Author’s response to reviews

**Title:** A rare case of confirmed Ceylon krait (Bungarus ceylonicus) envenoming in Sri Lanka resulting in neuromuscular paralysis

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**Author’s response to reviews:**

1. Reviewer #1: General comments:

Although the authors assert that "this case report adds knowledge to the limited literature available on Ceylon krait envenomation; a rare but potentially fatal clinical entity", it is disappointing that little/no comment is made on the possible management strategies. There is a lack of primary "take-away" lessons from this case report.

I HAVE INCLUDED A SECTION ON THE MANAGEMENT

Indian polyvalent anti-venom may not be effective for Ceylon krait envenoming in Sri Lanka, because it may not neutralize the Ceylon krait venom and pre-synaptic neurotoxicity may be irreversible. Provided the very limited data available in literature one might have to consider the theoretical possibility of anti-venom been able to clear circulating free venom and preventing progression of neuromuscular dysfunction. So management of a Ceylon Krait bite still remains an enigma. Therefore, the safety and benefits of anti-venom need to be weighed up along with the clinical status of the patient, before deciding on anti-venom therapy.

Cover page

- Please change "Registar" to "Registrar".

**CORRECTED**

Abstract

- Please change "frequently habitats near" to "frequents habitats near".

- Please change "26 year old" to "26-year-old".
- Please change "anti venom" to "anti-venom".

- Please change "on clinical manifestations following envenoming is lacking" to "on the clinical manifestations following envenomation is lacking".

CORRECTED

Introduction

- Please change "manly distributed it the" to "mainly distributed in the".

- Please change "frequently habitats near" to "frequents habitats near".

CORRECTED

Case presentation

- Please change "Twenty six year old" to "A 26-year-old".

- Please change "presented to Toxicology Unit of Teaching Hospital" to "presented to the Toxicology Unit of Teaching Hospital".

CORRECTED

- What was his respiratory rate?

- Was Partial Thromboplastin Time (PTT) prolonged?

- Did the patient undergo Tensilon (edrophonium) testing or a neostigmine trial to determine if anticholinesterase therapy may be beneficial?

- What was the supportive care plan for the patient? What was the fluid regimen (if any)?

INFORMATION INCLUDED IN THE CORRECTED VERSION OF THE MANUSCRIPT

Discussion

- It is important to mention that the decision to administer anti-venom may not be a straightforward one and must balance the potential benefit with the risk of adverse reactions.

DISCUSSED
- Please correct the typo in "She he had bilateral ptosis".
- Please change "Anti venom" to "anti-venom".

CORRECTED

Therefore, the imported venom is unlikely to be effective for native Sri Lankan species." It is hard to say that the anti-venom administered did not contribute to the survival and full recovery of the patient. Particularly for snakes with presynaptic neurotoxins (and also for some species with only postsynaptic neurotoxins), it is important to commence anti-venom early, as soon as first signs (e.g. ptosis or ophthalmoplegia) become apparent (citation: Warrell DA. Treatment of snakebite in the Asia-Pacific Region: a personal view. Snakes of Medical Importance (Asia-Pacific Region). 1990:641-70.)

- Please share some relevant clinical insights or primary "take-away" lessons of this case report.

I AGREE WITH YOUR COMMENTS AND I DID NECESSARY MODIFICATION IN THE DISCUSSION ADDRESSING THE ABOVE FACTS AND COMMENTS

Conclusion

- Please change "Ceylon krait is an endemic elapid in Sri Lanka which frequently habitats" to "Ceylon krait is an endemic elapid in Sri Lanka that frequents habitats".

CORRECTED

Terminology

Both terms, 'envenoming' (UK English) and ';envenomation' (US English) have been used throughout the text. Pease use either 'envenoming' or 'envenomation' and not both the terms.

I CORRECTED. TERM ENVENOMING IS USED THROUGHOUT THE TEXT

The term 'deadly venomous' is erroneous and misleading. This is because death is a summative effect of all toxic effects of a snake bite plus many other factors such as the general health of the victim, bite to antivenom delay, efficacy and the effectiveness of antivenom ect. (Please read the article: Silva et. al. Dangerous snakes, deadly snakes and medically important snakes. The journal of venomous animals and toxins including tropical diseases 2013; 19 (1): 26 . Please use 'venomous' instead of 'deadly venomous'.

CORRECTED
Abstract: The statement "It frequently habitats near human dwellings" is not accurate. The species is not common. It inhabits shaded home gardens and forests in the wet-zone of Sri Lanka. Please correct accordingly.

CORRECTED

Case presentation: It would be great to have a photograph of the snake specimen involved in the bite, if available, as a figure.

No photograph is available of the snake specimen involved in the bite as the snake was not brought to the hospital.

Single fiber electromyography: Please state the time at which this was performed (or time from bite), and the muscle (orbicularis oculi?). It appears that the 'mean jitter' is probably less accurate to present as most probably the jitter values of the individual fibers are unlikely to have a normal distribution. Therefore please state the Median jitter, jitter range and the Inter Quartile Range of the jitter. Also, please state the number of individual fibers sampled. Alternatively, the authors can include a scatter plot comparing the jitter values of the sampled fibers on the first recording (while neurotoxicity is still there) and the recording after two weeks. What is the reference upper normal limit of the jitter you have used? Please state.

AVAILABLE INFORMATION FROM THE SFEMG AND RNS INCLUDED

Figure 1: please use a better quality scan of the RNS trace

BETTER IMAGE ATTACHED

Please include any photos of the patient with neurological signs

PATIENT'S FACE PHOTOS AVAILABLE WITH PARTIAL PTOSIS AND OHTHALMOPLEAGIA. BUT DUE TO PATIENT'S PRIVACY CONCERNS AND JOURNAL'S POLICY FACE PHOTOS NOT INCLUDED

5th paragraph of the case presentation: "(which the only available antivenom available at the moment in Sri Lanka)" should be corrected as "(which is the only available antivenom at the moment in Sri Lanka)"

CORRECTED

Discussion: Last paragraph - The authors have raised the point that the Indian polyvalent antivenom is ineffective and probably not efficacious for Ceylon krait envenoming (because the Indian antivenom was not raised against Ceylon krait). Whilst this may be true, the authors have raised the above argument based on the fact that the patient's neurotoxicity progressed despite early antivenom treatment. Rather than a problem with the antivenom, such effect is most likely be due to the pre-synaptic neurotoxins in the Ceylon krait venom which start damaging the motor nerve terminal irreversibly before the antivenom was given. Once the neurotoxins start the
damage to motor nerve terminal, the process is irreversible and heals with the natural recovery of the motor nerve terminal by 3 to 5 days, as experimentally shown with the beta bungarotoxin (major pre synaptic neurotoxin of the many-banded krait). This means that even if the antivenom is fully efficacious (i.e. the antivenom has enough anti-Ceylon krait antibodies to neutralize the neurotoxins), still there wouldn't be a clinical effectiveness (no measurable clinical improvement). Exactly similar observation was made previously where the Indian krait bites resulted similar response to Indian Polyvalent antivenom, despite the circulating venom antigens were fully neutralized by antivenom promptly. It would be worthwhile discussing the above in the discussion.

ADDITIONAL INFORMATION ADDED AND THE ABOVE FACTS ARE DISCUSSED

References

Reference 6: Please format the first author's name accurately (Surname first, then the initials).

CORRECTED

The manuscript reviewed by someone who is fluent in English