Author’s response to reviews

Title: Severe Viperidae envenomation complicated by shock, acute kidney injury, and gangrene presenting late at the emergency department: a case report

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Author’s response to reviews:

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The Editor-in-chief,

BMC Emergency Medicine.

Dear Sir/Madam,

We are writing to submit our manuscript entitled “Severe Viperidae envenomation complicated by shock, acute kidney injury, and gangrene presenting late at the emergency department: a case report” for consideration for publication in BMC Emergency Medicine.

We have addressed all reviewers’ queries and have used the track changes options of MS Word to modify the paper so as to account for their comments and suggestions.

We hope that you will find this revised version suitable for publication.

Sincerely,

On behalf of all co-authors
Kavita Morparia, MD (Reviewer 1):

Kavita Morparia, MD (Reviewer 1): Thank you for the interesting case. A few suggestions:

1) Reviewer comments: in the case history, it is mentioned that 20 hrs have elapsed since the patient was brought to the hospital, but also that she immediately sought treatment from a local healer. This should be clarified.

Authors’ revision: Page 3, Line 13 to 20: The patient was bitten, but first sought treatment from a traditional healer who administered an unknown complementary and alternative medicine. Is due to no amelioration of her symptoms 20 hours following the bite incident that she decided to seek treatment at our emergency department.

2) Reviewer comments: how is it relevant that the patient did not have a snake bite previously?

Authors’ revision: We have deleted the sentence.

3) Reviewer comments: when mentioned that snakebite causes more deaths than measles and polio—it should be specified what geographic area that refers to.

Authors’ revision: We agree with you. This statement has been deleted.

4) Reviewer comments: a brief review of treatment strategies for snakebites may be beneficial to the emergency medicine population. There is some, but this can be expanded.

Authors’ revision: Page 9: line 15 to 24 and Page 10, Line 1 to 17: We have revised this accordingly in the abstract.

5) Reviewer comments: the conclusions are too broad-reaching for a case report.

Authors’ revision: Page 11, Line 1 to 16: The conclusion has been ameliorated.
6) Reviewer comments: how this case report is unique can be emphasized by noting other cases in literature and how this one was similar or different.

Authors’ revision: Page 6, Line 21 to 24: We have revised this accordingly in the abstract.

Martin Rohacek (Reviewer 2): Tochie present an interesting case of Viperidae envenomation with a fatal outcome. I have the following comments.

Background

1) Reviewer comments: Page 2 line 56 “Snake bites kill more people each year than either poliomyelitis or measles.” This sentence needs a reference.

Authors’ revision: we agree with you. This statement has been deleted.

2) Reviewer comments: Page 3 line 2: Scarce instead of scare? Line 7: Metalloproteinase instead of metalloprotein?

Authors’ revision: Page 3 Line 20: scare had been corrected to scarce. Page 7 Line 23 and page 8 line 11: Metalloproteinase had been corrected to metalloprotein.

Case

3) Reviewer comments: Page 3 line 13: shock in this case might be of anaphylactic, or septic origin, or both.

Authors’ revision: we revised the cause of shock to be mixed in the case presentation and discussion sections (anaphylactic and septic).

4) Reviewer comments: Page Line 34: Vertigo is a sensation of spinning dizziness that is related to a problem of the inner ear. Isn't it dizziness instead of vertigo?

Page 4: Glasgow come scale score instead of Glasgow coma score.
Authors’ revision: Page 4 Line 16; vertigo had been corrected to dizziness. Page 6 Line 6; Glasgow coma score had been corrected to Glasgow coma scale.

Discussion:

5) Reviewer comments: Page 5: Sepsis as a cause for shock, besides anaphylaxis, should be discussed here.

Authors’ revision: Page 8 line 13 to 8: the diagnosis of septic shock has been discussed

6) Reviewer comments: Page 6 line 13: Proliferative GN is not likely because it takes more time to develop, patient was oligo/anuric from the beginning.

Authors’ revision: Page 8 line 3: this has been deleted

Rajendra Raman (Reviewer 3): This is a very interesting case report. It highlights the fatal consequences of delayed presentation to healthcare facilities for a potentially treatable disease, as well as the disproportionate burden of snakebite suffered by disadvantaged socioeconomic groups. The report is well-written, and the case is highly relevant to the practice of emergency medicine.

I have two concerns related to the content of the case report, one minor and one major.

1) Reviewer comments: My minor concern relates to the use of the term "gas gangrene" in the Abstract (p2, lines 16/17). I note that in the remainder of the report the term "gangrene" is used, not "gas gangrene". The diagnosis of "gas gangrene" (also known as clostridial myonecrosis) would require at least a description of gas in the affected tissues, if not confirmation of the presence of known gas-forming organisms. In the absence of these findings, I would suggest using only the term "gangrene" in the Abstract.

Authors’ revision: Page 2 line 14: the term “gas” has been deleted
2) Reviewer comments: My major concern relates to the diagnosis of anaphylaxis. It is clear that this patient was profoundly shocked, as evidenced by hypotension, tachycardia, anuria and ultimately cardiac arrest. However, these findings could easily be explained by the combination of toxic, hypovolaemic and septic shock in the context of envenomation, gangrene and compartment syndrome, without invoking the diagnosis of anaphylaxis. The authors cite a case of snake-bite-induced anaphylaxis (reference [8], de Medeiros et al. 2008). However, that patient presented within minutes of the bite, reported respiratory symptoms (dyspnoea and cough) and pruritus, and showed a generalised urticarial rash on examination. The clinical suspicion of anaphylaxis was further strengthened in that case by demonstration of IgE against Bothrops venom in the patient's serum. I understand that IgE immunoassays may not be available at the authors' institution; however, I feel that at least some clinical features of anaphylaxis other than shock (e.g. rapid onset, respiratory involvement, urticaria) should be present in order to make this diagnosis. Did the authors note any signs of anaphylaxis other than shock? If not, I would suggest that they remove references to anaphylaxis from their report - I feel that even without anaphylaxis, they still have a very interesting case to present.

Authors’ revision: Many thanks for your comment. Although the patient did not immediately presented with signs of anaphylaxis (urticarial lesions, marked hypotension, tachycardia, tachpnoea, anuria. Her we incriminate the allergen to be the snake venom). However, we believe there was also a septic component in state of shock and this has be discussed in the discussion section page after the snake bite incident, we have clinical argument to support that there was an anaphylactic component in her state of shock.

3) Reviewer comments:

The remainder of my comments relate to terminology, spelling and references:

In the Title, replace "viperidae" with either "Viperidae" (capitalised) or "viperid".

P2 Line 9, replace "Echis occellatus viper" with "Echis ocellatus viper" (change to spelling of "ocellatus", italicise "Echis ocellatus", and un-italicise "viper")

P3 Line 7/8, replace "metalloproteins" with "metalloproteinases" for consistency with the rest of the report

P3 Line 11, replace "vipiridae" with either "Viperidae" or "viperid" (note spelling and capitalisation)

P3 Line 25/26, replace "Echis occellatus viper" with "Echis ocellatus viper" (change to spelling of "ocellatus", italicise "Echis ocellatus", and un-italicise "viper")

P3 Line 42/43, remove "fast" (this is already implied by the rate of 138)
P3 Line 46/47 "limp" should read "limb"

P4 Line 10 change "thrombopenia" to "thrombocytopaenia" for consistency

P4 Line 17/18 "haemodynamic unstable" should read "haemodynamically unstable"

P4 Line 19 "thrombocytopenia" should read "thrombocytopaenia" for consistency

P4 Line 21 "mmanagement" should read "management"

P4 Line 22/23 "polyvalent anti-venom serum, transfusion of three units" should read "polyvalent anti-venom serum and transfusion of three units"

P4 Line 35/36 "diaphoretic and diuresis 0,35ml/kg/h" should read "diaphoretic and had a diuresis of 0,35ml/kg/h"

P4 Line 39/40 "Glasgow coma score" should read "Glasgow Coma Scale" (note capitals)

P5 Line 2 "because its often" should read "because it is often"

P5 Lines 3-7 could be changed to: "In sub-Saharan Africa, recent estimates suggest that about one million bites by venomous snakes occur with 100,000 to 500,000 cases of envenomation and up to 30,000 deaths per year". (This clarifies that all three statistics refer to annual figures.)

P5 Lines 18/19 change "echymoses" to "ecchymoses"

P5 Lines 20/21, for consistency, change "hemorrhage" to "haemorrhage", "hematemesis" to "haematemesis", "malena" to "melaena" and "hematuria" to "haematuria"

P5 Line 22 change "species" to "families".

P5 Line 44/45. I am not sure of the relevance of reference [12] (Nagahiro et al. 2004). This paper is a retrospective review of intermittent pneumatic compression for preventing pulmonary embolism in post-operative patients. As far as I can see this paper does not discuss coagulopathy relevant to snake bite, does not mention DIC, and only mentions thrombocytopaenia in the context of heparin therapy. Was this reference included accidentally?

P5 Line 44/45 change "thrombopenia" to "thrombocytopaenia" for consistency

P5 Line 56/57 change "ischemic" to "ischaemic"

P5 Line 58/59 change "hemorragins" to "haemorrhagins"
P5 Line 60/61 change "anemia" to "anaemia"
P6 Line 3/4 change "delimma" to "dilemma"
P6 Line 21 change "poor prognostic factor" to "poor prognostic factors"
P6 Line 23 change "patients" to "patient"
P6 Line 40 change "re-enforce" to "reinforce"

Authors’ revision: We have revised all these comments accordingly in the abstract