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CASE REPORT
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Bothrops Envenomation in Dogs: Local and Systemic Manifestations

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ABSTRACT

***Background*:** Snakebite envenoming is a condition that affects humans and domestic animals worldwide. Identification of the snake species involved in the envenomation is infrequent. *Bothrops* envenomation presents typical clinicopathological features. This report describes epidemiological, clinical, and pathological data of 2 cases of *Bothrops* envenomation in dogs, including the first case of *Bothrops moojeni* snake striking a domestic animal in Brazil.

***Cases*:** *Case 1*. A dog was witnessed to have a *Bothrops moojeni* snakebite on a farm. In the first 24 h, acute lameness, pain, diffuse swelling, focal bleeding at the left forelimb, and increased whole-blood clotting time were observed in the envenomed dog. Polyvalent antivenom was administered in addition to fluid therapy, analgesics, corticosteroids, and antibiotics. On the 5th day, the animal presented spontaneous bleeding at the wound site, thrombocytopenia, and increased whole-blood clotting time. An additional dose of polyvalent antivenom was administered, and local treatment at the snakebite site was initiated. After 13 days, the dog showed no clinical or laboratory changes and recovered entirely. *Case 2*. A mongrel dog was taken for a necropsy to determine the cause of death. Grossly, major findings included swelling in the nasal plane that extended to the neck and dissecting hemorrhage in the subcutaneous tissue and adjacent musculature. Hemorrhages were observed in the heart, parietal pleura, left forelimb, lumbar region, and perirenal tissue. Marked necrosis and disruption of small blood vessels and lymphatics within the deep dermis and subcutaneous tissue were the main microscopic findings close to the snakebite site. Additionally, degeneration and necrosis of muscle fibers and dissecting hemorrhage were observed in the head and neck tissues surrounding the snakebite site. Kidneys showed marked interstitial hemorrhage and acute tubular nephrosis.

***Discussion*:** *Bothrops* envenoming is characterized by local (hemorrhage, dermonecrosis, and myonecrosis) and systemic (coagulative disorders, systemic hemorrhage, and acute kidney injury) changes due to the effect of the main venom components such as phospholipase A2 and metalloproteinases. These changes are hallmarks for the bothropic envenomation, supporting the diagnosis in cases 1 and 2. In *case 1*, the dog developed a *Bothrops moojeni* snakebite envenomation, but the immediate treatment with antivenom allowed a favorable outcome. In *case 2*, gross and microscopic findings supported the presumptive diagnosis of fatal bothropic envenomation. A marked local reaction such as swelling, pain, bleeding, bruising, and tissue necrosis was observed in *case 1*. In *case 2*, the most significant local changes were swelling and edema at the head and neck, hemorrhage in the subcutaneous tissue, and adjacent musculature. Systemic effects were observed clinically as spontaneous bleeding, thrombocytopenia, increased whole-blood clotting time (*Case 1*), systemic hemorrhages, and acute tubular nephrosis (*Case 2*). A proper treatment probably prevented the development of acute renal failure in *Case 1*. Herein, we show the first case of accidental snakebite envenomation by *B. moojeni* in a dog in Brazil. Information is scarce on the identification of venomous snake species striking domestic animals. Fast detection of well-determined clinical and pathological findings of *Bothrops* envenomation is essential for a correct diagnosis, therapeutics, and a good prognosis, even in cases with an unknown history.

Keywords: *Bothrops moojeni*, venomous, coagulative disorders, canine, snake, snakebite.

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INTRODUCTION

Accidental snake envenomations have been reported in humans [12] and domestic animals worldwide [3]. The Viperidae family includes venomous snakes with a high potential to generate severe envenomation, organic sequelae, and death [12]. In Brazil, cases of snake envenomation in humans occurred by the genera *Bothrops*, *Crotalus*, *Lachesis*, and *Micrurus* [11], while domestic animals were affected only by *Bothrops* and *Crotalus* [10,11,15,16,19]. *Bothrops* genus comprises one of the most dangerous venomous snakes in Latin America and is responsible for more than 90% of snake bites in humans [5] and also causes most snake envenomations in domestic animals in Brazil [15,16,19,21]. *Bothrops moojeni* has a broad natural distribution in South America, causing most of the accidents in humans in the Cerrado Biome [6], but it has not yet been reported to affect domestic animals [3].

Bothrops envenomation has a clinical presentation characterized by a marked local reaction such as pain, swelling, hemorrhage, edema, tissue necrosis, and frequent bleeding; systemic reactions include coagulation disorders and acute kidney injury (AKI) [15]. The diagnosis of bothropic envenomation is mainly based on the historic, clinicopathological findings and typical laboratory changes since the snake species are mostly not determined, and accidents are often unwitnessed [15]. In dogs, clinical aspects, therapeutics, and snake species involved in the envenomation have been rarely reported. Herein, we describe the first case of *Bothrops moojeni* snake envenoming in a dog. Additionally, we characterize clinicopathological features and therapeutics in 2 dogs with *Bothrops* envenomation.

CASES

Case 1. A 7-year-old bitch mongrel dog, weighing 19.7 kg, from a farm in the municipality of Jataí, Goiás, Midwestern Brazil, was found presenting acute lameness, restlessness, pain, diffuse swelling, and focal bleeding at the left forelimb (assumed as the snakebite site) [Figure 1 A]. The bitch was referred for clinical evaluation and intensive care at the Veterinary Medical Teaching Hospital of the Federal University of Jataí (UFJ). Heart and respiratory rates were unremarkable. Laboratory tests revealed mild neutrophilia (13.8 x10^3/µL; Reference range: 3-11.5 µL) [9], increased whole-blood clotting time (Activated coagulation time (ACT) > 6 min).

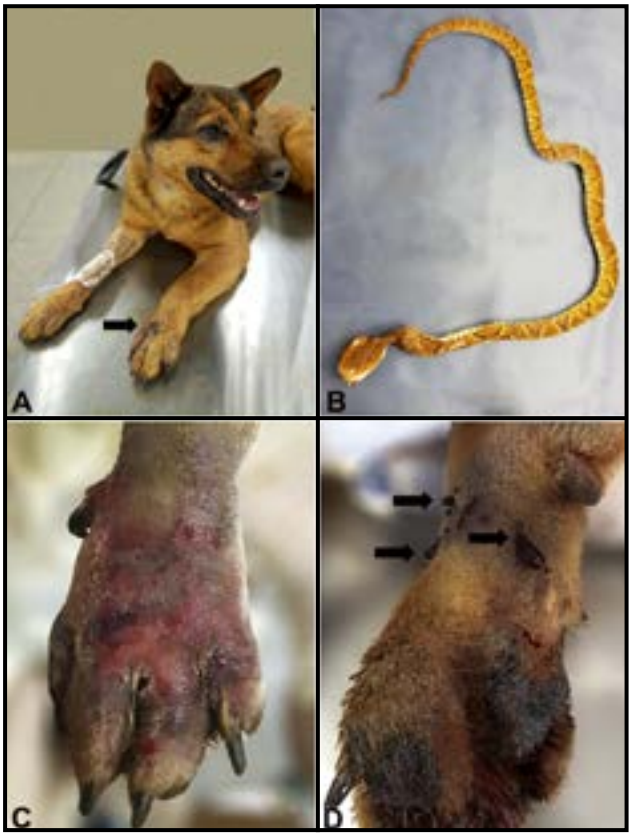

Figure 1. *Bothrops moojeni* envenomation in a dog (Case 1). A- Left forelimb swelling and local hemorrhage (arrow) at the snakebite site. B- *Bothrops moojeni*. C- Left forelimb. Edema and bruises after claw clipping (Day 2). D- Spontaneous bleeding (black arrows) surrounding the snakebite site (Day 5).

The dog's owner killed the snake, which was identified as *Bothrops moojeni* (Figure 1 B) at the Herpetology Laboratory, Butantan Institute, São Paulo, Brazil. Intensive care included intravenous therapy[1] [Ringer's lactate solution], analgesic[2] [dipyrone - 25 mg/kg, IV, TID, 5 days], opioid[3] [methadone - 0.3 mg/kg, IM, TID, 5 days], antibiotics[4] [ceftriaxone - 50 mg/kg, IV, BID, 5 days], and polyvalent snake antivenom[5] [20 mL, IV, sufficient to neutralize 100 mg of *Bothrops* sp. venom]. On the second day, the dog was sedated[6] [fentanyl - 2.5 µg/kg and ketamine:1 mg/kg, IV], and the snakebite site was inspected, revealing edema and bruisers (Figure 1 C). Necrosis and spontaneous bleeding at the snakebite site (Figure 1 D), thrombocytopenia (104.2 x10^3µL; RR: 200-500 x10^3µL) [9], ACT > 7 min, and neutrophilia (18.7 x10^3/µL; RR: 3-11,5 x10^3/µL) were observed on day 5. Another single dose of polyvalent snake antivenom [20 mL, IV] was given to the dog that was also medicated for 7 days with corticoids[6] [hydrocortisone - 10.0 mg/kg, IV, BID], antihistamine[7] [promethazine

- 1.5 mg/kg, SC], and antibiotics[6] [amoxicillin and clavulanate potassium - 30.0 mg/kg, VO, BID]. Topical wound cleaning with chlorhexidine 2%[8] solution was performed daily. No laboratory and clinical abnormalities were observed after 13 days of the snakebite, and the dog recovered entirely.

Case 2. An adult male mongrel dog weighing approximately 25 kg was referred for a necropsy to the Veterinary Pathology Laboratory of the University of Brasília (UnB), Brazil, without previous medical history. The animal was in good body condition and showed congested mucous membranes and marked swelling in the face, which extended from the nasal plane to the base of the left ear and neck. Due to the marked local reaction and gross features, the head was considered the snakebite site. At necropsy, extensive edema and dissecting hemorrhage in the subcutaneous tissue (Figure 2 A) and adjacent to the base of the tongue, trachea, esophagus, submandibular lymph nodes, and salivary glands were observed. Lungs were non-collapsed and diffusely red. There was perirenal hemorrhage, and the kidneys were diffusely dark red, with cortical pale radiating stripes on the cut surface. Petechiae and ecchymosis were observed in the epicardial, endocardial, parietal pleura, and intercostal musculature. Subcutaneous suffusions were detected in the left forelimb and lumbar region.

Microscopically, severe necrosis and rupture of the microvasculature and lymphatic vessels in the skin and subcutaneous tissues were remarkable. Muscle fibers degeneration and necrosis associated with dissecting hemorrhage were observed in the face and neck close to the snakebite site. Moderate multifocal tubular degeneration and necrosis, interstitial hemorrhage (Figure 2 B), and hyaline casts were the major renal injuries in the lethally envenomed dog.

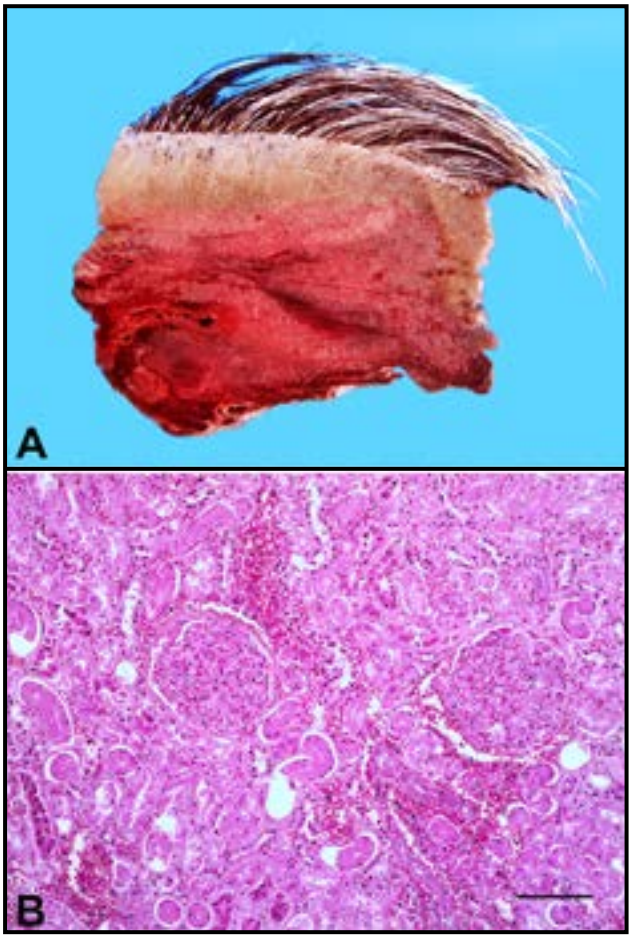

Figure 2. *Bothrops* envenomation in a dog (Case 2). A- Skin and subcutaneous tissue. Diffuse dissecting hemorrhage. B- Kidney. Multifocal degeneration and tubular necrosis and hemorrhage [HE; bar=100 µm].

DISCUSSION

Clinical and gross hallmarks of the *Bothrops* envenomation observed in domestic animals may enable and are essential in the proper diagnosis and therapeutics. In *case 1*, the diagnosis of *Bothrops* envenomation was based on the animal history, the snake species recognition, clinical features, laboratory abnormalities, and animal recovery after antivenom therapy. Given the hallmarked pathological features, the presumptive diagnosis of fatal *Bothrops* envenomation was enabled in *case 2*. The clinical and pathological findings in both dogs with *Bothrops* envenomation were similar to those previously reported in domestic animals [10,15,16,19].

Some of the main limitations in the diagnosis of snake bite envenomations worldwide include snake capture and identification; access to a specialist for snake identification; and the fact that most snake bites are not witnessed [11,17]. On the other hand, *Bothrops* envenomations have well-determined pathological features considered for a presumptive diagnosis in cases lacking a clinical history, such as in case 2. Additionally, the visualization of fang marks is relevant in diagnosing snakebites, but they are not usually identified at the snakebite site in the accidental bothropic envenomation of domestic animals [15,19,22], such as observed in both dogs reported here. The snake identification as *Bothrops moojeni* in *case 1* was crucial for a fast and accurate diagnosis, appropriate treatment, and a better prognosis.

Bothrops moojeni is a lethal venomous snake commonly known as the Brazilian lancehead pit viper

and indigenous to the states of Pará, Maranhão, Mato Grosso, Mato Grosso do Sul, Minas Gerais, São Paulo, Paraná, and Goiás, where in the latter *case 1* was recorded [6,13,21]. Presumptive fatal envenomations by *B. moojeni* were reported in 3 caged psittacine birds in a Brazilian Zoo [8]. Experimental envenomations by *B. moojeni* venom were lethal for a horse weighing 525 kg [20] and promoted clinical signs and death in sheep [7]. In Brazil, a few accidental snakebite envenomings in domestic animals had the snake identified [15,16,19], and they have been related to *Bothrops alternatus* [10], *B. jararaca* [10,22], *B. neuwiedi* [18], and *B. pauloensis* [4,10].

Epidemiological data are scarce on the *Bothrops* envenomation in domestic animals, but most cases have been affecting 1-4 years-old dogs, and about 60% of the cases occur in rural areas in Southern Brazil [19]. A *Bothrops moojeni* was found within the avian facilities after the detection of 3 cases of presumptive fatal *Bothrops* envenomation in caged psittacine birds [8]. In *case 1*, the animal envenoming occurred on a farm, but in case 2, the dog's location was ignored. Regarding the snakebite site, the left anterior limb was affected in case 1, while in case 2, the head and neck; these anatomical sites are considered more frequently involved in dogs [14,19] and horses with *Bothrops* envenomation [10,15].

The clinical course in dogs with bothropic envenomations may vary from superacute (up to 6 h), acute (6-24 h), and subacute (4-5 days) [19]. In *case 1*, the affected dog had a subacute evolution and a complete remission of clinical signs within 13 days after treatment initiation. Unfortunately, clinical course records in *case 2* were not available. Experimentally envenomed sheep ranged from a favorable clinical outcome with the disappearance of clinical signs within 5 days, and the death in approximately 24 h with the development of a subacute envenomation after the *B. moojeni* venom inoculation in different doses [7]. In a horse experimentally envenomed by *B. moojeni* venom, the clinical course was also subacute and a fatal outcome developed in about 2 days [20].

Dogs are known for having an intermediate sensitivity to the *Bothrops* envenomation [1], and fatal accidents are uncommon [19]. Thus, other factors must be considered in the clinical evolution and outcome in affected animals, as evidenced in *case 2*. Differences in the amount of venom inoculation in natural bothropic accidents have been reported in livestock and assuredly can influence the clinical course and outcome [21,22]. Therefore, it is possible to speculate that individual sensitivity, favorable conditions, and dose of *B. moojeni* venom inoculation have influenced the clinical evolution, outcome, and successful therapeutics in the naturally envenomed dog.

Envenomation-associated systemic changes such as thrombocytopenia and increased blood clotting time observed in *case 1* are possibly a consequence of combined activities of serine proteases and metalloproteinases within the *Bothrops* venom resulting in coagulopathies [17]. Additionally, metalloproteinases cause degenerative lesions in the vessel wall predisposing to vascular fragility and hemorrhages [17], which were also detected as fractions of the *B. moojeni* venom [6]. An increased blood clotting time is a significant change observed in humans envenomed by *B. moojeni* [13]. Bleeding disorders are also one of the main hallmarks of *Bothrops* envenomation in domestic animals [15,16]. As a result of the systemic manifestation of *Bothrops* envenomation, spontaneous hemorrhages in tissues and organs are expected, such as those detected in *case 1*, and multiple hemorrhagic areas in the lethally affected dog.

A severe renal injury is another systemic change related to *Bothrops* envenomation, as observed in *case 2*. Acute kidney injury (AKI) has been reported in humans and animals with *Bothrops* envenomation as a consequence of tubulotoxic damage associated with pigmenturia (myoglobinuria/hemoglobinuria), impaired perfusion, or venom-direct effects [12,15]. Horses with fatal *Bothrops* envenomation showed severe AKI [15], which was associated with the worst prognosis in humans [17]. Despite *B. moojeni* venom causing nephrotoxicity experimentally in rats [2], no significant renal injury was detected in *case 1*, and the dog showed a good prognosis and complete clinical recovery.

Hemorrhages, tissue necrosis, and edema were relevant local pathological features affecting snakebite sites in *cases 1* and *2*. Phospholipase A2 within *Bothrops* venom has been associated with tissue degeneration and necrosis [17]. In humans, severe necrosis of the skin and tissues adjacent to the snakebite site predisposes to secondary bacterial contamination, which may lead to terrible sequels and amputation of limbs [17]. Accidental *B. moojeni* snakebite has also promoted severe tissue damage and sequels in envenomed

humans [13], mainly related to metalloproteases and phospholipases within the venom [6].

Even considering many variables in the treatment of *case 1,* the early and correct application of antivenom sufficient to neutralize 200 mg of *Bothrops* sp. venom was appropriate for those conditions, with the achievement of full recovery. In humans with *B. moojeni* snakebite, a total dose of 187 ± 26 mg of *Bothrops* antivenom was recommended to treat all cases of envenomation [13]. The use of antibiotics and corticoids possibly reduced inflammation and contributed to preventing further local complications at the snakebite site in the dog struck by *B. moojeni*, a typical sequel in humans with *Bothrops* envenomation [13,17]. In *case 1*, the swift identification of the snake and referral of the dog for veterinary care enabled a correct diagnosis and proper treatment, resulting in the complete recovery of the patient, as previously recommended for increasing the success of treatments [11].

The first case of accidental snakebite envenomation by *B. moojeni* in a dog in Brazil is shown herein and evidenced by the scarcity of information about identifying venomous snake species striking domestic animals. Clinical and pathological data and features provided in *cases 1* and *2* are essential to support a fast presumptive diagnosis of *Bothrops* envenomation in dogs, proper therapeutics, and a good prognosis even in cases with an unknown clinical history.

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