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Mini Review

Review Myonecrosis due to Snake Poisoning: Mechanism and Clinical Significance

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Received: October 26, 2022; **Published:** November 04, 2022

Abstract

Tissue damage is a common symptom of snakebite especially in Viperidae and Crotalidae snakes. In the early stage of tissue damage, swelling is common. At a more advanced stage of snakebite damage more tissues are destroyed. Most snake venom studies have concentrated in neurotoxins. In this review article the mechanism of myonecrosis due to snake venom and its component myotoxin *a* are described and its significance to clinical manifestation are discussed.

Keywords: *Snake Venom; Snakebite; Muscle Damage*

Clinical symptoms

Swelling

Swelling of the tissue near the bite site is the first symptom due to snakebite of a pit viper (Viperidae and Crotalidae). Recently many components of snake venoms have been isolated and their chemical structures have been identified. Chemical structure and its effect have also been studied by many investigators. The snakebite clinical manifestation is the combined effects of all components present in the venom. Therefore, it is important to understand how these components manifest in a clinical effect.

In the review article, there are many examples of swelling at an early stage of snakebite and two illustrated examples. Figure 1A and 1B show examples of swelling in a human and a dog. In figure 1A a Japanese man living on Amami Island cut his own leg in order to save his life (Figure 1A). Swelling is not restricted to humans but also happens in animals. Figure 1B shows the early bite effect in the US Army's patrol dog (Figure 1B). Eventually tissue is damaged at a more late stage of necrosis (Figure 2); in this photo a man lost a finger due to myonecrosis. Another common damage is bleeding due to the destruction of blood vessels. In this review article only myonecrosis is discussed. Destruction of blood vessels is another big topic that needs to be described by a separate article.

In earlier days I visited an Indian physician who told me that there was a hemorrhage in the eye. After many years later I studied the effect of various snake venoms on eyes and found that his statement was correct. This is logical because blood carries the injected venom to circulate to many parts of the body.

Apparently, the eye is one weak spot against venom. Normally there is bleeding at the site of snakebite. So far the doctor's recommendation is to stop bleeding. Due to our recent findings it is better to let it bleed for a while instead of stop bleeding immediately so that venom will not be circulated to other parts of the body [1].

Figure 1A ***Figure 1B***

Figure 2

Mechanism of myonecrosis

Before looking for muscle damage, normal muscle structure viewed by electron microscope (Figure 3A) showing repeating fibers. Initial observation of the muscle damage is swelling sarcoplastinum (Figure 3B) subsequently the loss of regular muscle fiber (Figure 3C). Eventually the muscle fiber completely collapsed (Figure 3D).

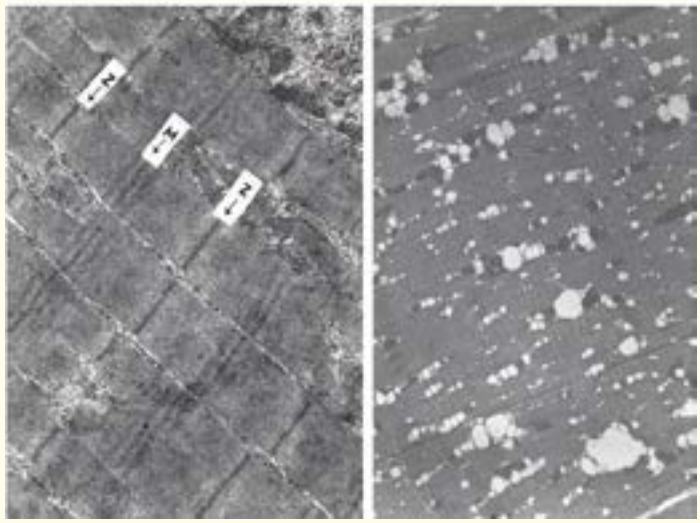

Figure 3A ***Figure 3B***

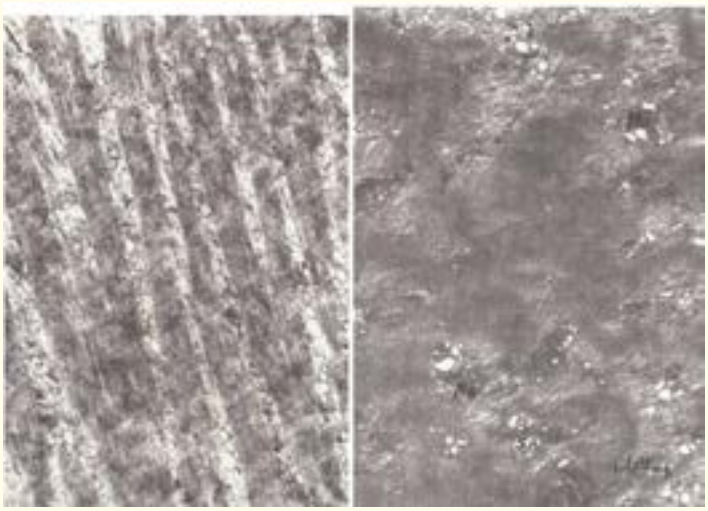

Figure 3C ***Figure 3D***

We found that there are at least two tissue damaging components in pit viper venom. One is viriditoxin that is a high molecular weight tissue damaging component [2,3]. The other is myotoxin *a*, which is a low molecular weight component. We made extensive study on myotoxin *a* so we will discuss mainly on myotoxin *a* in this review article.

Action of myotoxin *a*

There are several components in a given snake venom that are responsible for myonecrosis. In my laboratory only one component myotoxin *a* was extensively studied and the result is summarized in this review article. I hope the future scientists who want to pursue the mechanism of snakebite continue to study venom component study. I am 92 years old and am no longer working on actual snake venom research except an occasional review article.

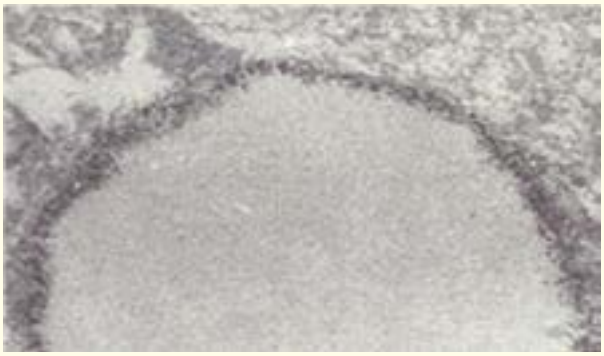

Figure 4: *Binding of myotoxin a to SR (sarcoplasmic reticulum).*

Further study showed that myotoxin *a* binds to Ca-ATPase [4,5].

Myotoxin a was cleaved to two fragments N-terminal fragment and C-terminal part. Only the N-terminal peptide had myotoxic activity (Figure 5).

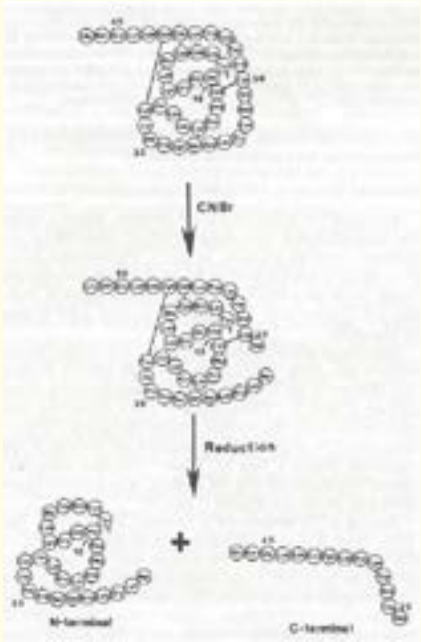

Figure 5: *Fragments of myotoxin a showing only the N-terminal Peptide showed myotoxic activity.*

Nucleotide sequence encoded myotoxin a was identified as shown in figure 6 [6,7].

Figure 6: *Nucleotide study showed only some portion of RNA was Actually translated into myotoxin a.*

Conclusion

Snake venom is a mixture of many compounds. Therefore, it shows complex toxicological symptoms. One of the pronounced pathological effect is damage of the muscle. On this review article, clinical symptom was briefly described. In order to find the mechanism of myonecrosis, morphological change of the muscle was examined under electron microscopy. For further study one of the components, myotoxin *a* was isolated and its structure-function was studied. Nucleotide sequence for the toxin was further studied and its RNA expressed for myotoxin *a* was shown.

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Volume 10 Issue 12 December 2022