

Response to the reviewers

Dear editors,

Thank you very much for your letter, and the comments. Due to rewriting most of my paper, we are quite sorry for delaying the submission of our revised manuscript.

According to the editor and reviewers' comments and requests, we have made extensive modification based on our original manuscript. All corrections and supplementary materials are labeled in pink for the editor, green for the Reviewer #1, blue for the Reviewer #2, orange for the Reviewer #3, purple for the Reviewer #4 in our revised version of manuscript. Our detailed point-by-point responses to the concerns are as follows.

Response to reviewers

Editor comments

Many thanks for the comments and suggestion from the editor. All corrections and supplementary materials are labeled in pink for the editor in our revised version of manuscript.

Comment 1

Our policy for the Case Report manuscript requires the title to include the disease name, the number of cases, and the phrase "literature review". In addition, the description of the paper as a literature review must be supported by the manuscript's content. Please update the reference list and add references with accompanying textual content that will strengthen the manuscript as a literature review of the appropriate and up-to-date case-related information. Please note that if authors only add the words "literature review" to the title, but do not revise the textual content of the manuscript to provide a literature review, the manuscript will be rejected.

[Reply] Many thanks for this suggestion. We have read the requirements of *World Journal of Clinical Cases* carefully, and our revised manuscript follows the rule of this Journal.

Comment 2

A short running title of less than 6 words should be provided.

[Reply] We accept this criticism and add the short running title, showing as “**Millard-Gubler syndrome with vertebrobasilar artery dissection**”.

Comment 3

Please provide the author contributions. Authors must indicate their specific contributions to the published work. This information will be published as a footnote to the paper. See the format in the attachment file-revision policies.

[Reply] Thanks for this advice. We have added the author contributions, showing as “**Author contributions: Hu WL designed the research; Li XT and Yuan JL collected the data; Li XT and Yuan JL wrote the paper**”.

Comment 4

Please offer all ORCID number like this:

Charles H Halsted (0000-0001-6711-887X); Charles H Halsted (0000-0001-6711-887X).

[Reply] We accept this criticism and advice. We have offered all ORCID number, showing as “**ORCID number: Xuanting Li (0000-0002-4874-3554); Junliang Yuan (0000-0002-9443-9203); Wenli Hu (0000-0001-6532-5410)**”.

Comment 5

Telephone and fax should consist of +, country number, district number and telephone or fax number, e.g. Telephone: +86-10-59080039, Fax: +86-10-59080039.

[Reply] We accept this criticism and advice. We have added the Telephone and fax, showing as “**Telephone: +86-10-85231370; Fax: +86-10-85232985**”.

Comment 6

Informed consent statement.

[Reply] We have offered another informed consent statement with the autography of the patient meeting your requirements.

Comment 7

Conflict-of-interest statement:

Please offer signed pdf format. A conflict-of-interest statement is required for all article and study types. In the interests of transparency and helping reviewers to

assess any potential bias in a study's design, interpretation of its results or presentation of its scientific/medical content, the BPG requires all authors of each paper to declare any conflicting interests (including but not limited to commercial, personal, political, intellectual, or religious interests) in the title page that are related to the work submitted for consideration of publication. In addition, reviewers are required to indicate any potential conflicting interests they might have related to any particular paper they are asked to review, and a copy of signed statement should be provided to the BPG in PDF format.

[Reply] We accept this criticism and advice, and offered a signed pdf format of the conflict-of-interest statement.

Comment 8

CARE Checklist (2016) :

In order to improve the quality of Case Report manuscripts, authors should download and complete the 'CARE Checklist (2016) of information to include when writing a case report' to ensure that the manuscript meets the requirements of the CARE Checklist (2016). Authors must state on the title page of the manuscript that the guidelines of the CARE Checklist (2016) have been adopted (see below). Authors must upload the PDF version of the completed checklist to the system.

[Reply] We accept this advice. We have provided a completed CARE Checklist (2016).

Comment 9

Abstract:

An informative, structured abstract of no less than 250 words should accompany each manuscript. Abstract should include background, case summary, and conclusion. The Abstract will be structured into the following sections, adhering to the word count thresholds indicated in parentheses: BACKGROUND (no more than 80 words):What does this case report add to the medical literature? Why did you write it up?CASE SUMMARY (no more than 150 words):Chief complaints, diagnoses, interventions, and outcomes. CONCLUSION (no more

than 20 words):What is the main “take-away” lesson from this case?

[Reply] We accept this criticism and advice. We have rewritten the abstract to meet your requirements, showing as

“Abstract

BACKGROUND

Millard-Gubler syndrome (MGS) is caused by a lesion in the brainstem at the level of the facial nerve nucleus, and it is also a rare ventral pontine syndrome. Vertebrobasilar artery dissection (VAD) is an uncommon cause of ischemic stroke. To the best of our knowledge, this is the first case reporting the coexistence of MGS and VAD in an acute ischemic young stroke patient.

CASE SUMMARY

We herein described an unusual case of acute ischemic young stroke patient, presenting with acute right peripheral facial palsy, right abducens palsy and contralateral hemihypesthesia, indicating as MGS. After receiving dual antiplatelet therapy with aspirin and clopidogrel, as well as rosuvastatin, the patient recovered significantly. The high-resolution magnetic resonance imaging (MRI) indicated a diagnosis of VAD.

CONCLUSION

Our finding further demonstrated high-resolution MRI is a useful technique to early detect underlying dissection in posterior circulation ischemic stroke”

on page 2, line 6-22.

Comment 11

Please offer the audio core tip, the requirement are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications:

Acceptable file formats: .mp3, .wav, or .aiff

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

[Reply] We accept this criticism and advice. We have offered an audio core tip meeting your requirements, which was uploaded as an attachment.

Comment 12

Please rewrote the case report as the format of the case report. Thank you.

[Reply] We accept this criticism and advice. We rewrote the case report according to your requirements as the format of the case report, showing as

“CASE PRESENTATION

Chief complaints

A 49-year-old male presented with dizziness and slurred speech for two days.

History of present illness

Two days before admission, the patient experienced sudden dizziness and nausea, followed by slurred speech, dysphagia, and choking.....

History of past illness

He suffered from hypertension for seven years.....

Physical examination

On admission, his neurological examination revealed right peripheral facial palsy, right abducens palsy, and left hemihypesthesia, suggesting the presence of MGS.....

Laboratory testing

The laboratory tests showed elevated plasm cholesterol (7.83mmol/L), glycosylated hemoglobin (9.0%) and homocysteine (15umol/L), and normal low density lipoprotein (1.4mmol/L)

Imaging examination

The chest X-ray film showed mild pneumonia.....

FINAL DIAGNOSIS

According to the typical symptoms, physical examination and imaging manifestations, this patient was diagnosed as acute ischemic stroke presenting as MGS causing by the VAD.

TREATMENT

The patient was given dual antiplatelet therapy with aspirin and clopidogrel, as well as rosuvastatin.

OUTCOME AND FOLLOW-UP

Nine days after his admission, he recovered significantly and was discharged from our department with mild residual right facial palsy and left hemihypesthesia.

DISCUSSION

MGS is caused by a lesion in the pons at the level of the facial nerve nucleus. This lesion involves the facial nerve nucleus, the abducent nerve, and the corticospinal tract.....

EXPERIENCES AND LESSONS

As for the acute ischemic stroke in young patient, artery dissection should be considered in the clinical works.....” on page 4-10.

Comment 13

Acknowledgment of the funds:

The approved grant application form(s) will be released online together with the manuscript in order for readers to obtain more information about the study and to increase the likelihood of subsequent citation. Our purpose of publishing the approved grant application form(s) is to promote efficient academic communication, accelerate scientific progress in the related field, and improve productive sharing of research ideas. In addition, a copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format.

[Reply] We accept this criticism and advice. We have offered the approved the grant application forms as attachments.

Comment 14

Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please provide PubMed citation numbers for the reference list, e.g. PMID and DOI, which can be found at <http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed> and <http://www.crossref.org/SimpleTextQuery/>, respectively. The numbers will be used in the E-version of this journal. Thanks very much for your co-operation.

[Reply] We accept this criticism and advice. We have changed the format of the reference list including all authors and Pubmed citation numbers.

Comment 15

Figure file names should identify the figure and panel. Avoid layering type directly over shaded or textured areas in the figure. Uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”.

[Reply] We accept this criticism and advice. We have removed the layering type from the figures and rewritten the figure file names, showing as “Figure 1. Brain MRI and MRA showed multiple infarctions and occlusion and stenosis of vertebral artery. A-C: Diffusion weighted imaging showed acute multifocal infarctions in pons, ventral of medulla oblongata, cerebellopontine angle and left occipital lobe; D: Brain MRA indicated the occlusion of left vertebral artery and the severe stenosis of proximal right vertebral artery.

Figure 2. High-resolution MRI showed the dissection of basilar artery and left vertebral artery. A, B: The eccentric periluminal hematoma of basilar artery; C, D: The eccentric periluminal hematoma of left vertebral artery” in Figure Legends section on page 15, line 2-6 and page 16, line 1-3.

Figure 1.

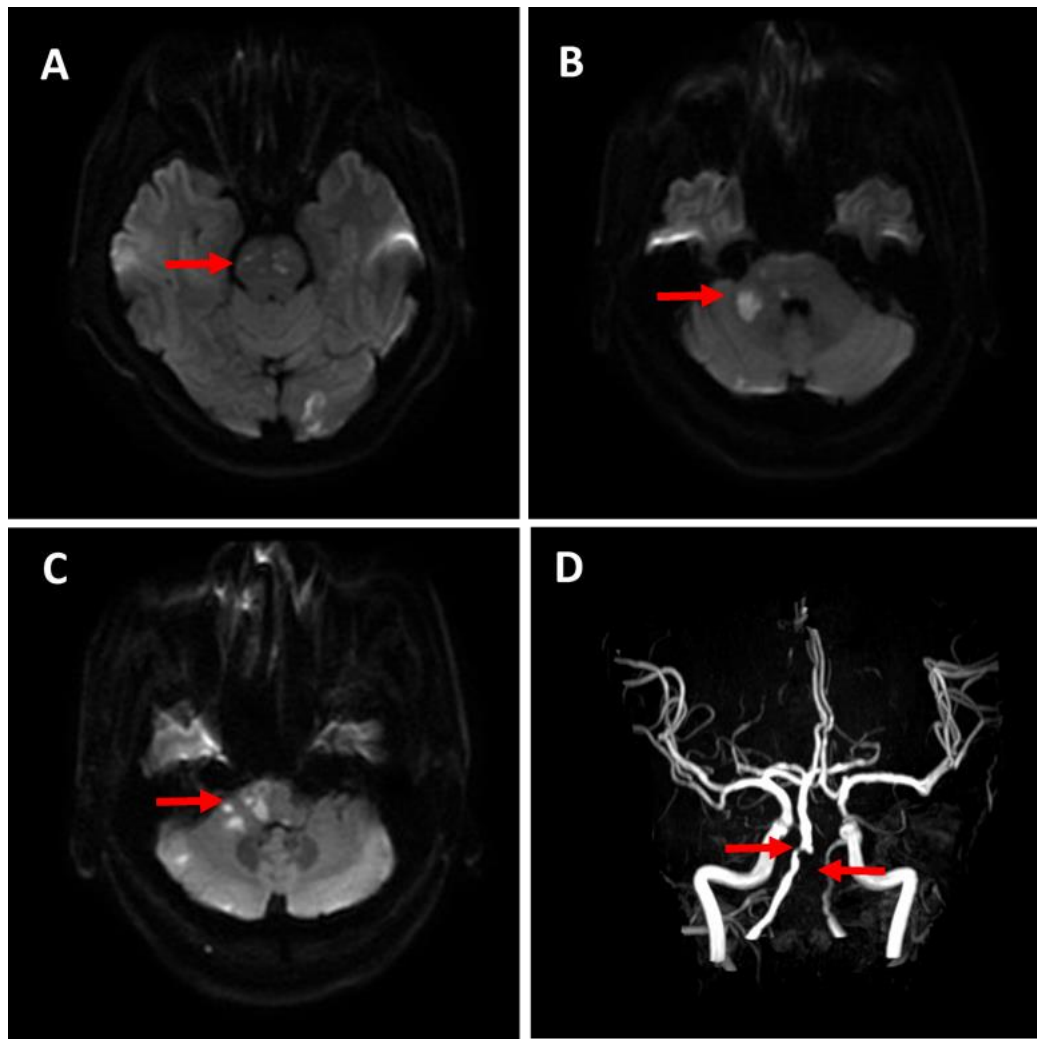
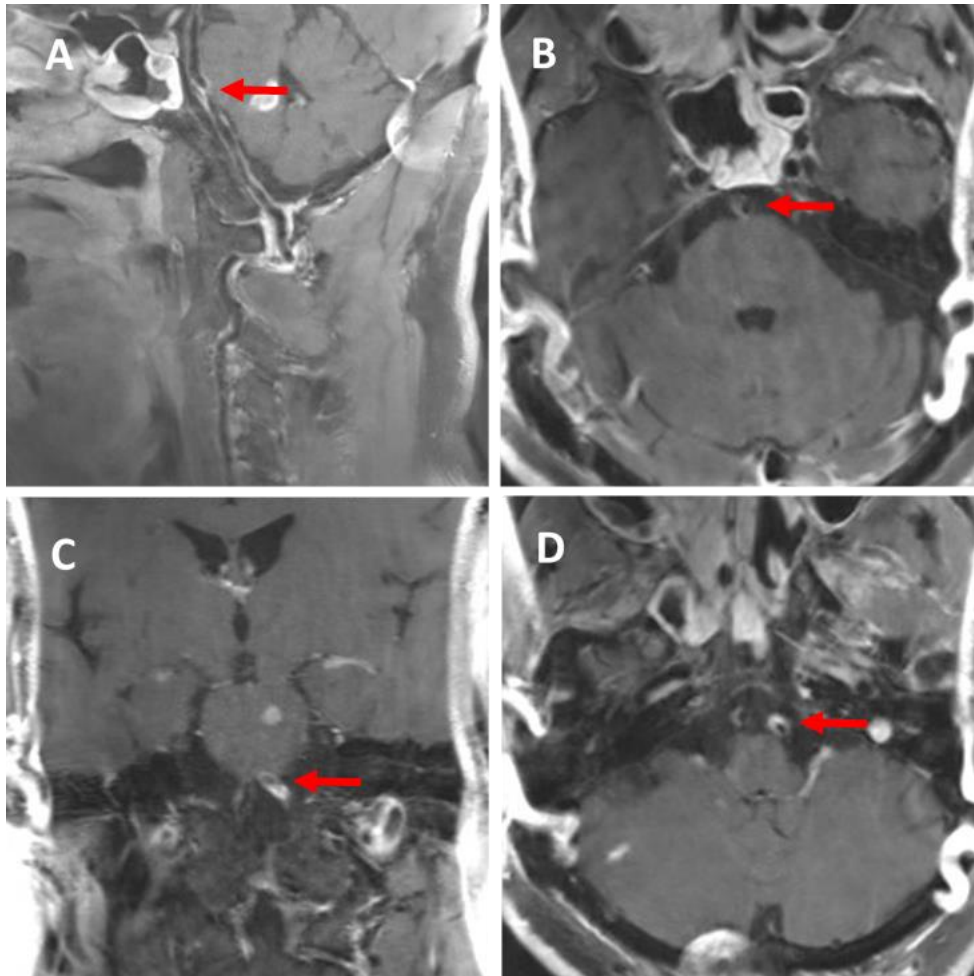


Figure 2.



Comment 16

您提供的知情同意书不是很清晰，请提供更清楚地版本

[Reply] We accept this criticism and advice. We have uploaded a clearer picture of the signed informed consent downloaded from the hospital digital medical record management system.

Comment 17

请提供 41239-CAREchecklist-Eng-20160131 文件

[Reply] We accept this criticism. We have completed the 41239-CAREchecklist-Eng-20160131 and uploaded it as an attachment.

Comment 18

请按我们最新的病例报告书写格式修改文章。（格式要求提供在附件中，文章应如何修改也做了批注）

[Reply] We accept this criticism. We have rewritten the manuscript and correct the format to meet your requirement of case report. The details are mentioned above on

page 3-6 of this file.

Reviewer #1

Many thanks for this reviewer's comments. All corrections and supplementary materials are labeled in green for the Reviewer #1 in our new version of manuscript.

Comment 1

Revision should include the removal of any repeated phrases such as “this is the first case reporting”... ..“only quite a few cases...”. Language editing is needed.

[Reply] We fully accept this reviewer's criticism. We have already removed the repeated phrases and delete the sentence “To our knowledge, this is the first case report of MGS due to posterior circulation ischemic stroke, which was caused by the VAD” from our manuscript in the DISCUSSION section. Besides, we have corrected some inappropriate words, and our revised version of manuscript has been further edited and polished.

Comment 2

Detail about DWI (1.5T or 3T?, manufacturer and model of MRI scanner, b values, fat saturation method) and MRA (contrast agent and dosage) is needed.

[Reply] We fully accept this reviewer's great advice. We have added more details about the neuroimaging technic, showing as “The parameters of MR examination were as follows from 3-Tesla system (Discovery MR750, GE Medical Systems, Milwaukee, Wis., USA): MR angiography (MRA) (repetition time 21 ms; echo time 3.4 ms; slice thickness 0.9 mm), axial T2-weighted (repetition time 5838.7 ms; echo time 107.3 ms), axial T1-weighted imaging (repetition time 1800 ms; echo time 27.7 ms), axial diffusion weighted imaging (DWI) (repetition time 3000 ms; echo time 65.3 ms, b value 1000), and coronal fluid-attenuated inversion recovery sequences (repetition time 7500 ms; echo time 121.1 ms).....Brain MRA without contrast agent indicated the occlusion of left vertebral artery and the severe stenosis of proximal right vertebral artery (Figure 1, D)” in CASE PRESENTATION section on page 5, line 10-22.

Comment 3

Specific comments: 1. High-resolution MRI>MRI (throughout, HR is meaningless, sounds like advertising) .

[Reply] Many thanks for the reviewer's criticism and advice. High-resolution MRI is expected to be more helpful and aid in differentiating intracranial artery dissection from other vascular pathologies in comparison to luminal angiographic techniques, such as CTA, MRA, and DSA [1]. In order to avoid confusion, we have rewritten the sentence according to the viewer's advice, changing "HR-MRI" to "high-resolution MRI" in all the manuscript.

Comment 4

Specific comments: 4. Fat sat>fat saturation. 5. Page 4 line 6: black blood MRI>black blood t2-weighted MRI.

[Reply] Many thanks for the reviewer's criticism and advice. We have rewritten the sentence according to the viewer's advice, changing "fat sat" to "fat saturation", "black blood MRI" to "black blood T2-weighted MRI" in all the manuscript.

Comment 5

Specific comments: 2. ...only quite a few cases...: unclear!

[Reply] We fully accept the reviewer's criticism and advice. We have rewritten the sentence more clearly, showing as "As far as we know, only 5 cases reported MGS caused by cerebral infarction" in INTRODUCTION section on page 4, line 8-9, and "To date, there are only 5 case reports of MGS due to cerebral infarction" in DISCUSSION section on page 6, line 16-17. Besides, we have added a table of the features of these 5 Millard-Gubler syndrome cases according to the suggestion of reviewer#3 on page 7-9.

Comment 5

Specific comments: 3. Last line page 3: delete (However...patient).

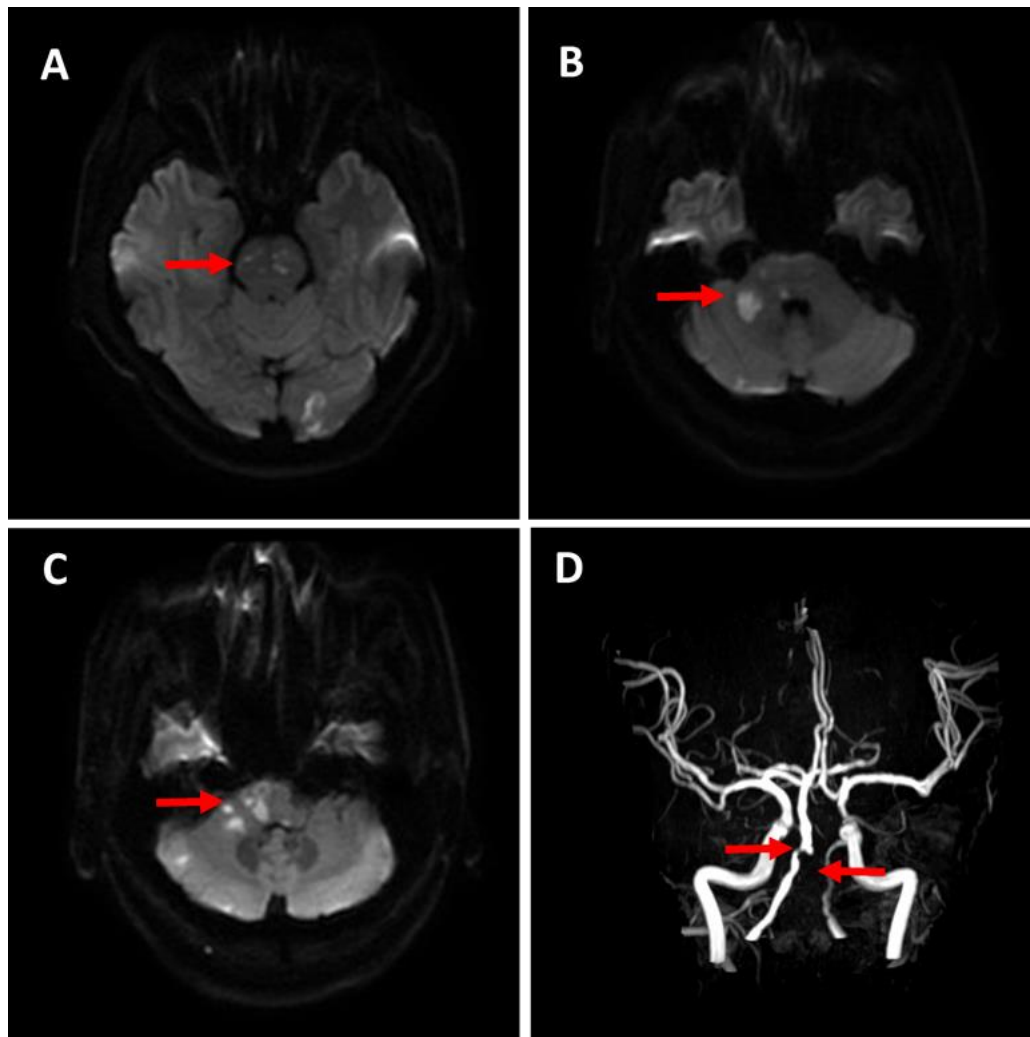
[Reply] We accept the reviewer's advice and delete the sentence "However, digital subtraction angiopathy was rejected by this patients" in DISCUSSION section.

Comment 6

Specific comments: 6. Fig.1: remove redundant text from images.

[Reply] We accept the reviewer's good advice. We have removed the redundant text

from images on Fig.1.



Comment 7

Specific comments: 7. Fig.1D: add arrows to indicate occlusion and stenosis.

[Reply] We fully accept the reviewer's great advice. In order to display important findings more visually, we have added arrows to indicate occlusion and stenosis on Fig.1D.

Reviewer #2:

Many thanks for this reviewer's comments. All corrections and supplementary materials are labeled in blue for the Reviewer #2 in our new version of manuscript.

Comment 1

This is an interesting case report of Millard-Gubler Syndrome due to

vertebrobasilar artery dissection. The case itself is interesting.

[Reply] Many thanks for the positive appraisal.

Comment 2

For differential diagnosis, more details of laboratory data such as blood cell counts, and serological tests should be presented.

[Reply] We fully accept the reviewer's good advice. We have added more details of laboratory data and serological tests, showing as "The laboratory tests showed elevated plasma cholesterol (7.83mmol/L), glycosylated hemoglobin (9.0%) and homocysteine (15umol/L), and normal low density lipoprotein (1.4mmol/L). For the blood routine, his white blood cell was mildly elevated ($10.63 \times 10^9/L$) and other items were normal. The chest X-ray film showed mild pneumonia" in the CASE PRESENTATION section on page 5, line 5-10.

Reviewer #3:

Comment 1

Millard-Gubler syndrome, also known as ventral pontine syndrome, is one of the crossed paralysis syndromes, which are characterised by cranial nerves VI and VII palsies with contralateral body motor or sensory disturbances. The vertebrobasilar dissection is not unusual but the age is indeed. The manuscript is of some interest, although it needs to be reviewed by an English-speaking neurologist (UK-USA/CAN/AUS/NZ). I found several aspects and terms that need to be reviewed carefully.

[Reply] Many thanks for the reviewer's positive appraisal, and we accept the criticism. We have corrected some inappropriate words, and our new version of manuscript has been further edited and polished with the help of English-speaking neurologist from USA.

Comment 2

It may be interesting and valuable to add a table of similar case reports so far.

[Reply] This is an excellent idea, and many thanks for the reviewer's advice. We performed an electronic literature search for reports (case reports or case series) on

Millard-Gubler syndrome causing by cerebral ischemic stroke from inception to October 31th, 2018. We searched the PubMed database and Web of Science using the following terms “Millard-Gubler syndrome” and “stroke”/“infarct”/“cerebral infarction”. The table of Millard-Gubler syndrome cases causing by cerebral ischemic stroke reported in the prior literatures is listed as follow:

Table 1. The characteristics of Millard-Gubler syndrome cases causing by cerebral ischemic stroke from 1993 to 2018.

Author	Time	Age, y	Sex	Medical History	Physical Examination	MRI	MRA	Others
Yasuda Y[2]	1993	60	male	NA	right peripheral facial nerve palsy, left hemiparesis , tongue deviated to the left, exaggerated deep tendon reflex and equivocal left Babinski's reflex	cerebral infarction in the right ventral pons	occlusion of both vertebral arteries	
Matlis A[3]	1994	76	male	hypertension, ischemic heart disease, type II diabetes mellitus	slight dysarthria, peripheral right facial palsy, flaccid left hemiparesis, brisk left deep tendon reflexes and positive left Babinski's reflex	cerebral infarction in the right anteromedial pons	NA	
Onbas O[4]	2005	56	male	NA	left facial paralysis, right hemiparesthesia and exaggerated deep tendon reflexes	acute cerebral infarction in the left ventral part of the pons	stenosis of basilar artery	

Rose DZ[5]	2010	45	male	HIV		horizontal diplopia, left acute cerebral unremarkable	facial paralysis and right infarction in the left pons	MRSA meningo-vasculitis causing by the restricted diffusion of pus in the subarachnoid space
Ahdab R[6]	2013	63	male	diabetic and hypertensive		right facial palsy involving the lower facial muscles and the orbicularis oculi but sparing the frontalis muscle and left hemiparesis	acute infarction in the ventro-medial aspect of the medulla and limited to the right pyramid	cerebral diffuse atherosclerotic changes of the basilar trunk with multisegmental mild to moderate narrowing, especially in the distal third

MRI=magnetic resonance imaging; MRA=magnetic resonance angiography; NA=not available; HIV=human immunodeficiency virus; MRSA=methicillin-resistant Staphylococcus aureus

Reviewer #4:

Comment 1

This case report from China reported a young adult male with vertebrobasilar artery dissection presenting as Millard-Gubler Syndrome. The manuscript is simple and well written

[Reply] Many thanks for the reviewer's positive appraisal.

Comment 2

However, some issues need to be addressed. Firstly, although neurological examination is reported appropriately, please state whether the rest of the physical examination and laboratory results revealed anything important such as fever, leukocytosis, as this is important for the differential diagnosis.

[Reply] Many thanks for the reviewer's positive appraisal, and we accept the criticism. We have added the rest of the important physical examination and laboratory results, showing as "Before the onset of the illness, he didn't suffer from fever or cervical pain.....The other cranial nerves and motor exam were normal. On admission, his blood pressure was 141/85 mmHg. The laboratory tests showed elevated plasma cholesterol (7.83mmol/L), glycosylated hemoglobin (9.0%) and homocysteine (15umol/L), and normal low density lipoprotein (1.4mmol/L). For the blood routine, his white blood cell was mildly elevated ($10.63 \times 10^9/L$) and other items were normal. The chest X-ray film showed mild pneumonia" in CASE PRESENTATION section on page 4, line 22-23 and page 5, line 2-10.

Comment 3

Secondly, did you perform further investigation on his high blood pressure? To be diagnosed with high blood pressure at 42 years old raises the concern for secondary causes for this diagnosis.

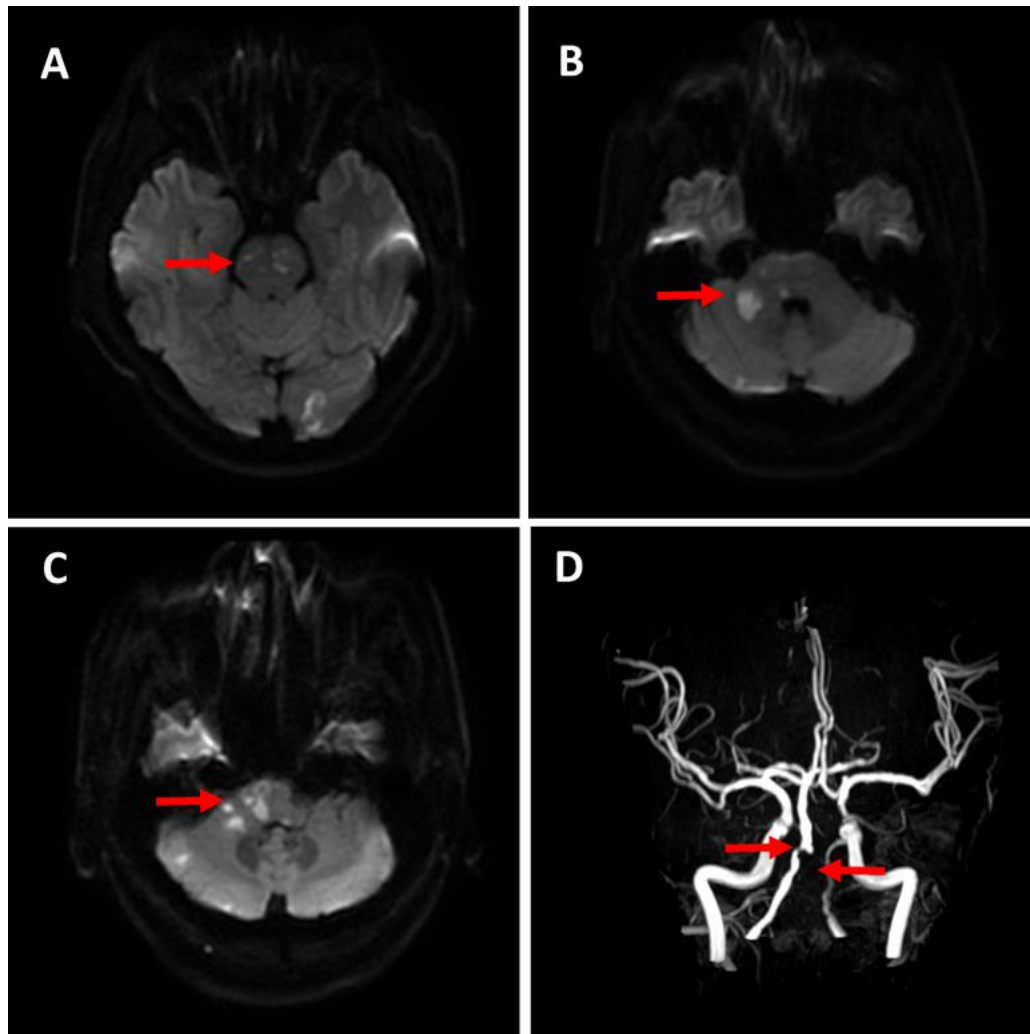
[Reply] Many thanks for the reviewer's criticism, and it is interesting and worth thinking. We measured the patient's blood pressure daily, and his systolic pressure was 135-144mmHg and diastolic pressure was 85-96mmHg. Unfortunately, we did not perform further investigation on his high blood pressure. Making a speculation, acute elevated blood pressure maybe one of the reasons to cause the dissection of the

basilar artery and vertebral artery of this patient.

Comment 4

Finally, as Figure 2, please use arrows within Figure 1 to remark important findings, as this would help non-neurologist physicians.

[Reply] Many thanks for the reviewer's good advice, and we accept the criticism. We have added arrows in Figure 1 to remark important findings.



Reviewer #5:

Comment 1

good case report

[Reply] Many thanks for the reviewer's positive appraisal.

Reviewer #6:

Comment 1

accepted

[Reply] Many thanks for the reviewer's positive appraisal.

We have revised the manuscript in line with all the editor and reviewers' comments and we hope that the new manuscript can be acceptable for publication. If you have any questions, please feel free to contact us.

Many thanks for your processing on our work.

Best regards,

Xuanting Li

References

1. Jung SC, Kim HS, Choi CG, Kim SJ, Lee DH, et al. (2016) Quantitative Analysis Using High-Resolution 3T MRI in Acute Intracranial Artery Dissection. *J Neuroimaging* 26: 612-617.
2. Yasuda Y, Matsuda I, Sakagami T, Kobayashi H, Kameyama M (1993) Pontine infarction with pure Millard-Gubler syndrome: precise localization with magnetic resonance imaging. *Eur Neurol* 33: 331-334.
3. Matlis A, Kleinman Y, Korn-Lubetzki I (1994) Millard-Gubler syndrome. *AJNR Am J Neuroradiol* 15: 179-181.
4. Onbas O, Kantarci M, Alper F, Karaca L, Okur A (2005) Millard-Gubler syndrome: MR findings. *Neuroradiology* 47: 35-37.
5. Rose DZ, Parra-Herran C, Petito CK, Post MJ (2010) Restricted Diffusion of Pus in the Subarachnoid Space: MRSA Meningo-Vasculitis and Progressive Brainstem Ischemic Strokes - A Case Report. *Case Rep Neurol* 2: 101-110.
6. Ahdab R, Saade HS, Kikano R, Ferzli J, Tarcha W, et al. (2013) Pure ipsilateral central facial palsy and contralateral hemiparesis secondary to ventro-medial medullary stroke. *J Neurol Sci* 332: 154-155.