Author's response to reviews

Title: Life threatening intracerebral haemorrhage following Saw scaled viper (Echis carinatus) envenoming-Authenticated case report from Sri Lanka

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Author's response to reviews: see over
Dear Dr Tom,

Hereby, we would like to submit our revised manuscript for consideration for publication in your journal. We would like to thank the reviewer for his comments in response to which the manuscript was thoroughly revised. A point-by-point response in bold type to the reviewer’s remarks is given below.

**Reviewer:** Georges Mion

1. Have the authors an explanation why bites are considered as rarely fatal in Sri Lanka? Is the treatment particularly well codified? Do most victims receive antivenom therapy?

*We have clearly addressed these issues in our manuscript. Saw scaled viper envenoming in Sri Lanka characterized by minor bleeding manifestations. Neither serious bleeding manifestations nor fatalities have been reported in Sri Lanka. Anti venom serum is recommended by the management guidelines of Sri Lanka. Therefore most of the clinicians treat saw scaled viper envenoming with antivenom serum.*

2. I disagree with the authors statement that antivenom was inefficient. Clearly, antivenom was administrated 3 hours after the bite and the headache had begin yet. So, I think the blood was completely incoagulable and the bleeding took place early, before the administration of antivenom.

*Blood was clearly coagulable after antivenom administration. So, despite the persistence of headache after antivenom administration, the authors cannot rule out that the treatment was efficient. As they state in the title, an intracranial bleeding is life threatening. Antivenom had probably stopped the extension of the intracranial hemorrhage, explaining that the patient could survive without a surgical intervention. There is no reason why antivenom would have stopped headache and neurological signs as long as the hematoma was present.*

*So the real question is not whether antivenom was efficient, but whether antivenom should have been administered as soon as the patient came to local hospital, when the local bleeding could be a sign of systemic envenomation.*

*On admission to the local hospital our patient did not have any clinical or haematological evidence of systemic envenoming. According to the management guidelines antivenom serum is not indicated only for localized envenoming. Once the detection of systemic*
envenoming he was immediately treated with antivenom serum. There was no delay. His neurological deficit was progressive even after antivenom serum administration, which clearly indicated either inadequate antivenom was used or antivenom was less effective in prevention of progression of neurological deficit. We agree that we couldn’t say the antivenom was ineffective. We have changed the word “ineffective” to “less effective”.

3. Can the authors explain whether the dose of 10 vials is the usual dose, and how much is the total liquid amount administered (200 or 2000 mL)?

Each vial of antivenom serum was dissolved in 10 ml of sterile water and diluted with 200ml of normal saline to a total volume of 300ml and was infused intravenously over an hour as stated in the management guideline of Sri Lanka.

4. The neurological signs indicate a third cranial nerve paralysis, and the CT brain clearly shows a deviation of middle line and a ventricular collapse thus involving, despite the normal fundoscopic examination, a rise in intracranial pressure, explaining headache.

Initial enlargement of the opposite pupil was a false localising sign of intraparenchymal haemorrhage. Because of the intra-axial fascicular arrangement of fibres within the third nerve, the peripherally located pupilloconstrictor fibres are most vulnerable, such that unilateral mydriasis may be the earliest sign. This may evolve to a complete, false localising, third nerve palsy before the ipsilateral third nerve becomes involved. (ref J Neurol Neurosurg Psychiatry. 1994 Sep;57(9):1126-8. Initial enlargement of the opposite pupil as a false localising sign in intraparenchymal frontal haemorrhage. Chen R, Sahjpaull R, Del Maestro RF, Assis L, Young GB).

5. What do you call “blood picture”?

Blood picture means peripheral blood smear. Since normal blood picture do not add to the manuscript, we have removed it from the manuscript to avoid unnecessary confusion.

6. I disagree that VICC is characterized by slightly prolonged PT. In Echis envenoming, PT as APTT and fibrinogen are very markedly disturbed (Ref Mion G, Larréché S. Antivenom therapy is efficient in Viperidae bites, fresh frozen plasma probably not. Am J Emerg Med. 2009;27:247-8).

We agree to some extent and we have deleted the word ‘slightly’.
Reviewer: Sidgi Hasson

Abstract

Comments:
1- Authors used abbreviation in the abstract. this is uncommon.
2- The authors used SSV at the end. The SSV meant Saw- scaled viper is a general term for Echis subspecies of Echis carinatus, Echis ocellatus and Echis coloratus.

We have rewritten the abstract and we have not included the abbreviation. Out of the Echis subspecies only Echis carinatus is found in SriLanka. Therefore in our manuscript Saw-scaled viper meant to Echis carinatus.

Introduction

Comments:
1 Un proper use of abbreviation i.e., SSV should be stated earlier i.e., first line.

2 Introduction looks to me as a summary more than an introduction. Introduction should illustrate adequately the issue of snake venom and snake envenomation with its clinical complications in a constructive way.

3 I suggest authors should re-write a proper introduction.

We have rewritten the introduction in an illustrative way and have used the abbreviation properly.

Case report

Comments:

1 Authors claim that the killed snake was identified. My question to the authors who identified the killed snake and if they can state his/her proficiency.

We have already stated that the killed snake was identified by the attending medical officer and one of the authors (CAG- Prof Christeine Ariaranee Gnanathasan MBBS, MD (Col), MRCP (UK), M Phil, FRCP (UK). Professor in Medicine; Consultant physician and an expert in snake bite and antivenom). She has done M Phil on snake identification and epidemiology. She is a clinical herpetologist.

2 The authors claim they brought the killed snake and at the same time they showed a photograph “Figure1” of a life one?? I am not convinced that is
adequate.

Unfortunately we don’t have the photograph of the killed snake. It was brought in a denatured condition. If this figure do not add to the manuscript, we are happy to remove it.

3To me the photograph is for *Echis ocellatus* more than for *Echis carinatus*!!!.

We are surprised by your comment because *Echis ocellatus* is not found in SriLanka!!!.

4The authors stated that “On admission to the local hospital, there was local bleeding at the bite site with fang marks” the fangs of the *Echis* viper [*E. Carinatus, E. Ocellatus, E. colaratus*] usually 5mm. Therefore, it is unlikely to see the fangs marks and would be be very hard to recognize specially if there is bleeding. I recommend that the authors should remove such statement.

It is shocking. Even few millimeters of fangs mark can be easily identified by careful examination of experienced clinician. Anyway we have removed the word ‘with fang marks’ as you have suggested.

5The authors stated that “there was no evidence of systemic envenoming” how come such statement was concluded without prior laboratory investigation and findings.

We have changed the sentence to “there was no clinical evidence of envenoming”.

**Discussion**

1The general introduction in this section is too long and should be placed in the main introduction section instead.

We have rewritten the discussion as suggested.

2The authors stated that “We believe that VICC and direct endothelial injury due to haemorrhagin in the venom were responsible for the fatal intracerebral haemorrhage in our patient” it is very difficult to use the word believe. I recommend the authors should use the results or the finding of “VICC is characterized by prolonged 20WBCT, slightly prolonged PT and PTTK and a marked increase in fibrinogen degradation products.” suggest or may be due rather than believe.

We have rewritten the sentence as “VICC and direct endothelial injury due to haemorrhagin in the venom might be responsible for the near fatal intracerebral haemorrhage in our patient”.

3The authors stated the abbreviation of AVS? What AVS abbreviation meant to be.
AVS means antivenom serum.

The authors referred to a previous study “In a study included 167 cases of VICC following snake bite envenoming in Australia, showed AVS was ineffective in restoration of coagulopathy” where is the reference?.

We have given the reference.

The authors stated that “This case report is intended to increase the vigilance for fatal intracerebral hemorrhage following SSV envenoming in Sri Lanka” my question is that how many cases being reported with similar finding?

Yes we agree. This is the first case report from Sri Lanka. Therefore we have changed the sentence as “This case report is intended to bring awareness of this fatal complication of SSV envenoming in Sri Lanka.

Reviewer: Geoffrey Isbister

This is a single case of a snake that has been well described. It is novel because it is uncommon in Sri Lanka and not been reported to cause fatalities in Sri Lanka. My advice would be that this is better placed in a local journal, rather than an international journal since it is applicable to Sri Lanka and doesn't really add to our understanding of the snake internationally.


Editorial comments:

Could we please ask you to clarify the fate of the patient detailed in your manuscript? In the report of your case, you state that "He was discharged home a week later in good health without any neurological deficit". However, we find other references throughout the manuscript to "the fatal intracerebral haemorrhage in our patient". Could we therefore ask you clarify whether your patient died as a result of the bite?

We have used the word “fatal” or “life threatening” to indicate the seriousness and severity of the intracranial hemorrhage. As we have stated that He was discharged home a week later in good health without any neurological deficit. Since the word “fatal” caused the confusion, we have changed it to “near fatal”.

Please include Authors' Contributions, Competing Interests and Acknowledgements sections in your manuscript.

We have included the author’s contribution and competing interest.

We feel that your manuscript would benefit from some corrections being made to the English used.

The manuscript has reviewed by one of our English colleague. However he has failed to find any major errors in the use of English and grammar.

We feel that the revised manuscript is a suitable for publication in the BMC Emergency Medicine. Thank you again in advance for your kind consideration of this paper.

In anticipation of your response, on behalf of the co-authors,

With kind regards,

V.Jeevagan