

Answering Reviewers

Dear Editors and Reviewers,

We are grateful to the reviewers for the valuable and helpful comments of our manuscript NO # [85715] with the title “**Subintimal recanalization for non-acute occlusion of intracranial vertebral artery in an emergency endovascular procedure: A technical case report**” which we are submitting as a CASE REPORT to *World Journal of Clinical Cases*. We appreciate the promoting comments to our case study, and we have accepted and revised as recommended in this revised manuscript. The point-by-point responses are provided below. We hope that the explanations and revisions of our work are satisfactory.

● Response to reviewer's # 1 comments

General comments: This case is interesting and well illustrated, ...

1. comment: Some terms should be improved (e.g. “correctly stress” (P3, L51,61; P13,L282) (stress?); “this article reports” (P3,L59) (this report?))

Reply:

We apologize for our error.

- a. We have changed [..., we **correctly stress** the need for caution when...] to [..., we **emphasize the necessity for caution** when...];
- b. We have changed [..., **this article reports** the first successful case of...] to [..., **this article details** the first successful case of...].

2. comment: On the L48 the time of last clinical evaluation should be explained.

Reply:

- a. We have added the time of last clinical evaluation in the CASE

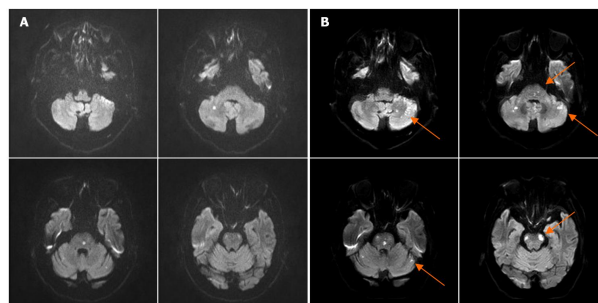
SUMMARY of Abstract: [The patient's Modified Rankin Scale was 1 at three months postoperatively.]

3. comment: The text and some figures could be shortened if space is critical.

Reply:

We have reduced the number of words in the text and figure legends.

- a. Because the clinical significance of the subintimal tracking and re-entry technique is still controversial and there isn't enough evidence to support its use in the endovascular treatment of intracranial arterial occlusion. Additionally, a specific case report cannot be generalized, **so we removed a paragraph from the DISCUSSION section that reviewed its clinical significance.** We have deleted this paragraph: [~~In contemporary coronary CTO PCI strategies, the results of various studies comparing intraplaque versus subintimal tracking techniques on clinical outcomes are contradictory. Additionally, histological studies on the subintimal canal of peripheral arteries discovered that, although it may initially appear to be thrombogenic, the subintimal canal eventually undergoes arterial wall remodeling and neo-cellularization.~~].
- b. Since the original Figure 1 was composed of numerous pictures that gave the impression of being bloated, **we divided it into Figures 1 and 2,** which represent brain magnetic resonance imaging and cerebral angiography, respectively. **The word count of the figure legends, which was changed from 489 to 445 words, was also reduced.** E.g.



Copyright © The Author(s) 2023.

Figure 1 The brain diffusion-weighted magnetic resonance imaging at different time intervals. A: Diffusion-weighted magnetic resonance imaging

(DW-MRI) at initial admission; B: DW-MRI on day 4 of admission showed multiple infarcts enlarged than before (orange arrows).

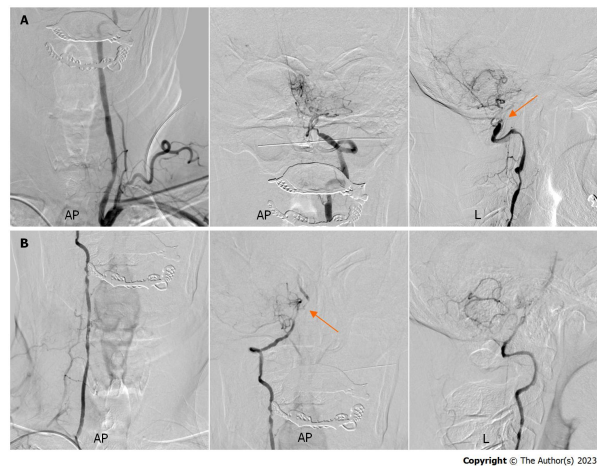


Figure 2 Digital subtraction angiography of bilateral vertebral arteries. A:

The left intracranial vertebral artery (VA) has been occluded with a blunt proximal stump (orange arrow); B: The right VA has been occluded near the junction of the basilar artery (BA), and the BA was supplied by the anastomosis of the right VA branch vessels (orange arrow). AP: anterior-posterior; L: lateral.

4. comment: The line “to our knowledge, which has not been reported previously” (P4,L80-81) is unnecessary and could be deleted.

Reply:

We have deleted this sentence: ~~[to our knowledge, which has not been reported previously].~~

● Response to reviewer's # 2 comments

1. comment: Are there any metabolic anomalies in this patient that would rule out the differential diagnosis?

Reply:

Thank you very much for your comments, which are valuable for our clinical evaluations and aid in enhancing precise diagnosis and treatment.

Cerebrovascular disease can be **etiologically diagnosed** with the aid of laboratory examinations, and **toxic metabolic encephalopathy** can be ruled out with the aid of laboratory tests pertaining to human metabolism.

The patient was admitted to the hospital with **no consciousness disorder, no fever, no headache, etc; and deny a history of chronic alcoholism, surgery, and unusual exposure history.** His **laboratory examinations such as routine blood tests, blood biochemistry, immune indexes did not show any significant abnormality.** The patient's condition deteriorated despite standardized drug therapy during hospitalization. On the fourth day of admission, he **presented with drowsiness and limb weakness, but no fever, no headache, no nausea or vomiting, and no behavioral or personality changes.** **Immune indexes were slightly elevated [white blood cells count was 10.21×10^9 /L (normal range: $3.5-9.5 \times 10^9$ /L), C-reactive protein was 55.63 mg/L (normal range: 0-6 mg/L), and procalcitonin was 0.09 ng/mL (normal range: 0-0.05 ng/mL)]; nevertheless, liver and renal function, electrolytes (sodium, potassium, calcium), and blood glucose levels were normal. Brain magnetic resonance imaging (MRI) showed no occupying lesions or characteristic demyelinating changes.**

On the second day of admission, the patient had already received cerebrovascular imaging (brain MRI, cerebral digital subtraction angiography, and intracranial vessel wall MRI), and a definitive diagnosis of **acute cerebral infarction coupled with bilateral vertebral artery occlusion** had been made. **We prioritized the etiology as being of vascular origin** because the patient's clinical presentation was consistent with the characteristics of cerebrovascular disorders (impaired function of the ascending reticular activating system due to ischemia in the posterior circulation leading to altered consciousness; multiple infarcts in the brainstem and cerebellum leading to focal neurologic deficit symptoms).

Atherosclerosis, cardiac or aortic origin emboli, and vasculitis are the primary causes of intracranial artery occlusion. Heart failure or atrial

fibrillation were not present in the patient, and cardiogenic embolism was mainly ruled out.

Because of the patient's modestly elevated inflammatory markers, **vasculitis-related cerebral occlusion may need to be ruled out.** However, the patient's vascular imaging signs, including the cerebral angiography and vessel wall MRI, were not consistent with vascular inflammatory alterations. We hypothesized that **the elevated inflammatory markers may have been caused by the stress of the disease.**

We regarded atherosclerosis-associated non-acute occlusion as a high possibility given the patient's coexisting **cerebrovascular risk factors** (hypertension, hyperlipidemia), as well as **vascular imaging patterns** (bilateral intracranial vertebral artery occlusion combined with moderate stenosis of the left middle cerebral artery).

In addition, **according to the patient's clinical history, laboratory examinations and imaging, we can exclude the etiologic diagnosis of toxic metabolic encephalopathies, such as encephalopathies caused by electrolyte disorders, hepatic encephalopathy, uremic encephalopathy, septic encephalopathy, Wernicke encephalopathy, and so on.** **We did not perform further cerebrospinal fluid analysis and pathogen testing to screen for central nervous system infections due to inadequate indications.** Furthermore, after the intracranial vertebral artery was recanalized, the patient's symptoms significantly improved, which in some ways supports our theory about a vascular etiology.

● Response to Editorial comments

1. comment: Authors are requested to send their revised manuscript to a professional English language editing company or a native English-speaking expert to polish the manuscript further. When the authors submit the subsequent polished manuscript to us, they must provide a new language

certificate along with the manuscript.

Reply:

The manuscript has been polished for type and grammar correction by the professional English language editors. A new language certificate has been submitted along with the manuscript.

2. comment: Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/ definition.

Reply:

Based on the correct abbreviation rules, we have made changes in the manuscript.

For example, in the figure legends, we have changed [Figure 1 The MRI DWI image at different time intervals...] to [Figure 1 The brain diffusion-weighted magnetic resonance imaging at different time intervals.]; and changed [Figure 2 HRMRI T1WI axial and CPR images.] to [Figure 3 The high-resolution magnetic resonance imaging of bilateral vertebral arteries].

3. comment: Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Reply:

We have provided the original figure document using PowerPoint, and submit as "85715-Figures.pptx" on the system.

The figures are original. We have added the following copyright information (Copyright ©TheAuthor(s) 2023) in the bottom right-hand side of

PowerPoint (PPT).

4. comment: Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. Authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision.

Reply:

Thanks to Company editor-in-chief for let us know the new tool-the RCA. We visited RCA database and obtained more information and we did supplement the highlights for the latest cutting-edge research results.

Thank you for accepting reviewing our manuscript.

Yours sincerely,

Fu Jun-Feng