case of anti-NMDAR encephalitis with syphilis.”, “A 32-year-old man was admitted to our hospital with complaints of cognitive decline, diplopia, and walking instability during the previous six months. He developed dysarthria, difficulty swallowing, and involuntary shaking of his head, neck, and limbs during the month prior to presentation.”, “According to the patient’s weight, he was treated with intravenous methylprednisolone 1g Qd for five days, with the dose gradually decreased for 6 months, and immunoglobulin 25g Qd for five days;” and “This case shows anti-NMDAR encephalitis can combined with syphilis which should be recognized to avoid misdiagnosis and treatment delay. ”.

(7) We have shortened the part of core tip to 100 words, and the details are as follow: “Anti-N-methyl-D-aspartate-receptor (NMDAR) encephalitis is a common type of autoimmune encephalitis characterized by complex clinical signs and various imaging manifestations. We present a rare case of anti-NMDAR encephalitis combined with

syphilis, developing in a previously healthy immunocompetent male patient.” and “In order to avoid misdiagnosis and delay of treatment, this case emphasizes anti-NMDAR encephalitis can present in combination with syphilis.”.

(8) According to the common unit guidelines, we modified the units in history of present illness, as follows: “More than 6 months prior to admission, he developed diplopia and his right eye showed outward inclination after long-term emotional stress and fatigue.” and “According to the patient’s weight, we treated him with intravenous methylprednisolone 1g Qd and immunoglobulin 25g Qd for five days, and his symptoms improved.”.

(9) We added the content of personal and family history in our article, as follows:

“Personal and family history

The patient is a married 32-year-old male with a height of 180cm and a weight of 62.5kg, Han nationality, engaged in fitness instructor. He has no history of drug use, drinking or bad sexual life, but has a history of smoking. His parents are both in good health.”.

(10) We modified the content and format of the subtitle, as follows: **“Physical examination upon admission”, “Final diagnosis”, “Treatment” and “Outcome and follow-up”**.

(11) We deleted the one-used acronym and standardized the grading, as follows: “The patient’s score on the Montreal Cognitive Assessment examination was 24/30. His Mini-Mental State Examination score was 28/30.”

(12) We added the time of the imaging examination, as follows: “Brain magnetic resonance imaging (MRI) scans one month before admission showed T₂ hyperintensity of the brain stem, bilateral internal capsules, and the right frontal lobe; the right ventricle was enlarged (Figure 1). Repeat brain MRI scans on admission showed abnormal symmetrical signals in the pons, mesencephalon, bilateral medial temporal lobe, and bilateral basal ganglia (Figure 2).”.

(13) We have changed the format of the citations, as follows: “Some literatures outlined the best treatment for anti-NMDAR encephalitis, including the combination of tumor resection, immunotherapy, intensive care, and rehabilitation including physical therapy^[24].”.

(14) We added the acknowledgments in our article, as follows: **“ACKNOWLEDGMENTS**
We are very grateful to the patient and his family. The study was supported by the

National Natural Science Foundation of China(funding numbers: 81571057), and Tianjin Science and Technology Project(funding numbers: 16ZXMJSY00010). “.

(15) We modified the care checklist (2016) statement, as follows: “The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016). “.

(16) We added the S-Editor’s name, as follows: “ **S-Editor:** Le Zhang”.

(17) According to the format of the illustrations, we have changed the illustrations and notes. The illustrations can be seen in the file name of 55225- manuscript. The notes are as follows: “ **Figure1: Brain magnetic resonance imaging scans 1 mo before admission.** A: T2 weighted image shows high signal of brain stem (black circle); B: T2 weighted image shows high signal of bilateral internal capsule (black arrow); C: T2 weighted image shows high signal of the right of frontal lobe (black circle); D: T2 weighted image shows the right ventricle is enlarged (black arrow).” and “**Figure2: Brain magnetic resonance imaging scans on admission.** A: T2 weighted image shows high signal of pons (black circle); B: T2 weighted image shows high signal of mesencephalon and bilateral medial temporal lobe (black circle); C: T2 weighted image shows high signal of bilateral basal ganglia (black arrow); D: T2 weighted image shows high signal of bilateral basal ganglia (black arrow).”.

We have upload the funding agency copy of approval document (file name: 55225- the funding agency copy of approval document.doc) and the image file (file name: Manuscript No55225-image files.ppt).

2 Revision has been made according to the suggestions of the reviewer

(1) According to your suggestion, we have revised the title to: “Anti-N-methyl-D-aspartate-receptor antibody encephalitis combined with syphilis: A case report”.

(2) We have address newer theory of anti-NMDAR encephalitis for enriching our article. This newer theory is “It has been reported that the dysfunction of postsynaptic glutamate transmission at the synapse leads to increased release of γ -Aminobutyric acid and

decreased secretion of glutamate in anti-NMDAR encephalitis, so glutamate therapy can be used in anti-NMDAR encephalitis^[31]. In the future, we can try the glutamate therapy in more patients with anti-NMDAR encephalitis to observe the clinical effect." The literature cited by this new theory is "Tzang R F, Chang C H, Chang Y C, Lane H Y. Autism Associated With Anti-NMDAR Encephalitis: Glutamate-Related Therapy. *Front Psychiatry* 2019; **10**: 440 [PMID: 31293459 DOI: 10.3389/fpsyt.2019.00440]".

(3) Because one of the cited references is earlier and does not have a DOI number, we have replaced this reference in our article, and its related contents have been replaced as well. This reference is "Xu X, Lu Q, Huang Y, Fan S, Zhou L, Yuan J, Yang X, Ren H, Sun D, Dai Y, Zhu H, Jiang Y, Zhu Y, Peng B, Cui L, Guan H. Anti-NMDAR encephalitis: A single-center, longitudinal study in China. *Neurol Neuroimmunol Neuroinflamm* 2020; **7** [PMID: 31619447 DOI: 10.1212/NXI.0000000000000633]". The related contents of this reference is "In China, the patients often suffer from mental illness and epilepsy, but the proportion of potential tumors is very low^[17]".

3 References and typesetting were corrected

All the references in the article have been changed according to the format required by the magazine. This reference is "Xu X, Lu Q, Huang Y, Fan S, Zhou L, Yuan J, Yang X, Ren H, Sun D, Dai Y, Zhu H, Jiang Y, Zhu Y, Peng B, Cui L, Guan H. Anti-NMDAR encephalitis: A single-center, longitudinal study in China. *Neurol Neuroimmunol Neuroinflamm* 2020; **7** [PMID: 31619447 DOI: 10.1212/NXI.0000000000000633]". The literature cited by this new theory is "Tzang R F, Chang C H, Chang Y C, Lane H Y. Autism Associated With Anti-NMDAR Encephalitis: Glutamate-Related Therapy. *Front Psychiatry* 2019; **10**: 440 [PMID: 31293459 DOI: 10.3389/fpsyt.2019.00440]".

The above changes are marked in red fonts highlight in our manuscript for your convenience.

Thank you again for publishing our manuscript in the *World Journal of Clinical Cases*.

Sincerely yours,

Zhi-Hong Shi

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