CASE REPORT

FIRST RECORD OF ENVENOMATION BY Bothrops brazili IN THE BRAZILIAN AMAZON REGION

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ABSTRACT

Snakebites in Brazil are most frequently inflicted by *Bothrops* spp. but there are no records of envenomation by *Bothrops brazili*. We hereby report on the first confirmed case by this snake, which took place in a primary forest in the State of Pará, in the Brazilian Amazonia, while the victim was felling trees. After being bitten, the man presented with clinical manifestations including pain and edema that extended to the thorax and further complications such as necrosis and abscess. This is the first record of a *B. brazili* bite in the literature, whose manifestations are similar to those inflicted by other *Bothrops* spp. with a favorable evolution.

KEY WORDS: Snakebite; envenomation; sequelae; Bothrops brazili; Brazilian Amazon.

INTRODUCTION

Envenomation resulting from snakebites are a major public health issue worldwide, with more than 5 million bites per year, with around 350,000 cases in the Americas alone (Chippaux, 1998). In Brazil, it is estimated that around 30,000 snakebite cases occur annually (Brasil, 2022), with the most incriminated snakes belonging to genera *Bothrops, Crotalus, Lachesis* and *Micrurus* (Brasil, 2001). The genus *Bothrops* is the most frequent in Brazil, with about 29 species, from which seven are recorded from the Brazilian Amazon region, including *Bothrops brazili* (Nogueira et al., 2020). *B. brazili*, described

Received for publication: 29/6/2023. Reviewed: 17/11/2023. Accepted: 1/12/2023.

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in 1953 by Hoge, is scarce, and morphologically can be distinguished from other species in the genus by the lack of an ocular stripe, the back is brown with dark drawings in the shape of a triangle, the belly is cream-colored and its general color is pinkish or coppery iris (Hoge, 1953; Campbell & Lamar, 2004). They can be found in the Amazonian Forest areas of Brazil, Bolivia, Colombia, Ecuador, Peru, French Guiana, Guyana, Suriname and Venezuela (Campbell & Lamar, 2004). The most important characteristic of *B. brazili* is the abundant production of venom when compared to other snakes of the Viperidae family, which is one of the factors that make envenomation by this species very serious, because in addition to the toxicological activity of components of the venom, a high venom volume is also injected per bite (Zavaleta & Campos, 1992).

The main clinical manifestations of *Bothrops* envenomation are those resulting from inflammatory and hemorrhagic manifestations (Gutiérrez, 2002). The injury may cause pain, swelling and necrosis in the bite' site, and its complications may result in permanent physical disability (Magalhães et al., 2022). Although potentially dangerous, envenomation by *B. brazili* has not been described before in the world literature, so we are reporting the first case of proven envenomation by *B. brazili* in humans in the Brazilian Amazon.

CASE REPORT

A 52-year-old man, was bitten by a snake that was called by the victim "surucucu" in the distal part of the right leg, measuring about 1.5 meters in length and killed by its companions (Figure 1), it was later identified as *B. brazili*. This was on December 9, 2019, at around 2:00 pm, while walking with short boots in a primary forest in the rural area in the Municipality of Ulianópolis, Pará, Brazil, in the Brazilian Amazon (03° 45' 32'' S, 47° 29' 26'' W) (Figure 2). Immediately after the envenomation, he had pain, bleeding and swelling at the site. About 30 minutes later, the edema was extended to his knee.

The victim tied his leg with his shirt just below the knee and he was taken to the Municipal Hospital of Ulianópolis. On the way, he reported two episodes of emesis. About three and a half hours after the injury, he was admitted to the hospital, with local pain and edema up to his right thigh, the severity being classified as moderate. Eight ampoules of polyvalent Bothropic antivenom (Butantan Institute, 10 mL per vial, of the F(ab')2 fraction of heterologous immunoglobulins) were administered. The next day, he had blisters on the dorsum of the foot and on the distal part of the injured leg and reported vomiting and urine with a reddish color, suggesting hematuria, and black stools (melena).

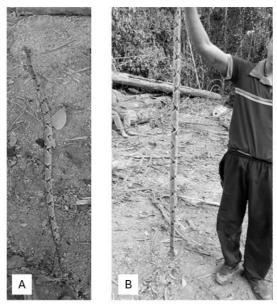


Figure 1. Bothrops brazili snake specimen responsible for envenoming seen in two views: (A) the snake on the ground and (B) a person holding the snake.



Figure 2. Map of the State of Pará-Brazil, indicating the City of Ulianópolis where the snakebite incident occurred.

On the second day, the edema ascended to the right part of the abdomen and chest. He underwent treatment for eight days, during which abscesses in the leg and areas of necrosis on the dorsum of the right foot developed. On the ninth day, he was transferred to the João de Barros Barreto University Hospital (HUJBB) in Belém, Pará, a reference center for injuries involving venomous animals, for treatment of complications. On admission, he was conscious, oriented, with pallor of the mucous membrane and mild pain in the injured limb, without fever, however, with necrosis on the dorsum of the right foot and edema up to the thigh (Figure 3A). When asked about the medications and laboratory tests performed previously, he was unable to mention them, and he was not accompanied by a previous hospitalization report. At HUJBB, he was medicated with clindamycin (600 mg, intravenously, 8/8 hours for seven days) for bacterial infection and underwent laboratory tests (Table). On the fifth day, a venous echo Doppler examination of the affected limb was performed. Then, he underwent surgical intervention with debridement of the necrotic area on the dorsum of the foot and drainage of the leg abscess (Figure 3B and Figure 4). He remained hospitalized for nine days and was discharged for outpatient follow-up.



Figure 3. Right lower limb of the victim envenomed by *Bothrops brazili*, Pará, Brazil, showing: (A) edema on the ninth day post-envenomation and (B) abscess on the right leg.

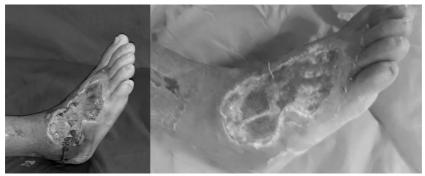


Figure 4. Debrided necrotic lesion on the dorsum of the right foot, caused by *Bothrops brazili* envenomation, Pará, Brazil.

This report was approved by the Research Ethics Committee of the João de Barros Barreto University Hospital of the Federal University of Pará (UFPA), approval number CAAE: 59203420.6.0000.0017.

Table. Laboratory parameters recorded during hospitalization of *Bothrops brazili* envenomation victim at the João de Barros Barreto University Hospital, Belém, Pará, Brazil.

Parameters*	18/12/2019	22/12/2019	26/12/2019	Reference ranges
Red blood cells	3.51	3.29	3.19	4.1 to 6.0 million/mm3
Hemoglobin	10.7	10.0	9.7	13.5 to 17.8 g/dL
Hematocrit	32	30.5	29.8	41 to 54%
Leukocytes	12,300	8,400	6,200	3,600 to 11,000mm ³
Platelets	466,000	799,000	613,000	140,000 to 400,000mm ³
PT	14.20	-	11.10	12 to 18 seconds
PTT	88.00	-	130.00	70 to 100%
INR	1.08	-	0.87	0.8 to 1
APTT	27.90	-	25.20	27 to 40 seconds
Urea	28	15	16	10 to 40mg/dL
Creatinine	0.7	0.8	0.7	0.7 to 1.3mg/dL
Sodium Potassium Total calcium AST ALT Total bilirubin Glycemia	133 4.5 8.7 36 22 0.8 118	131 4.2 8.9	136 4.5 - 23 26 23	130 to 146 mmol/L 3.5 to 5.5 mmol/L 8.5 to 10.5 mg/dL Up to 41U/L Up to 33U/LTAP= 0.3 to 1.2 mg/dL 70 to 99 mg/dL

*INR: International normalized ratio; PT: Prothrombin time; PTT: Prothrombin time (PTT); APTT: Activated Partial Thromboplastin Time; ALT: alanine transaminase; AST: aspartate aminotransferase.

DISCUSSION

In the Brazilian Amazon, around 10,053 envenomation by snakes occur on average per year, with *Bothrops* spp. being the most incriminated (Chippaux, 2017; Souza et al., 2018; Brasil, 2022). Among this genus, the species of medical importance in the country are *B. atrox, B. bilineatus, B. brazili, B. marajoensis, B. mattogrossensis, B. moojeni,* and *B. taeniatus* (Nogueira et al., 2020), with *B. atrox* being the most frequent involved in injuries (Pardal et al., 2004; Silva & Pardal, 2018). However, to the best of our knowledge, there are no records in the literature of envenomation by *B. brazili* in Brazil or other Amazonian countries. It is a rare snake, and its habitat corresponds to "solid land" in forests, and places with scarce human activity (Bernarde & Almeida, 2019), similarly to the area where the accident reported

here took place, where the victim was felling trees. The literature suggests that activities related to agropastoral and extractive procedures favor exposure to venomous animals, mainly snakes (Pardal et al., 2015; Silva & Pardal, 2018). Matos & Ignotti (2020), when analyzing the trend in the incidence rate of snakebites in the Brazilian Amazon biomes, found an increase in the incidence rate per 100,000 inhabitants from 37 in 2003 (6,822 accidents) to 42 in 2012 (8,405 accidents), that is, about four times the average rate in the country.

This case report describes an envenomation case by *B. brazili*, in the southeast section in the State of Pará, in the Brazilian Amazon region, by an adult specimen. According to Campbell & Lomar (2004), *B. brazili* can reach 70 to 90 cm in length. The envenomation described here is the first human case by *B. brazili* reported in the world literature despite being a snake distributed in several South American countries. Species identification was performed based on current taxonomic keys for the genus *Bothrops* (Hoge, 1953).

According to the National Information System for Notifiable Diseases of the Ministry of Health of Brazil, in the period 2017-2021, 32.6% of all cases of envenomation by snakes of the Viperidae family in Brazil were registered in the States from the Brazilian Amazon, being the genus *Bothrops* the most incriminated (Brasil, 2022). Here we report a proven case of envenomation by *B. brazili*, which is popularly known as "surucucu." This name is also used in the Amazon to describe other *Bothrops* spp. and *Lachesis* spp. (Silva et al., 2019), which causes confusion when there is no proof of the species involved in the injury, a situation we believe that has contributed to the underreporting of *B. brazili* envenomations in the Amazon area.

The severity of this envenomation was initially classified as moderate. According to Gutiérrez (2002), bothropic venom has proteolytic or inflammatory, coagulant and hemorrhagic activities, responsible for the appearance of local and systemic clinical manifestations. In Brazil, snakebite cases are classified according to their severity as mild, moderate or severe (Brasil, 2001). Severity depends on the snake species, the composition and the amount of injected venom. Mild envenomation present with pain, edema or local paresthesia; moderate envenomation present with local pain, local and ascending edema, local and systemic bleeding, whereas the severe cases, in addition to the local symptoms and signs presented by the moderate, the edema becomes more intense, and blisters and necrosis in the affected segment can be present, abundant systemic bleeding may occur, together with oliguria, anuria and shock. In all severities, the clotting time can be normal or altered (Brasil, 2001).

The clinical manifestations presented at the site of the bite, as well as the systemic manifestations presented by the victim of *B. brazili*, are similar to other *Bothrops* spp. envenomation (Pardal et al., 2004; Batista et al., 2020). However, as it is a large snake, it is believed that the amount of venom introduced may be greater, which can lead to greater severity (Zavaleta

& Campos, 1992). In the Amazon, hemorrhagic stroke has been reported, due to envenomation by *B. marajoensis* (Pardal et al. 2015), and hemolytic uremic syndrome (HUS) after a *B. atrox* bite (Araújo et al., 2021).

The increase in local severity reported in this case may have been contributed by the use of a tourniquet, with the appearance of necrosis and abscesses. It has been reported that *Bothrops* spp. envenomation in the Amazon region led to 7% of abscesses and 2% of necroses (Silva et al., 2021). According to Ribeiro et al. (2001), the use of tourniquet is statistically associated with the development of necrosis, due to the presence of phospholipase A2 in viper venoms (Gutiérrez, 2002). The use of a tourniquet is not recommended in Brazil (Brasil, 2001).

The patient presented edema at the site, which reached the right part of the abdomen and chest. Kallel et al. (2018), describe an injury by a snake of the Viperidae family in French Guiana, on the left foot, in which the edema extended to the left part of the thorax. It is reported that viperid venom causes an inflammatory process in tissues, which act in a complex way leading to edema, cell infiltration and pain (Gutiérrez, 2002). This extensive edema presented by the victim, possibly resulted from the injection of a large amount of *B. brazili* venom.

As we have no records of laboratory tests from the initial care unit in Ulianópolis, it is possible that the victim experienced a change in coagulation parameters, as the victim had anemia and reported reddish urine, which suggests blood loss. *Bothrops* spp. envenomation can lead to bleeding due to blood incoagulability, as a result of the coagulant and hemorrhagic activities found in their venoms (Gutiérrez, 2002).

At the reference hospital (HUJBB), laboratory tests were performed to assess the clinical condition, and treatment with antibiotics was indicated to control the infection, as the victim had necrosis on the dorsum of the right foot and an abscess on the leg (Figure 4). Laboratory tests did not show impairment of renal or hepatic function, or changes in some elements of the ionogram. However, the blood count showed a decrease in red blood cells, hemoglobin and hematocrit, and an increase in leukocytes in the first test. This decrease in blood count elements suggests that there was some bleeding, possibly due to hematuria and melena during the initial admission. Meanwhile, the increase in leukocytes is due to the local infectious condition. Silva and Pardal, (2018) found leukocytosis in *Bothrops* spp. accidents in patients with local infection, while Araújo et al. (2021), even without local infection.

The victim underwent treatment with bothropic antivenom based on the moderate severity of the case. In Brazil, the bothropic antivenom is produced using a venom pool from the snakes *B. jararaca, B. alternatus, B. jararacussu, B. moojeni,* and *B. neuwiedi*. It is used for all envenomation caused by *Bothrops* spp. whose treatment protocol is established according to the criteria of the Brazilian Ministry of Health for the diagnosis and treatment of snakebites, which recommends three ampoules in mild cases, six ampoules in moderate cases and 12 ampoules in severe cases. Treatment considers the intensity of local and/or systemic manifestations (Brasil, 2001). In this case report, all clinical manifestations presented suggest a case of initial moderate envenomation that evolved to severe case. In this condition, the indication is 12 ampoules of the polyvalent antibothropic antivenom. According to Muniz et al. (2023), the bothropic antivenom neutralizes the lethal, hemorrhagic, myotoxic and phospholipase A2 activities of *B. brazili* venom from Brazil, which suggests that the Brazilian antivenom may be used for treating *B. brazili* envenomation.

Upon admission to the reference hospital, an evaluation was performed by the angiologist, who requested a venous echo Doppler examination, which showed no anatomical or hemodynamic changes in the examined limb. Imaging tests have been used to assess snakebite envenomation, such as ultrasonography (Tchaou et al., 2016), magnetic resonance imaging (Fonseca et al., 2002), among others.

On the fifth day, he underwent surgery with debridement of the necrosis of the dorsum of the foot, skin and subcutaneous tissue and an incision in the posterior-medial part of the leg, with drainage of the purulent abscess and partial removal of the necrotic Achilles tendon. Silva et al. (2021), showed that complications due to *Bothrops* spp. envenomation in the Amazon region reach 19%. These occur due to the direct toxicological action of the venom that leads to tissue destruction, resulting in different levels of necrosis, in addition to edema that can compress blood vessels and prevent vascularization of the extremities, causing compartment syndrome, which is exacerbated by injuries caused by bleeding, tourniquet use, or severe anemia caused by bleeding (Gras et al., 2012). However, we believe that surgical intervention can improve the patient's prognosis. According to Gras et al. (2012), many patients survive, with a high proportion of them suffering from complications and sequelae.

In conclusion this is the first report of *B. brazili* envenoming in the literature, which occurred in the Brazilian Amazon, State of Pará, whose clinical manifestations were similar to other *Bothrops* spp. envenomation. He evolved with complications and underwent surgery, with favorable evolution.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest to disclose.

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