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Volume 2 • Issue 2 • 2018

Scientia Ricerca

Mini Review

Multidisciplinary Advances in Veterinary Science

ISSN: 2573-3435

Systemic Rhabdomyolysis Secondary to Human Accidents by Stingrays. Perspectives for Early Recognition and New Emergency Clinical Approach: A Mini Review

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Received: May 15, 2018; **Published:** May 21, 2018

Abstract

Despite of high morbidity and growing incidence, stingray accidents are still commonly neglected. The excruciating pain inducing power results from the synergy of direct traumatic actions and inflammatory immune response, combined with the tissue toxicity of venom, particularly my necrosis. The painful stinging power of the stingrays was known and used by the Mayan people for rituals of blood and self-sacrifice. Pain is typically disproportionate to the size of the lesion. We want to call attention to a new phenomenon that can occur when the injury reaches a muscular area, even if minimal: the systemic rhabdomyolysis described in a human case in 2012 in a clinical case in which a fisherman was stung by a marine stingray, thought to be from the Dasyatis family and then reproduced in a laboratory in 2014. We suggest criteria for early recognition based on clinical and laboratory evidences, besides therapeutic measures to prevent the most feared complication that constitutes acute renal injury. Our main goal is to raise awareness for this new clinical issue.

Keywords: *Stingray accidents; Systemic rhabdomyolysis; Acute kidney injury; Preventive measures*

Volume 2 Issue 2 May 2018

Critical Discussion

Stingrays are cartilaginous skeletal aquatic animals (Chondrichthynes) similar to sharks and classified in the suborder of Elasmobranchs. They inhabit both hydrographic basins and temperate - freshwaters - and tropical oceans all over the planet. They have the trapeze-shaped body and are considered by some authors as "prehistoric super-fishes", surviving to the dinosaurs and dated by fossil findings, more than 150 million years ago in the Jurassic Period. Stingrays are demersal fish, because they live at the bottom of the seas and rivers and are characterized by having serrated stingers and venom pouch (many species) at the base of its dangerous whiptail. In this way, they draw traumatic risks to humans.

Citation: Antonio Augusto Masson*., et al.* "Systemic Rhabdomyolysis Secondary to Human Accidents by Stingrays. Perspectives for Early Recognition and New Emergency Clinical Approach: A Mini Review". *Multidisciplinary Advances in Veterinary Science* 2.2 (2018): 338-340.

They impose an increasing global risk to human health - sometimes sudden death when they reach vital organs from who venture into their habitat, such as bathers, divers, fishermen and surfers. However, other group's professional may also eventually become victims, such as sailors, aquarists, and veterinarians getting in touch with these animals, although not naturally aggressive, they usually react violently in self-defense when inadvertently stepped on (the most common scenario, given their habit of staying in the sandy bottom) or disturbed.

The excruciating pain inducing power resulting from the synergy of direct traumatic actions and inflammatory immune response, combined with the tissue toxicity of venom, particularly my necrosis. The painful stinging power of the stingrays was known and used by the Mayan people for rituals of blood and self-sacrifice. [1] Pain is typically disproportionate to the size of the lesion.

Despite of high morbidity and growing incidence, sting accidents are commonly neglected in Brazil - the country with the largest river network in the world. Many accidents are underreported because they occur generally in isolated locations and do not have high lethality, besides, the victims are usually "medicated by laymen with natural products". [2]

In contrast, these attacks can reach 2000 cases/year in the USA. The objective of this work is to discuss the phenomenon of systemic rhabdomyolysis (SR) with a serum peak of the creatine-phosphokinase muscle enzyme (CPK) not recorded in the medical literature until recently, as a result of a lesion accidentally inflicted by the stingray sting of the Dasyatis family on muscle mass of a fisherman's forearm, as an unique case reported by our group [3]

The theoretical possibility of even when the victim is reached in small muscle areas - feet, forearms - has drawn attention owing to increased risk of severe systemic inflammatory complications or my necrosis at a distance, leading acute kidney injury (AKI) by tubular deposition of myoglobin. It was demonstrated in experimental conditions that the venom extracts of two types of river stingrays caused coagulative necrosis of the gastrocnemius muscle of rats at the direct injection site, as well as in the contra lateral muscle that had been spared, characterizing the systemic effect at distance, similar to that observed in the case of the human patient.

Although findings in a single clinical case do not usually have the force of evidence, we are convinced that, in this particular case, SR resulting from an injury caused by stingray was reproduced "*in vitro*" unequivocally, confirming the pathophysiological phenomenon of SR reported in a real case, secondary to a small muscle area injury, justifying, until the level of our knowledge therefore, the concern and the need for adjustments in the therapeutic protocol in future similar events.

The same group emphasized importance of the SR phenomena: "One of the few reports of the toxic activity of stingray venom in human published by Masson., *et al*. (2012). My toxic activity was evidenced by increase in serum total CK and CK-MB (heart muscle activity in an individual injured in the arm by a marine stingray probably of Dasyatis family. The authors also showed an increase in C-reactive protein, suggesting a systemic inflammatory response" [5].

Recently it was published 3 human cases of stinging accidents with confirmed SR based on high muscle enzyme levels and evolutionary pattern of thrombocytopenia, presenting with heart disturbances and renal dysfunction [6].

Considering all evidence discussed so far, we propose a more in-depth debate on the subject due to the possibility of SR progressing to acute kidney injury (AKI). Moreover, we suggest prompt nephroprotection measures, such as generous venous hydration, urine alkalization, monitoring of flow and renal function within, at least, within the first 48-72 hours after an accident with a stingray spine, measures beyond those already established as analgesics, debridement and immersion of the injured site in hot water (43-46°C), for 30 to 90 minutes for pain relief (thermo labile venom). Early diagnosis can be made more safely when there is at least 1 clinical and 2 laboratory evidences, as shown in Table 1.

Clinical and laboratorial evidence	Reference
1) Trauma to human muscular tissue (even minor)	Masson., *et al*. 2012
2) C-Reactive Protein, CK (10.000 Units or more), CK MB peak serum levels	Masson., *et al*. 2012
3) Histological alterations of distal muscle biopsy (contralateral, if possible)	
with inflammatory infiltrate pattern and also my necrosis	Lameiras., *et al*. 2014
4) Platelet count decrease; CK and CK MB peak serum levels	Liang., *et al*. 2018
5) Cardiac impairment	Liang., *et al*. 2018

Table 1: *Chronology of early clinical and laboratory evidence of Systemic Rhabdomyolysis (SR) due to stingray accidents my toxicity and respective references.*

Finally, we reinforce the need of updating current treatment protocols for muscle stingray injury, even in small extension, emphasizing on early therapeutic measures of nephroprotection order to minimize the risk the most feared SR complication: AKI and its high morbimortality, particularly in small medical facilities in the most distant and few resources regions.

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