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Review

Snakebite by *Micrurus averyi* (Schmidt, 1939) in the Brazilian Amazon basin: Case report

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ABSTRACT

Micrurus snakes, commonly known as coral snakes, are responsible for 0.4% of the snakebites envenomings in Brazil. In this report, we describe a case of envenoming by *Micrurus averyi*, the black-headed coral snake, recorded in the western Brazilian Amazon. To the best of our knowledge, this is the first published case perpetrated by this species. The major complaint of the patient was an intense local pain and paresthesia. Examination of the bite site revealed edema extending from the left foot up the left leg that was accompanied by erythema involving the foot and distal third of the leg. Systemic signs at admission included nausea and drooling. The patient was treated with 100 mL of coral snake antivenom and intravenous analgesics (dipyrone) and was discharged 48 h post-admission with no complaints. The patient showed more intense local edema than that generally described in several other cases of *Micrurus* bites in Brazil.

Contents

1. Introduction

In Americas, the average annual incidence of snakebite is ~57,500/year (6.2 per 100,000 population) and mortality is close to 370 deaths (0.04 per 100,000 population) (Chippaux, 2017). The annual frequency of venomous snakebites reported by the Brazilian Ministry of Health since 2005 is ~22,000–23,000 cases/year (~11 per 100,000 inhabitants), i.e., a stable frequency. The data from 2001 to 2004 probably reflect under notification and not a trend towards an increase in the number of cases from 2005 to the present day. Snakebites incidence is higher in the Brazilian Amazon states, representing an occupational health problem for rural and riverine populations, with a rate of 55.4 cases/100,000 inhabitants

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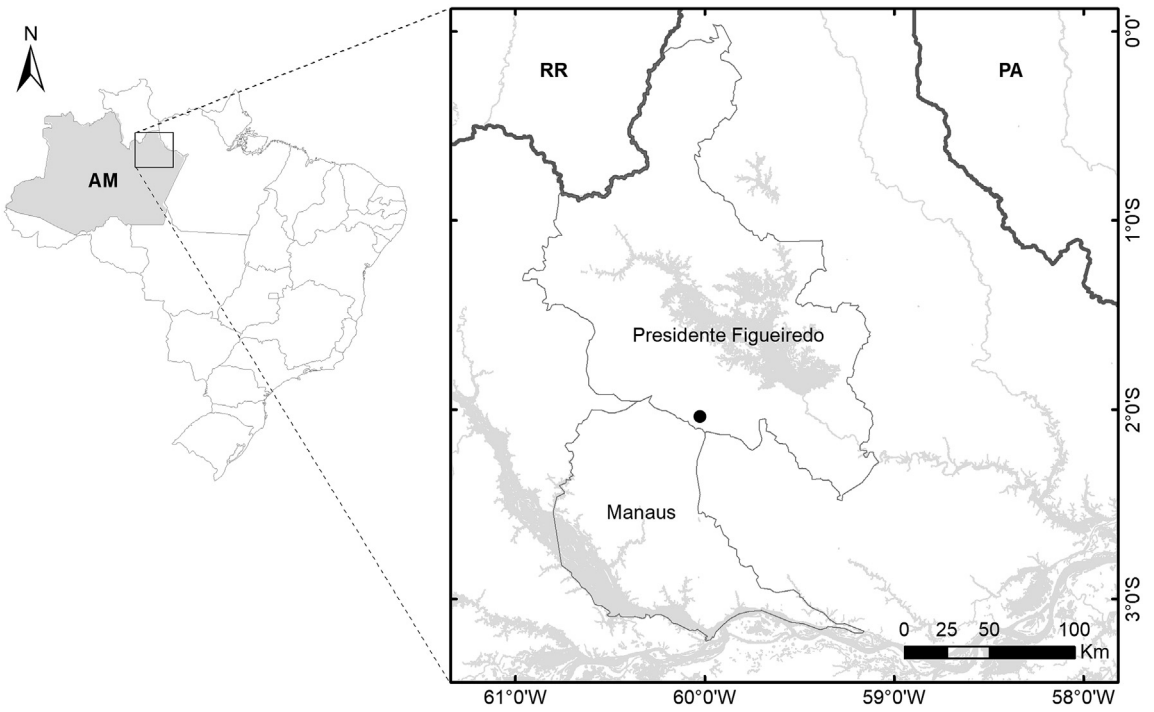

Fig. 1. The municipality of Presidente Figueiredo, in the state of Amazonas (Brazil), where the bite by *M. averyi* occurred (indicated by the black dot). (Map prepared by Erlane Cunha).

in 2015 (Brasil. Ministério da Saúde, 2016). *Micrurus* spp. snakes, commonly known as coral snakes, the Elapidae representatives of the New World, are responsible by 0.4% of the snake envenomings in Brazil (Brasil. Fundação Nacional de Saúde, 2001), the same proportion recorded in the Brazilian Amazon (Feitosa et al., 2015).

Most coral snake bites reported in Brazil was caused by *M. corallinus* and *M. frontalis*, with several patients showing signs of acute myasthenia (Bucaretchi et al., 2016). There are few clinical reports of envenoming by *Micrurus* spp. in the Brazilian Amazon, although bites by *M. filiformis*, *M. hemprichii* and *M. surinamensis* have been reported (Pardal et al., 2010; Wen et al., 2015). Neuromuscular blockade is the hallmark of systemic envenomation by *Micrurus* spp. *and* can progress to acute respiratory failure, the cause of death in this type of snakebite (Bucaretchi et al., 2016). Although rare, deaths can occur where respiratory support (mechanical ventilation) is unavailable, such as in remote locations in the Amazon region (Wen et al., 2015).

In this report, we describe a case of envenoming by *Micrurus averyi* (Schmidt, 1939), the black-headed coral snake in the municipality of Presidente Figueiredo, in the Brazilian state of Amazonas in the western Brazilian Amazon.

2. Case report

2.1. Clinical description

In July 2017, a previously healthy 7-year-old girl was admitted to the emergency service in Presidente Figueiredo, a municipality located 107 km from Manaus, capital of the state of Amazonas, Western Brazilian Amazon (Fig. 1).

The girl was accompanied by her father, who said that the hospital admission occurred 15 min after she being bitten in the foot (Fig. 2) by a coral snake, near the front door of their house, in the outskirts of the urban area, surrounded by a forest. The bite occurred at 10:00 p.m. The major complaint of the patient was intense local pain and paresthesia. Examination of the bite site revealed edema extending from the left foot all over the left leg associated with erythema in the foot and distal third of the leg. A purpuric spot measuring approximately 2 cm, surmounted by a hematic crust, corresponding to the bite site, was observed on the lateral face of the left foot (Fig. 2). Systemic signs at admission included nausea and drooling. Considering the early clinical manifestations that included important local features plus salivation, the local medical staff decided to treat the patient with 100 mL of coral snake antivenom intravenously (soro antielapídico bivalente, Instituto Butantan, São Paulo, SP, Brazil; Fab2; 1 vial = 10 mL; 1 mL of antivenom neutralizes 1.5 mg of reference *M. frontalis* venom in mice). Before antivenom infusion, the patient was pre-medicated intravenously with steroids plus H1 and H2 antagonists (IV hydrocortizone 500 mg, IV promethazine 50 mg, IV dexchlorpheniramine and IV ranitidine 50 mg); dipyrone (750 mg) was also given intravenously for pain relief. No acute adverse reaction to antivenom was observed in the patient's follow-up.

After antivenom administration, the patient was referred to the *Fundação de Medicina Tropical Dr. Heitor Vieira Dourado* (FMT-HVD) the tertiary reference center for snakebites treatment in the state of Amazonas. At the admission to this service, patient was afebrile and

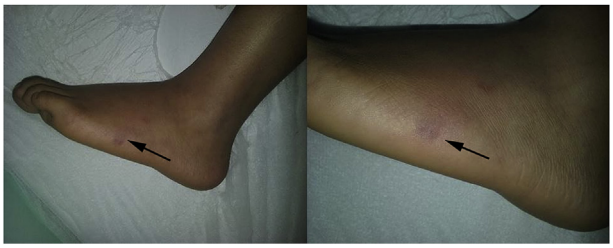

Fig. 2. The bite site (purple spot, ~2 cm long) on the lateral face of the left foot. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

denies coughing, diarrhea, sialorrhea or other complaints. Heart rate was 86 bpm and respiratory rate was 18 bpm. Normal heart and respiratory sounds. No signs of neurological focus and of meningial irritation. Otoscopy and oroscopy without alterations. No palpable visceromegalias and no lymph node enlargement. Abdomen flaccid and painless. The clinical features upon admission still included local pain and edema. Apart from mild leukocytosis (11,580 cells/mm3), all the laboratory results (whole blood clotting test, hemoglobin, platelets and blood serum levels of creatine kinase, lactate dehydrogenase and creatinine) were within the reference values for age. The patient received intravenous dipyrone every 6 h for two days, with progressive improvement in pain, and was discharged with no complaints after 48 h of hospitalization.

After 24 h of hospitalization, patient's general status remains normal, but she still complained of pain at the bite site, which improved with the administration of dipyrone. Diuresis and evacuation were present. Local manifestations improved and bite site presented no sign of bacterial secondary infection. Patient remained hospitalized for 48 h until discharge with no complaints. Oral dipyrone was prescribed in case of pain.

2.2. The cause of envenoming

Patient's father brought the offending snake to the FMT-HVD, where the specimen was kept in a 40% formalin solution until its identification by a herpetologist (P.S.B.) as an adult male *Micrurus averyi*, commonly known as 'the black-headed coral snake' (Fig. 3). The snake was killed in front of the main door of the wooden house, located close to a forest reserve. The snake's head was severed during capture and was not brought with the dead snake. The specimen presented 9 black rings along its body and 7 black rings along its tail. Without the head, morphometric analysis showed a total length of 45.5 cm and a length of 39.5 cm from the severed extremity to the cloaca.

3. Discussion

In the Americas, the main representatives of the family Elapidae are coral snakes of the genus *Micrurus*, of which 30 species occur in Brazil (Costa and Bérnils, 2015). The species most frequently involved in human envenoming are *M. corallinus*, *M. frontalis* and *M. lemniscatus* (Bucaretchi et al., 2016). In the present study, we report a case of human envenomation caused by *M. averyi* in the Brazilian Amazon. This species has a large geographical distribution

Fig. 3. The *Micrurus averyi* specimen responsible for the bite. Ventral (A) and dorsal (B) aspects.

in the Amazon basin, including Suriname and Guyana, where the species was first described (Schmidt, 1939) and the Brazilian Amazon, in the states of Amazonas, Pará, Mato Grosso and Roraima (Campbell and Lamar, 2004; Feitosa et al., 2015; Vanzolini, 1985; Velloso-Calleffo, 1997). These snakes occur in primary forests or in disturbed areas of crops and pasture, including records of some species (e.g., *M. lemniscatus* and *M. surinamensis*) in urban areas. Most species have fossorial or terrestrial habits, but two species (*M. lemniscatus* and *M. surinamensis*) have aquatic habits. *Micrurus* mainly feed on elongated vertebrates (other snakes, amphisbaenians, lizards, and caecilians) but also on fishes (*Callichthys*, *Gymnotus*, and *Synbranchus marmoratus*, predated by *Micrurus lemniscatus* and *Micrurus surinamensis*) and velvet worms (recorded for *M. hemprichii*) (Bernarde, 2014; Martins and Oliveira, 1999; Silva Jr and Aird, 2001). *Micrurus averyi* is a fossorial and cryptozoic forest species that may be active during the day and at night, when it feeds on lizards and snakes (Martins and Oliveira, 1999). In Manaus, this species is present in periurban forest (Reserva Adolpho Ducke) (Martins and Oliveira, 1999), which would explain the occurrence of this snake at the site of this accident.

The primary effect of *Micrurus* venoms is neurotoxicity that is mediated by pre- and postsynaptic neurotoxins. Presynaptic neurotoxins block neurotransmission by inhibiting acetylcholine release from nerve terminals, whereas postsynaptic neurotoxins act by blocking postsynaptic nicotinic receptors (Brasil. Fundação Nacional de Saúde, 2001). This neuromuscular blockade results in ptosis; ophthalmoplegia; dizziness; blurred vision; weakness; dysphagia; dyspnea; inability to walk; drooling and respiratory failure (Bucaretchi et al., 2016). Acute respiratory failure has been observed in accidents caused by *M. surinamensis* that occurred in the state of Pará, as a result of paralysis of the respiratory muscles. In this state, *M. filiformis* also causes envenomings with epigastric pain and vomiting (Pardal et al., 2010). At admission, the patient reported here presented with nausea and drooling as systemic manifestations, which ceased after antivenom administration. Although speculative, we may infer that the good outcome of this patient was attributable to the early medical assistance after the bite (around 15 min), with the use of coral snake antivenom. In Brazil, *M. corallinus* and *M. frontalis* venoms are used for the production of *Micrurus* antivenom (Wen et al., 2015). However, it was demonstrated by in vivo and in vitro neutralization assays that the coral snake antivenom produced in Brazil does not fully neutralize the activities of some *Micrurus* species venoms (Tanaka et al., 2010).

Local features, mainly paresthesia and pain, were frequently reported in *Micrurus* snakebites, with the pain being intense in some cases (Bucaretchi et al., 2016). In this work, the major complaint of the patient was intense local pain that required symptomatic medication at admission and during hospitalization. Envenoming by another Amazonian species, *M. filiformis*, has also been reported to cause pain and mild edema at the bite site (Pardal et al., 2010). In Amazonian Ecuador, a bite by *M. lemniscatus helleri* resulted in severe local pain with no other marked local effects (Manock et al., 2008). In the present case, examination of the bite site revealed also erythema and intense edema extending from the left foot all over the left leg associated with erythema in the foot and distal third of the leg. There are few references of edematogenic effects produced by *Micrurus* sp. venoms in humans (Bucaretchi et al., 2016; Pardal et al., 2010). However, a low edematogenic effect was described for *M. frontalis* and *Micrurus nigrocinctus* venoms in mice (Gutiérrez et al., 1980; Sanchez et al., 1992). Edematogenic activity was also observed for *M. ibiboboca*, *M. spixii*, *M. lemniscatus carvalhoi*, *M. frontalis frontalis*, *M. surinamensis surinamensis* and *M. nigrocinctus* venoms (Cecchini et al., 2005; Tambourgi et al., 1994). Moreover, it was noted also that PLA2 from *Micrurus* venoms have been shown to be edematogenic (Casais-e-Silva et al.,

2016; Rey-Suárez et al., 2017). Here, *M. averyi* venom caused intense edema and discrete hemorrhage in mice, as confirmed by histological examination (Barros et al., 1994), in agreement with the extensive edema seen in the present case.

Envenoming by *M. averyi* can cause important local alterations (edema, pain and paresthesia), without signs of systemic neurotoxicity. To the best of our knowledge, this is the first published case involving this species.

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