Reviewer's report

Title: Patient with pontine warning syndrome and bilateral posterior internuclear ophthalmoplegia: case report

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Reviewer: Gustavo Saposnik

Reviewer's report:

Summary: The authors presented a case report on 54-year-old woman who had 3 episodes of left-sided weakness before complete hemiplegia and bilateral posterior internuclear ophthalmoplegia. MRI demonstrated an acute right paramedian pontine infarct and MRA showed diffused mild atherosclerotic disease. Clopidogrel, atorvastatin and acarbose. After 23 days of hospitalization, she was discharged with severe left hemiplegia. They concluded by saying: 1) Pontine warning syndrome may be underestimated and understudied. 2) Posterior internuclear ophthalmoplegia is a rare clinical sign in cerebrovascular diseases, while it can help to locate a brainstem lesion rather than an internal capsular one. 3) Blood pressure lowering administration may be improper for patients with pontine warning syndrome. 4) Once infarct occurs following the transient ischemic attacks, these patients can be appropriate target for intravenous thrombolysis within an extended time window of up to 6 hours.

Strengths:
1- Well-written
2- Interesting case

Comments and suggestions:

1) Case description: the examination is well described. The results of investigations are vaguely described. For example, the authors stated that MRA showed diffused mild atherosclerosis. No imaging is provided. In the discussion, they mentioned proximal branch narrowing. This is somewhat confusing as readers would like to know whether this is due to large atherosclerotic disease or due to small vessel disease (branch disease as reported by Caplan in Neurology 1990). Please clarify and be consistent.

2) A clear explanation about the underlying mechanism is needed. Hypoperfusion is an uncommon mechanism in stroke. The evidence provided based on a case/s report is weak. Therefore, a thoughtful description of the pathophysiologica mechanisms is needed (? Penetrating branch disease rather than lipohyalinosis with hypoperfusion of the vascular territory of terminal arteries with no collateral flow).

3) Conclusions: The authors said “Once infarct occurs following the transient
ischemic attacks, these patients can be appropriate target for intravenous thrombolysis within an extended time window of up to 6 hours, in view of the pathological basis of basilar penetrating branch disease and of the poor clinical outcome”. This statement implied that patients with branch disease benefit from t-PA and even beyond the accepted time window. Although this reviewer may personally agree with the extended time window, there is no evidence than patients with penetrating branch disease benefit from thrombolytic therapy. This hypothesis has never been tested. Information from RCT using IV thrombolysis unlikely answer this question (penetrating branch disease was not in the CRF of the studies, most of required imaging include CT scan rather than MRI). In summary, this statement is misleading and is neither support from the manuscript nor from the current available evidence. I strongly suggest deleting this whole point. If anything the authors can mention about the erratic course and limitations with effective therapies in this context.

4) Minor comment: Please check for grammar and misspelling. For example: acabose instead of acarbose.

I hope the authors find these comments helpful.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests