Decision Letter (JCQ-2025-0040)

From: [redacted]
To:
CC:
BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0040

Body: 19-Jan-2026

Dear Dr Chu:

Manuscript ID JCQ-2025-0040 entitled "Diagnostic Challenges in Thrombotic Thrombocytopenic Purpura: A Case Report of Initial Misdiagnosis" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.
1. Access to https://mc.manuscriptcentral.com/jcq and log into the site.
2. Click "Author" at the top left of the screen at "Home" page.
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4. Click "create a revision" on the manuscript you are going to revise.
5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

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When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Richard S. Isaacs
Editor in Chief
Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author
Authors present the challenging atypical case of such a severe disease as thrombotic thrombocytopenic purpura. Description of such cases is quite important for understanding of pathogenesis of the disease and for improvement of diagnostics and therapy.
I'm satisfied with the manuscript and have no comments.

Reviewer: 2

Comments to the Author
Case report
This manuscript describes an iTTP case with a delayed diagnosis over several days.
Understanding the pathogenesis and clinical presentations of TTP is essential. It is also crucial to keep TTP in mind during clinical evaluation.
Dizziness frequently occurs as a neurological symptom in iTTP. Secondary iTTP often occurs with SLE or APS as the underlying condition.
The patient suffered from thrombocytopenia and hemolytic anemia. Thrombocytopenia caused by isoniazid was suspected. But, isoniazid seldom causes hemolytic anemia, except in individuals with G-6-PD deficiency. Given the mechanisms of Coombs-negative hemolytic anemia, drug-induced bicytopenia was unlikely.
The patient experienced multifocal bilateral cerebral and cerebellar infarctions without identifiable responsive vessels. The results do not match those seen in embolic strokes or strokes with an undetermined embolic source. Instead, they are typical of neurological symptoms caused by TTP, which is triggered by VWF-platelet thrombi. Hemolytic anemia observed in association with antiphospholipid syndrome (APS) typically demonstrates a positive Coombs test. Although the authors noted that the case was unusual, there was considerable signs indicating she had iTTP prior to the demonstration of ADAMTS13 deficiency.
Discussion
During the acute phase of iTTP, cardiac death is caused by microvascular thrombosis in the heart rather than coronary thrombosis (Kayashima et al., IJH 2021).
iTTP is an autoimmune disease in which anti-ADAMTS13 antibodies inhibit the activity of ADAMTS13, a protease responsible for cleaving unusually large VWF. As a result, VWF–platelet thrombi form, leading to thrombocytopenia, organ dysfunction, and hemolytic anemia. Plasmapheresis using FFP removes pathogenic antibodies and adds ADAMTS13, but the infused ADAMTS13 can trigger more anti-ADAMTS13 antibodies. This inhibitor boosting often occures. Therefore, immunosuppression combined with plasmapheresis is central to iTTP treatment.
As previously described, this case involves secondary TTP associated with SLE and APS. The figure shows that severe tuberculosis infection can sometimes trigger iTTP. In this patient, latent TB was present; however, iTTP and TB appear to be independent conditions.
Conclusion
Many signs indicate the possibility of iTTP. The presented case does not appear to be atypical TTP.

Date Sent: 19-Jan-2026

Author's Response to Decision Letter for (JCQ-2025-0040)

Diagnostic Challenges in Thrombotic Thrombocytopenic Purpura: A Case Report of Initial Misdiagnosis

Dear Editor and Reviewers,
We sincerely thank the Editor and the Reviewers for their careful evaluation of our manuscript and for their insightful and constructive comments. We appreciate the time and effort devoted to reviewing our work. Below, we respond to each comment point by point.

Reviewer 1
Authors present the challenging atypical case of such a severe disease as thrombotic thrombocytopenic purpura. Description of such cases is quite important for understanding of pathogenesis of the disease and for improvement of diagnostics and therapy. I'm satisfied with the manuscript and have no comments.
Response: We thank Reviewer 1 for the positive evaluation of our manuscript and for recognizing the importance of reporting such cases to improve understanding of TTP pathogenesis, diagnosis, and treatment. We appreciate the reviewer's supportive comments.

Reviewer 2
This manuscript describes an iTTP case with a delayed diagnosis over several days. Understanding the pathogenesis and clinical presentations of TTP is essential. It is also crucial to keep TTP in mind during clinical evaluation.
Response: We agree with the reviewer's comment. We have revised the title and the manuscript to consistently specify TTP as iTTP. As the reviewer pointed out, one of the primary aims of this case report is to highlight the importance of early clinical suspicion of iTTP, particularly in patients presenting with thrombocytopenia, hemolytic anemia, and neurological symptoms, even before confirmatory ADAMTS13 testing becomes available.

Dizziness frequently occurs as a neurological symptom in iTTP. Secondary iTTP often occurs with SLE or APS as the underlying condition.
Response: Thank you for your comment. In the revised manuscript, we emphasize in the Discussion that dizziness is a common neurological manifestation of iTTP. We also clarify that autoimmune diseases, such as SLE and APS, are well-recognized conditions associated with secondary iTTP, supporting the diagnosis in this case.
The patient suffered from thrombocytopenia and hemolytic anemia. Thrombocytopenia caused by isoniazid was suspected. But, isoniazid seldom causes hemolytic anemia, except in individuals with G-6-PD deficiency. Given the mechanisms of Coombs-negative hemolytic anemia, drug-induced bicytopenia was unlikely.
Response: We appreciate this important clarification. We have added this explanation to the Case Presentation section to clarify that a drug-induced cause was unlikely, specifically stating: "Considering the pathophysiology of Coombs-negative hemolytic anemia, INH-induced bicytopenia was deemed unlikely."

The patient experienced multifocal bilateral cerebral and cerebellar infarctions without identifiable responsive vessels. The results do not match those seen in embolic strokes or strokes with an undetermined embolic source. Instead, they are typical of neurological symptoms caused by TTP, which is triggered by VWF-platelet thrombi.
Response: hank you for your comment. We agree that the neuroimaging findings, multifocal bilateral cerebral and cerebellar infarctions without large-vessel occlusion, are more consistent with a microvascular thrombotic process than with an embolic stroke. We have revised the manuscript accordingly to emphasize this diagnostic clue, as follows: "Multifocal bilateral cerebral and cerebellar infarctions without identifiable responsible vessels suggest a microvascular thrombotic process rather than an embolic stroke."

Hemolytic anemia observed in association with APS typically demonstrates a positive Coombs test. Although the authors noted that the case was unusual, there were considerable signs indicating she had iTTP prior to the demonstration of ADAMTS13 deficiency.
Response: We agree with this observation. As the reviewer correctly notes, hemolytic anemia in APS is typically Coombs-positive, whereas our patient exhibited Coombs-negative hemolytic anemia, which further supports a diagnosis of iTTP. We have revised the manuscript accordingly to state: "iTTP was considered while ADAMTS13 activity results were still pending. APS was also included in the differential diagnosis; however, laboratory findings, including Coombs-negative hemolysis, made this diagnosis less likely."

Comment: During the acute phase of iTTP, cardiac death is caused by microvascular thrombosis in the heart rather than coronary thrombosis (Kayashima et al., IJH 2021).
Response: Response: We thank the reviewer for this valuable reference. We have incorporated this important point into the Discussion, emphasizing that cardiac complications in iTTP are primarily driven by microvascular thrombosis rather than epicardial coronary artery disease, as microvascular thrombosis is more frequently observed in iTTP cases ."In iTTP cases, microvascular thrombosis is more frequently observed.1"

iTTP is an autoimmune disease in which anti-ADAMTS13 antibodies inhibit the activity of ADAMTS13. Therefore, immunosuppression combined with plasmapheresis is central to iTTP treatment.
Response: We agree entirely. We have expanded the discussion to more clearly describe the pathophysiology of iTTP, including inhibitor boosting during plasma exchange and the critical role of early immunosuppressive therapy in combination with plasmapheresis.

As previously described, this case involves secondary TTP associated with SLE and APS. The figure shows that severe tuberculosis infection can sometimes trigger iTTP. In this patient, latent TB was present; however, iTTP and TB appear to be independent conditions.
Response: We agree with this interpretation. In the revised manuscript, we clarify that although severe infections may trigger iTTP, this patient had latent tuberculosis without evidence of active disease. We have added the following statement to the manuscript: "Despite these observations, the temporal association between TB and TTP varies across cases, and a definitive causal relationship has not been established, suggesting that TB may act as a potential trigger in some patients, while in others the coexistence may be incidental."

Many signs indicate the possibility of iTTP. The presented case does not appear to be atypical TTP.
Response:We appreciate this important comment and agree. We have modify the conclusion section as specified it as iTTP.

Once again, we thank the Editor and Reviewers for their insightful comments, which have significantly improved the clarity and quality of our manuscript.

Sincerely,
Chu Gary
California Northstate University College of Medicine
Email: garychumd@gmail.com

Reference
1. Kayashima M, Sakai K, Harada K, et al. Strong association between insufficient plasma exchange and fatal outcomes in Japanese patients with immune-mediated thrombotic thrombocytopenic purpura. Int J Hematol. Oct 2021;114(4):415-423. doi:10.1007/s12185-021-03197-5