

HEMOLYTIC-UREMIC SINDROME FOLLOWING SNAKEBITE: CASE REPORT

SÍNDROME HEMOLÍTICA-URÊMICA POR PICADA DE COBRA: RELATO DE CASO

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ABSTRACT

Objective: Describe case of hemolytic-uremic syndrome (HUS) following snakebite. **Method:** Observational and descriptive study, case report type, carried out at the Paragominas, Par  State, Brazilian Amazon. **Case report:** A woman was bitten by a snake, called jararaca, probably *B. atrox*, on her left foot, in the rural area of Paragominas, in 2019. She reported immediate pain, developed local edema and was referred to the Nova Esperan a do Piri  City Hospital. It was rated as a mild accident and four ampoules of the bothropic antivenom were administered. On the third day, the patient presented mucosa skin paleness and jaundice, being transferred to Paragominas Emergency Care Unit. The case rating changed to severe and another eight ampoules of bothropic antivenom administered. Blood count, bilirubin dosage, renal, hepatic and pancreatic function tests, all altered results. The peripheral blood smear showed the presence of schizocytes and helmet-cell. She was transferred to Intensive Care Unit and submitted to conservative treatment without plasmapheresis. After 22 days, she was discharged the hospital. **Conclusion:** This report describes the first HUS case, caused by snake envenoming, in the Brazilian Amazon region, with favorable evolution to specific treatment and conservative measures.

Keywords: Snakebite, *Bothrops*, Thrombotic Microangiopathies, Hemolytic-Uremic Syndrome.

RESUMO

Objetivo: Descrever caso de s ndrome hemol tica-ur mica (SHU) ap s picada de cobra. **M todo:** estudo observacional e descritivo, do tipo relato de caso, ocorrido em Paragominas, estado do Par , Amaz nia brasileira. **Relato caso:** Mulher picada por cobra, denominada jararaca, provavelmente *B. atrox* no p  esquerdo, quando caminhava em  rea antropizada, na zona rural de Paragominas, em 2019. Referiu dor imediata e desenvolveu edema local. Foi encaminhada ao Hospital Municipal de Nova Esperan a do Piri , para atendimento m dico. Foi classificado como acidente de gravidade leve, recebendo quatro ampolas do antiveneno botr pico. No terceiro dia, apresentou palidez cut nea mucosa e icter cia, sendo transferida para Unidade de Pronto Atendimento de Paragominas, sendo reclassificado como grave e sendo aplicadas oito ampolas do antiveneno botr pico. Realizados hemograma, dosagem das bilirrubinas, exames da fun o renal, hep tica e pancreatica, todos alterados. O esfrega o do sangue perif rico mostrou presen a de esquiz citos e *helmet-cell*. Foi transferida para Unidade de Terapia Intensiva, onde foi submetida a tratamento conservador, sem necessidade plasmaf rese. Recebeu alta hospitalar ap s 22 dias da internan o. **Conclus o:** O relato descreve o primeiro caso SHU, provavelmente causado pelo envenenamento da *B. atrox*, na regi o Amaz nica brasileira, com evolu o favor vel ao tratamento espec fico e medidas conservadoras.

Palavras-chave: Picada de Cobra, *Bothrops*, Microangiopatia Tromb tica, S ndrome Hemol tica-Ur mica.

1. INTRODUCTION

Thrombotic microangiopathies (TMAs) can cause hemolytic-uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP), which are severe diseases¹. The TMAs are a group of diseases in which there is fragmentation of red cells due to microangiopathic hemolytic anemia. This shear fragmentation occurs when mechanical forces break the physical integrity of the erythrocyte membrane². HUS is characterized by the presence of microangiopathic hemolytic anemia, generalized microvascular occlusion, caused by the deposition of platelet-rich thrombi, thrombocytopenia, and the presence of acute renal injury (ARI), while TTP presents neurological manifestations without the occurrence of ARI¹. Several causes are associated with microangiopathic hemolysis, including medicines³, toxins⁴ and snake venom⁵⁻⁹.

The HUS caused by snakebites has been reported in envenomings by *Hypnale hypnale*, *Hypnale zara* and *Hypnale nepa* in Sri Lanka⁶, by *Cerastes cerastes* in Europe¹⁰ and by *Bothrops jararaca* and *B. erythromelas* in Brazil^{5,8,9}, this syndrome being uncommon. For this reason, a case of HUS by snakebite, probably *B. atrox*, in the State of Pará, in the Brazilian Amazon, is being reported herein.

2. CASE REPORT

The observational and descriptive study, case report type, was carried on a 19-year-old female, snake bitten, informed by the victim as being jararaca, on January of 2019, at approximately 3 pm, in Vila Cacimão, Paragominas (02°59'45" south and 47°21'10" west), Pará State, Brazilian Amazon (Fig. 1).

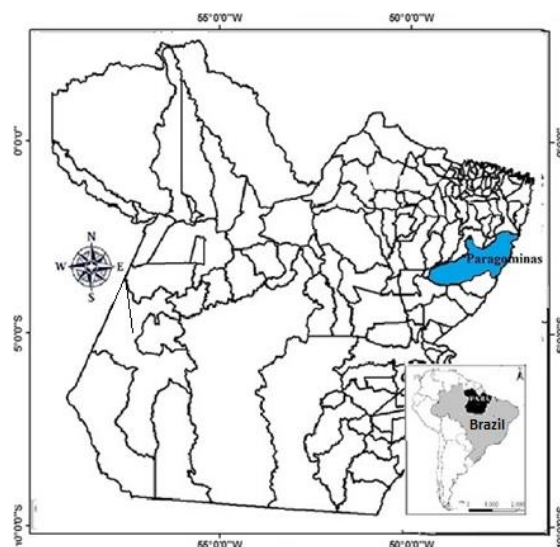


Figure 1. Map of the State of Pará-Brazil, indicating the City of Paragominas (in blue) where the snakebite incident occurred.

The victim was bitten on her left foot while walking in an anthropized rural area, near her house, by a snake approximately 90 cm long. She reported immediate pain and developed local edema. She was referred to the Nova Esperança do Piriá City Hospital six hours after the accident for medical assistance, not bringing the snake that bit her. It was rated as a minor accident and four ampoules of the bothropic antivenom (AV) from the Butantan Institute were intravenously (IV) administered. The following day, it evolved with oral bleeding and ecchymosis. On the third day, she presented mucosa skin paleness and jaundice, and was transferred to Paragominas Emergency Care Unit (ECU); she was hemodynamically stable, eupneic, afebrile, anuric and had the above-mentioned signs and symptoms. The case rating was changed to severe and another eight ampoules of bothropic AV were administered. Blood count, bilirubin dosage, renal, hepatic and pancreatic function tests were performed, which exhibited altered results (Table 1). In addition, peripheral blood smear showed the presence of schizocytes and helmet-cell (Fig. 2).

Table 1. Laboratory tests performed at the Paragominas Emergency Care Unit, Pará, Brazil.

Exams	January 6, 2019	January 7, 2019	Reference ranges (♀)
Red blood cells (RBC's)	1.61	2.16	3.9 to 5.4 million/ μ L
Hematocrit	12.1	16.5	35 to 47%
Hemoglobin	4.5	6.1	12.0 to 16.0 g/dL
VCM	75.2	76.4	80.0 to 100.0 fL
HCM	28.0	28.2	27.0 to 32.0 pg
CHCM	35.5	37.0	31.0 to 36.0 g/dL
RDW	19.5	17.3	10.0 to 16.0%
Leukocytes	10250	12300	4000 to 11000/ μ L
Platelets	110000	50000	140000 to 450000 μ L
APTT	23	22	24 to 40 seconds
Total Bilirubin	5.02	4.94	0,2 to 1.1 mg/dL
Direct Bilirubin	0.56	1.26	0,1 to 0,4 mg/dL
Indirect Bilirubin	4.46	3.68	0,1 and 0,7 mg/dL

Urea	371.3	427.3	16-40 mg/dL
Creatinine	13.19	14.06	0.6-1.2 mg/dL
AST	251	188.5	up to 31 U/L
ALT	151.2	121.8	up to 31 U/L
Amylase	1624	1366	up to 125 UI/L
Lipase	-	3000 U/L	up to 160 UI/L
Routine Urine – EAS	High RBC count	-	3 to 5 RBCs per field

She was transferred to the Intensive Care Unit (ICU) of the Paragominas Regional Hospital, where plasmodium, viral hepatitis and the human immunodeficiency virus (HIV) tests were performed, all of which being negativ. She was submitted to clinical support, symptomatic measures and no plasmapheresis was required; she had good progress, and was pronounced cured and was discharged from the hospital after 22 days of hospitalization for outpatient follow-up.

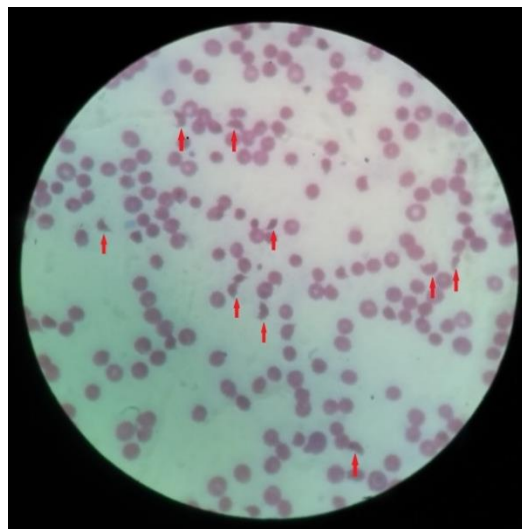


Figure 2. Blood smear showing schizocytes and helmet-cell, three days after the snakebite.

This manuscript 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: 07344919.7.0000.0017.

3. DISCUSSION

The reporting region in the State of Pará has recorded cases of envenoming by *Bothrops* and *Lachesis*, the symptoms of which being similar^{11,12}. The *Bothrops* genus is represented in Brazil by 26 neotropical species, *B. atrox* being abundant and widely distributed in the Amazon biome, occupying a range of habitats, from forests to open areas, including anthropized areas. They are called by the local population as *jararaca*, *surucucurana* and *comboia*^{11,13}. The genus *Lachesis muta* (*L.m.*) has two subspecies in Brazil, the *L. m. muta* found in the Amazon region, distributed in areas of preserved forests, not so abundant and known as *surucucu-pico-de-jaca*¹⁴. This case report does not confirm the type of snake that caused the envenoming; however, since the accident occurred near her house, an anthropized area, by a serpent called *jararaca*, the symptoms at the area of the body that was bitten and systemic bleeding are compatible with envenoming by *Bothrops*^{12,13,15}, since *Lachesis* is a snake found in preserved biomes, the local symptoms and systemic bleeding of which being similar to *Bothrops*; however, they cause stimulation of the vagus nerve, with the presence of colic, diarrhea and bradycardia^{12,16}, which was not found in the herein case.

Bothrops venom is a complex mixture of multiple enzymes and proteins that induce coagulopathy by consumption and thrombocytopenia¹⁷, thus prompting inflammatory, coagulant and hemorrhagic action^{17,18}, and leading to local, systemic manifestations and complications. Local manifestations include bleeding, oedema, ecchymosis, pain and blisters, while systemic manifestations include vomiting, sweating, bleeding (gingivorrhagia, hematuria, epistaxis and ecchymoses), blood incoagulability, thrombocytopenia and hypotension. Complications can be local such as necrosis, infections and compartmental syndrome^{12,13} and systemic ones, generally severe such as hemorrhagic stroke^{15,19}, acute renal injury^{8,20,21} and thrombotic microangiopathy^{5,7,9,22}, the latter being found herein.

In the clinical evolution, the patient presented mucosal skin paleness, jaundice, and anuria, while laboratory tests showed decreased red blood cells (RBCs) and platelet counts, increased indirect bilirubin, plasma creatinine, high RBCs in the urine, and the presence of schizocytes and helmet-cell in the peripheral blood smear (Table 1), which suggested it was a case of HUS-compatible MATs because it presented ARI. This syndrome has a complex pathophysiology, which arises from an endothelial cell lesion,

resulting from a complication or being precipitated by various diseases, conditions and treatments²³, including snakebite^{6,10,22}. In Brazil, the only reports described are Bucarety et al.⁵ and Malaque et al.⁸ caused by *Bothrops jararaca* in the Southeast region and Mota et al.⁹, by *B. erythromelas* in the Northeast.

The severity criteria for *Bothrops* envenoming, according to the Brazilian Department of Health¹¹, are classified as (i) mild; (ii) moderate and (iii) severe. This case report refers to a severe case with HUS. Snakebite is a major cause of ARI in tropical countries^{8,20}. Mohan et al.⁷ showed it accounts for 37.6% and Chugh²⁴ found 27% of acute cortical necrosis in renal biopsy, associated with snakebites.

Initially, the treatment was performed with specific AV. The AV is presented in a vial containing 10 mL of injectable solution of the fraction F(ab')₂ of specific and purified heterologous immunoglobulin, capable of neutralizing at least 5 mg of *Bothrops jararaca* venom (neutralization determined in mice) per mL of serum. Since the patient's clinical manifestations worsened, with complication of renal injury, she was transferred to another hospital for treatment in an Intensive Care Unit, where conservative measures were conducted, without the need for plasmapheresis. Following progressive improvement, she was pronounced cured and was discharged after 22 days of hospitalization. In Brazil, the reports of treatment of TMA were conservative, with complete recovery of the victims^{5,8,9}, which corroborates the herein report.

4. CONCLUSION

This report describes the first HUS case, probably caused by *B. atrox* envenoming, in the Brazilian Amazon region, with favorable progress to specific treatment and conservative measures.

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