

ENVENOMATION BY *Micrurus* CORAL SNAKES IN THE BRAZILIAN AMAZON REGION: REPORT OF TWO CASES

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SUMMARY

Two cases of proven coral snake bites were reported in Belém, Pará State, Brazil. The first case was a severe one caused by *Micrurus surinamensis*. The patient required mechanical ventilation due to acute respiratory failure. The second case showed just mild signs of envenomation caused by *Micrurus filiformis*. Both patients received specific *Micrurus* antivenom and were discharged without further complications. Coral snake bites are scarcely reported in the Amazon region and there is a broad spectrum of clinical manifestations, varying from extremely mild to those which may rapidly lead to death if the patient is not treated as soon as possible.

KEYWORDS: Envenomation; Coral snakes; *Micrurus surinamensis*; *M. filiformis*; Brazilian Amazon.

INTRODUCTION

Coral snakes are the main representatives of the Elapidae in the Americas, the genus *Micrurus* being the most important in terms of public health^{4,6}. Due to their large geographical distribution, coral snakes may be found in diverse environments^{6,13}. In Brazil, several species of *Micrurus* are found throughout the whole country and a great number of them live in the lowland rainforest or tropical jungle⁶. The Amazon region harbors the largest number of species of coral snakes, such as *Micrurus spixii* and *M. lemniscatus*, and the only species closely associated with water environments, the aquatic coral snake, *M. surinamensis*^{6,22}. These species live sympatrically in the Amazon basin³¹. Coral snakes are largely fossorial and seldom seen, even in very dense areas.

In contrast to viperids, the fangs of coral snakes are short, hollow structures that are permanently fixed in position on the anterior maxillary bones, which is a feature of proteroglyphous dentition. The short and small-sized fangs usually represent low risk to individuals wearing footwear and clothing. Most coral snake bites in human beings occur on the hands and usually involve a snake that was intentionally picked up and handled. This may explain the low number of *Micrurus* snake bites recorded. In 2007, of 22,763 snake bites reported in Brazil, 136 were attributed to the genus *Micrurus* and were without fatalities⁵. Most cases were reported in the Southern region, where *M. corallinus* is predominant, 11 occurred in Pará State.

Studies on *Micrurus* specific toxins are limited due to the fact that these animals are difficult to capture and keep in captivity, and are

known to produce only a small amount of venom. The genus *Micrurus* possesses a potent neurotoxic venom, which causes postsynaptic blockage of neuromuscular transmission by binding competitively to the acetylcholine receptors³⁸. The venom of *M. corallinus* also has a neurotoxin with presynaptic activity. These neurotoxins mainly cause cranial nerve paralysis in envenomed individuals, leading to so-called myasthenic or neurotoxic facies.

The first sign of peripheral nervous system involvement is usually ptosis, often followed by ophthalmoplegia, dysarthria and dysphagia. The descendent progression of envenoming may lead to dyspnea. Death can be a consequence of muscle paralysis and respiratory arrest. Specific antivenom is produced by the immunization of horses with *M. corallinus* and *M. frontalis* venoms. For other species, including the *Micrurus* species of the Amazon region, studies on their mechanisms of action and the neutralizing effects of antivenoms are rarely available². Clinical descriptions of patients bitten by *Micrurus* are still much needed and therefore we describe two cases in which the severity of envenomation varied considerably.

CASE REPORTS

Case 1: An 18 year-old male, Biology student, was reportedly walking on a university campus belonging to the University of Rural Amazon, Belém, Pará State, when he found an 80-cm coral snake (Fig. 1). In an attempt to capture the animal, he was bitten on the left thumb. Immediately, the patient pulled the snake off so the animal did not hold on to the site of the bite. Only one fang mark was visible. He did not

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Fig. 1 - *Micrurus surinamensis*, specimen responsible for severe envenoming (Case 1).

complain of having any pain but he mentioned paresthesia at the bite site that went up along the whole limb a few minutes after the accident. He had been sent to the reference hospital, João de Barros Barreto University Hospital, where he arrived within 20 minutes after the bite took place, bringing with him a *M. surinamensis* coral snake. Upon arrival, he complained of blurred vision and difficulty in speaking, walking and opening his eyelids. On examination, he was in respiratory distress (40 bpm), foaming at the nose and mouth, conscious but unable to speak. He was not cyanosed or in shock. The pulse rate and blood pressure were normal (100/80 mmHg). He was intubated and transferred to the Intensive Care Unit (ICU) where he was immediately put on a ventilator, followed by IV administration of neostigmine methylsulfate (0.5mL = 5 mg), preceded by atropine sulfate (1mL = 0.25 mg), and 100 mL of *Micrurus*



Fig. 2 - *Micrurus filiformis*, specimen responsible for mild envenoming (Case 2).

antivenom, produced by the Butantan Institute (São Paulo) in ampoules of 10 mL containing: F(ab')₂ horse antibodies, 1 mL neutralizing at least 10 mg of *M. frontalis* reference-venom in mice. In the ICU the patient was found to be unconscious. The chest was clear and heart sounds were normal. Initial laboratory studies were normal (Table 1). Approximately 12 hrs after the development of neurological symptoms, the patient was alert and following commands with a normal physical examination. Neostigmine administration did not apparently reverse any neurological manifestation. The patient could be weaned from artificial ventilation 48 hours after antivenom infusion. No further medication was required and the patient was discharged in a good condition on day 3.

Case 2: A 19 year-old male was handling a colored snake which

Table 1
Laboratorial data from a patient bitten by *Micrurus surinamensis* (Case 1)

Test	Date		
	11/April/2006 (before AV therapy*)	12/April/2006 (24hrs after AV therapy)	13/April/2006 (without artificial ventilation)
Arterial blood gas analysis			
pH	7.36	7.51	7.41
pCO ₂ (mmHg)	32	26	40
pO ₂ (mmHg)	379	198	283
HCO ₃ (mEq/L)	18	21	25
Total CO ₂ (mmol/L)	19	--	26
BE (mmol/L)	-6		+1
Std. BE	-6	-1	+1
Std. BC	20	--	25
Sat. O ₂ (%)	100	100	100
FiO ₂ (%)	40	50	50
Hemoglobin (g/dL)	13.2	--	--
Total leukocytes (count/mm ³)	18,500	--	--
Platelets (count/mm ³)	230,000	--	--

*Patient was already on artificial ventilation.

had been captured the day before in the village of Boa Vista in the Acará municipality, Pará State. He reported that he had been bitten on a left-hand finger and complained of mild pain. He stated that approximately one hour after the accident he noticed a mild swelling on the bitten limb and complained of epigastric pain. He mentioned two episodes of vomiting. Upon physical examination everything seemed normal apart from a small puncture wound on the fourth finger of the left hand with very mild edema. He had no blurred vision, ptosis or other symptom of neurotoxicity. He was given 100 mL of *Micrurus* antivenom and fully recovered while in the hospital. He was discharged 24 hours after the antivenom therapy with only mild edema on the hand, and remained asymptomatic. The snake was identified as a 50-cm specimen of *Micrurus filiformis* (Fig. 2) by the Herpetology Laboratory of the Emílio Goeldi Museum, Belém, Pará State.

DISCUSSION

Two cases of human *Micrurus* envenoming are here presented, one caused by *M. surinamensis* and the other by *M. filiformis*, which show the potential for severe envenoming and the variability of the clinical manifestations. In Brazil, *Micrurus* envenoming is relatively rare and most cases are due to *M. corallinus*, *M. lemniscatus* and *M. frontalis*^{6,9,20,32,39}.

Although broadly distributed across the whole country, the number of *Micrurus* accidents is negligible, when compared to cases involving *Bothrops* and *Crotalus* snakes⁴. The rarity of human accidents is attributed to the type of dentition and envenoming which would result from a bite on a small part of the body, such as fingers, which enables the snake to hold on and to inoculate its venom into tissues by means of a chewing motion²⁵. Contrary to this common view, Case 1 illustrates the capability of the coral snake in delivering a potentially severe bite without having to “chew” on the victim for a long period of time. Thus, envenoming should be diagnosed by the presence of the signs and symptoms of neurotoxicity. Fang marks may or may not be evident and when they are present, they are usually slight and may be seen as scratch marks. Even the absence of visible fang marks does not preclude the possibility of a bite with venom inoculation²⁵.

Micrurus venoms are known to possess neurotoxic properties³⁷. In most symptomatic cases neuromuscular paralysis is the most prominent and is caused by postsynaptic motor end-plate blockage of acetylcholine receptors, which produces similar effects to those seen in myasthenia gravis¹⁸ and curare poisoning²⁴. This prevents nerves from stimulating muscle contraction and leads to paralysis. Similar actions are described for other Elapidae venoms, such as *Naja* and *Bungarus* spp^{14,19}.

The two cases reported here presented different clinical aspects. The first progressed rapidly to respiratory distress while the other showed only mild edema without any neurological manifestations up to 24 hrs after bite. This broad spectrum of clinical manifestations in snake bites is generally known to occur. Cases of patients bitten by elapid snakes that did not receive antivenom and did not present neurological manifestations have been reported and characterized as asymptomatic or dry-bites⁶. It is important to point out that there are few studies available to understand the exact mechanism of action of *Micrurus* venoms, and some variation in their composition may be present among different species. Most experimental studies involve *M. frontalis* and *M. corallinus*

venoms, since these two species are the most frequent cause of *Micrurus* envenoming in Brazil³³. *M. surinamensis* venom is known to contain postsynaptic toxins³³. One experimental study with *Micrurus* venoms from the Amazon, including *M. spixii*, *M. averyi*, *M. lemniscatus* and *M. surinamensis*, showed no coagulant activity but edematogenic effects, except for *M. surinamensis*². Another study evaluated the biological and enzymatic activities of *M. surinamensis* venom but not those of *M. filiformis*⁸.

Antivenom administration is recommended as the most efficacious treatment for envenoming by coral snakes^{6,17}. Specific *Micrurus* antivenoms, produced in Brazil by the Butantan Institute (São Paulo) and the Ezequiel Dias Foundation (Minas Gerais), are produced in horses immunized with the venoms of *M. corallinus* and *M. frontalis*²⁹. However, some studies suggest that the neutralizing capacity of antivenoms may be improved by including venom from other *Micrurus* species in the venom pool used in the immunization protocol^{1,10,15,36}.

The assumption that commercial antivenoms may be used in the treatment of bites by any Brazilian *Micrurus* species, even for other South American coral snakes contrasts with the scarcity of clinical studies on envenoming by *Micrurus* coral snakes, which are limited to case reports^{3,6,21,27,40}. Unusual symptoms of envenoming by *M. lemniscatus* have been described²¹ in which the patient had severe pain in the bitten limb, despite repeated doses of potent analgesics, and no response to anti-cholinesterase or specific antivenoms was observed, either. In contrast, our patients had no intense local pain, but the Case 2 patient presented mild local swelling and pain, which is in accordance to experimental reports that have shown that some *Micrurus* venoms may induce myotoxicity and local lesions².

Reports on *Elapidae* snake bites in Australia have suggested that pressure immobilization bandaging of the affected limb could impede the egress of toxins from the site of the bite and delay the onset of life-threatening systemic involvement^{23,35}. On the other hand, experimental studies have suggested that attaining the recommended pressure levels is technically very difficult and the effective use of this method might require extensive training and experience²⁶. Because of this and time wastage concerns, in Brazil emphasis is given to improving antivenom supply and distribution, and instructions are that all victims should be transported to the nearest medical treatment facility as soon as possible.

Neurologic signs and symptoms of envenoming can be apparent in minutes, or be delayed for as long as 12 hours. In Case 1, the rapid onset of clinical manifestations indicates the severity of envenoming and the necessity of prompt intervention, not only with antivenom, but also with intensive care supportive measures. Moreover, improved methods of reversing the effects of neurotoxicity are needed. Even when administered early, antivenoms did not promptly reverse paralysis. Improvement in neurological signs was not seen until 24 hours after antivenom administration. Ancillary treatment has been recommended with anti-cholinesterase drugs; Edrophonium Chloride could benefit those patients bitten by a coral snake with postsynaptic neurotoxic venom⁴¹, and neostigmine had demonstrated the potential to reverse neuromuscular paralysis^{9,39}. Even when used in several occasions in clinical practice, no standard protocol has been followed. Our patient, for instance, had received a half dose of that used in other studies⁵. The failure of neostigmine in reversing neurotoxicity in Case 1 may be partially attributed to an insufficient dose.

On the other hand, the very mild symptoms observed in Case 2 suggest that coral snake bites are not necessarily always severe. There is no generally accepted clinical classification for severity of accidents, and an empirical dose of 10 ampoules of antivenom is usually given, regardless of severity. A review of the classification of severity is thus needed to adjust the amount of antivenom to the real necessity in case of mild, moderate or severe envenoming, as exists for *Bothrops* and *Crotalus* envenoming.

Coral snakes are widely distributed in almost all major ecological regions of the New World, and a great number live in the lowland rain forest, particularly in the Amazon region of Brazil²². This area harbors the largest number of species of coral snakes, such as *Micrurus spixii* and *M. lemniscatus*, as well as the only species closely associated with water environments, the aquatic coral snake, *M. surinamensis*³⁰. From all the *Micrurus* spp. that are found in Brazilian Amazon, *M. surinamensis* is one of the largest in girth and length, reaching up to 1,350 mm⁶. It inhabits humid tropical forests and secondary forests, near water flows of the Amazonas and Orinoco Rivers, in the Northern and Central parts of South America^{11,12,14,30}. A proteomic analysis of the venom of the fish-eating *M. surinamensis* provides an overview of its protein composition, the specific pharmacological features of which differ from other *Micrurus* species²⁸. *Micrurus filiformis* is also broadly distributed in the Amazon basin and may be found in secondary forests, low altitude mountains, open fields, and humid forests^{7,16,30}.

In general, coral snakes are not abundant in nature, thus the scarcity of specimens is one reason why they are not well known, and their elusive habits are a key for their success in at least partially avoiding decimation by humans. But, as colorful and distinctive snakes, they sometimes appeal to humans to be handled and observed. With the increasing spread of the habit of keeping snakes as pets, it is important to identify elapids and distinguish them from false coral snakes, and also to spread information about first aid and treatment.

CONFLICT OF INTEREST

The authors of this study are not part of any association nor do they have commercial relationships that might represent conflicts of interest in the writing of this study

RESUMO

Envenenamento por coral do gênero *Micrurus* na Amazônia brasileira: relato de dois casos

Dois acidentes por coral verdadeira são descritos em Belém, Pará. O primeiro caso foi decorrente de envenenamento por *Micrurus surinamensis*, no qual a vítima necessitou ventilação mecânica por insuficiência respiratória. O segundo, causado por *Micrurus filiformis*, apresentou apenas manifestações leves. Ambos os pacientes receberam soro antielapídico específico e evoluíram sem complicações. Acidentes por coral verdadeira na região Amazônica são raramente descritos e podem cursar com um largo espectro de alterações, que variam desde quadros de envenenamento muito leves até manifestações com risco de óbito.

ACKNOWLEDGMENTS

The authors would like to thank all the health professionals of Hospital Universitário João de Barros Barreto, who contributed to the quality of patients' medical assistance. The authors are also grateful to Dr. Regina Dórea, for kindly reviewing the article.

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Received: 26 November 2007

Accepted: 8 October 2010