

Envenomation by Brown Spider (*Loxosceles* sp.) in a German Shepherd Bitch - Laboratory and Anatomopathological Findings

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ABSTRACT

Background: Although small in size, the brown recluse spider (*Loxosceles* sp.) often has the habit of hiding in intradomestic and dark places, causing accidents in humans and animals. Brown spiders are not aggressive, but bites occur when they are compressed, attacking quickly and leaving immediately, making difficult the spider recognition. The bite is usually painless or similar to a mosquito bite, hampering to perceive the accident, mainly for the owner of small animals. There is currently no antivenom available for veterinary use against arachnid bites, and the delay in suspicion and diagnosis of loxoscelism are usually fatal. This report aimed to describe a case of dermonecrotic lesions suspected of *Loxosceles* sp. bite in a young German Shepherd bitch.

Case: A 6-month-old bitch German shepherd dog, weighing 27 kg, was admitted with a history of swelling in the right forelimb for over a week. Clinical examination revealed stupor, pale mucous membranes, and enlarged lymph nodes. Edematous hematomas on the forelimb, spreading widely over the ventral abdominal region were noted, including necrosis and a small double perforation (~0.3 cm) in the axillary region, like inoculation by spider chelicerae. Leukocytosis, elevated platelet aggregation, and high fibrinogen led to the suspicion of a brown spider bite. Uremia, hypoalbuminemia, and elevated alkaline phosphatase, together with urinalysis (intense proteinuria and occult blood) indicated acute kidney failure. The radiography showed soft tissue enlargement in the right forelimb. Ultrasonography revealed liver condition and splenomegaly. Despite administering emergency supportive care, the patient died 12 h after admission. Necropsy revealed necrotic dermatitis and necrohemorrhagic myositis, renal (acute toxic tubular) and hepatic necrosis, pulmonary edema, splenic congestion, myocardial infarction, and stroke, showing critical systematic alterations compatible with the myonecrotic and hemorrhagic action of the brown spider venom. Although the spider was never found, this case reinforces the prompt treatment and thorough clinical inspection for the accurate diagnosis of loxoscelism.

Discussion: The bitch presented the viscerocutaneous form of loxoscelism, there is an aggressive and fatal presentations, with necrotic areas in the forelimb and ventral abdomen, besides leukocytosis, platelet aggregation, thrombocytopenia, proteinuria, and occult blood in urine. Considering that the swelling in the forelimb was noticed by the owner for more than a week and that the dog was belatedly taken to the veterinary hospital, its clinical condition has worsened, compromising the systemic organs. *Loxosceles* sp. venom inactivate the serum hemolytic complement, inducing rapid coagulation and occlusion of small capillaries, and subsequent tissue necrosis. Necrotic signs are mainly caused by proteins belonging to the phospholipase D family (“dermonecrotic toxins”), which are also responsible for hemolysis, thrombocytopenia, and renal failure. Due to the delay in obtaining veterinary intervention since the history and the systemic complications, the animal died. The necropsy showed intense necrosis at the muscular level and in systemic organs, as noted in the right forelimb, kidneys, liver, brain, and heart. The pathological findings were compatible with accidents with poisonous animals in which their toxins have myonecrotic and hemorrhagic action. Together with the presence of small double perforation in the forelimb, suggestive of inoculation by spider chelicerae, the clinical diagnosis was concluded. Although the spider was never found, this case reinforces the prompt treatment and thorough clinical inspection for the accurate diagnosis of loxoscelism.

Keywords: brown spider, *Loxosceles* spp., loxoscelism, dog, poisoning, toxicology.

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INTRODUCTION

Loxosceles sp. ("brown spiders") comprises more than a 100 species [15] and is present on different continents, as *L. laeta* in South America, the USA, Finland and Australia; *L. gaucho* in Brazil and Tunisia; and *L. rufescens* in Mediterranean countries [16], America, Africa, China and Australia [15], showing a global distribution. Brown spider is not aggressive, but bites occur when they are compressed, attacking quickly and leaving immediately, making difficult the spider recognition [13]. Moreover, the bite is usually painless or similar to a mosquito bite [16], hampering to perceive the accident, mainly for the owner of small animals.

Due to its small size, measuring about 1-3 cm in total length [2] and its high intra-domicile infestation capability, brown spiders play the leading role in spider envenomation [5], and 6,390 human accidents were caused by *Loxosceles* sp. (loxoscelism) only in 2022 in Brazil [3], mainly in Southern Brazil [16]. In this region, although only 8 cases of accidents with brown spiders have been recorded in dogs and cats between 2020 and 2021 [4], this does not correspond to reality, since accidents are scarcely diagnosed and/or reported, due to the owner's difficulty in recognizing them. In this way, the veterinary diagnosis is often based on history, clinical signs, and geographic region [13].

Although Brazil is known for being self-sufficient in the production of antivenom serums [5], there is no anti-arachnid serum available for veterinary use, and the delay in suspicion and diagnosis of loxoscelism are usually fatal. This report describes a case of dermonecrotic lesions suspected of *Loxosceles* sp. bite in a young German Shepherd bitch.

CASE

A 6-month-old German Shepherd unneutered bitch weighing 27 kg was admitted at the Veterinary Clinic Hospital (UFPEL, Pelotas, RS). The owner noticed swelling in the right forelimb for more than a week and administered the antibiotic azithromycin (500 mg) and silver spray to the lesions (twice a day) for a week on his own, without a veterinary prescription. No improvement was noted in the animal during this period.

Clinical alterations showed stupor, pale mucous membranes, tachycardia (110 bpm) and enlarged prescapular and axillary lymph nodes, but no fever (38.4°C). Edematous hematomas on the forelimb, spreading widely over the ventral abdomen were noted,

including necrosis and a small double perforation in axillary region, like inoculation by spider chelicerae, with exudative and putrid smell.

Leukocytosis (19,900/ μ L; ref. 6,000-17,000/ μ L), platelet aggregation (++; ref. absence), low platelets (113×10^3 / μ L; ref. 200-500 $\times 10^3$ / μ L), and high fibrinogen (1,000 mg/dL; ref. 150-490 mg/dL) led to the suspicion of a brown spider bite. Uremia (70.65 mg/dL; ref. 21.4-59.92 mg/dL), hypoalbuminemia (1.52 g/dL; ref. 2.6-3.3 g/dL), and high ALP (649.8 IU/L; ref. 21-102 IU/L) indicated possible hepatic and renal alterations. The high protein-creatinine urinary ratio (2.75; ref. <0.5), and occult blood (++; ref. absence), along with uremia, indicated acute kidney failure.

Radiography showed soft tissue enlargement in the right forelimb (Figure 1A). Ultrasonography showed enlarged liver (Figure 1B), splenomegaly, and large medial iliac lymph node (0.99 cm, Figure 1C). The other organs were found within the physiological parameters for the species.

Adding these alterations to the suspicion of a brown spider bite, an emergency support treatment was instituted. Fluid therapy with Ringer-Lactate was initiated upon patient admission, followed by prednisone¹ (1 mg/kg, 12/12h), and enrofloxacin² (10 mg/kg, 24/24h), in addition to urinary catheterization. Due to the patient's severe pain, tramadol¹ (5 mg/kg) associated with dipyrone³ (25 mg/kg) was applied for analgesia. The lesions were cleaned and debrided, and a topical ointment containing gentamicin sulphate, sulphanilamide, sulfadiazine, urea and vitamin A (Vetaglós[®])⁴ was applied. Due to the absence of veterinary antiloxoscelic serum, it was not possible to administer specific treatment. In the following 12 h, the patient still had severe pain and an analgesic infusion was performed in a continuous way. Unfortunately, the patient died on the same day of hospitalization.

In the necropsy, a small double perforation (~0.3 cm = 3 mm) compatible with spider chelicerae bite was noted (Figure 2A). The large tracts of muscle tissue (Figure 2B), necrosis and hemorrhage (Figure 2C & D) and cellulitis (Figure 2E) were characteristic of necro-hemorrhagic myositis and necrotizing dermatitis, respectively. In the systemic organs (Figure 3), there was a hemoperitoneum, an enlarged spleen, and the presence of darkened contents in the stomach, whose gastric mucosa was reddish. Pancreas was hemorrhagic and liver showed massive hemorrhagic hepatic

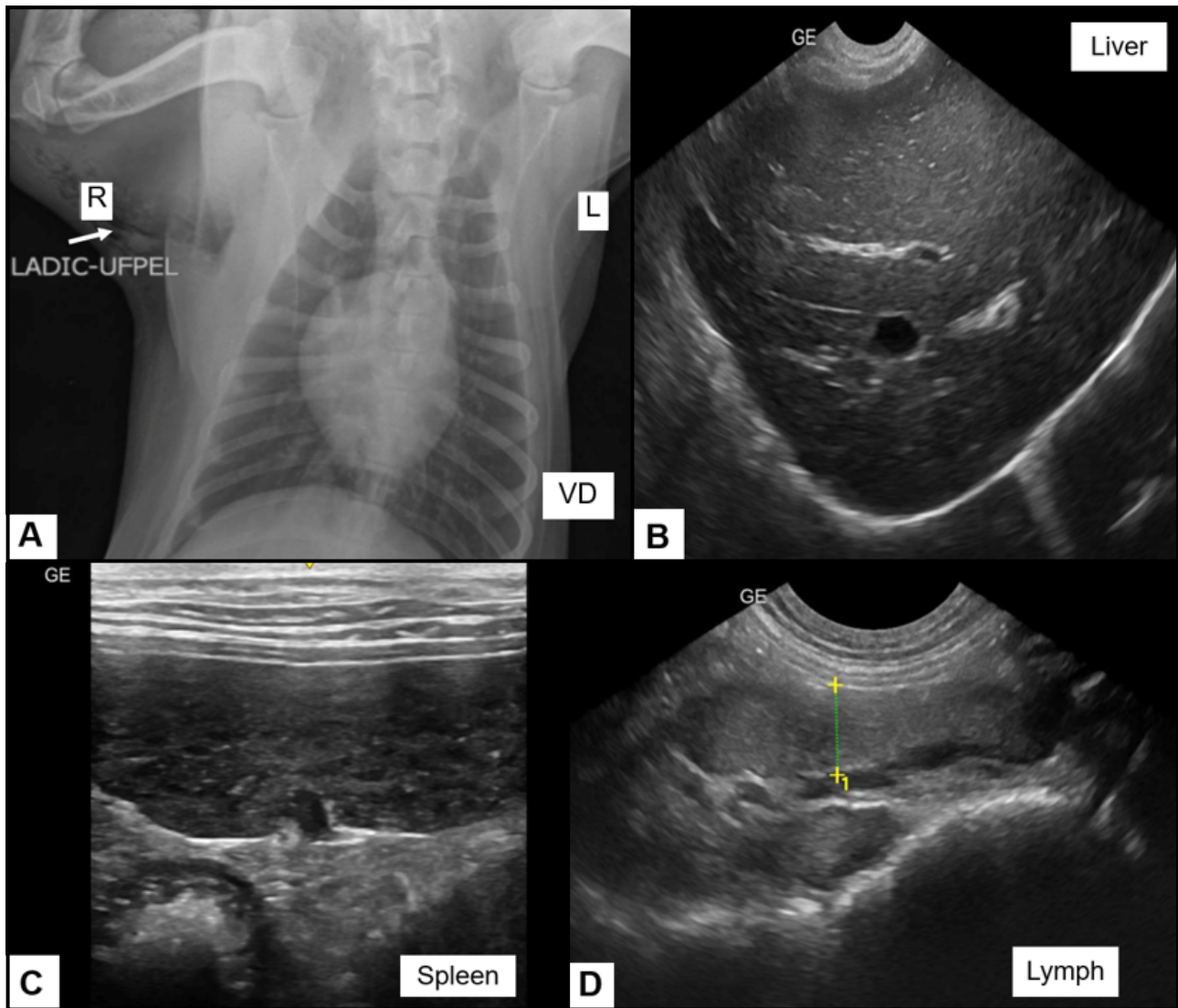


Figure 1. Chest X-ray (A) in ventrodorsally (VD) projection in a 6-month-old bitch German Shepherd, non-neutered, treated in Pelotas, RS (Southern Brazil) with a history of edema in the right thoracic limb for more than a week. Note the increase in soft tissue volume (white arrow) in the right limb (R) compared to the left limb (L). Ultrasound examination showed liver alterations, which presented increased dimensions and decreased echogenicity (B), as well as splenic alterations, whose spleen presented reduced echogenicity and parenchyma with a “tied” appearance, due to the presence of small rounded and hypoechoic areas (C). Furthermore, dimensioning the medial iliac lymph node by 0.99 cm revealed that it had an enlarged dimension (D, reference value: 5 mm).

necrosis. Microscopically, the stomach, duodenum, pancreas, and liver presented massive hemorrhagic necrosis, especially in the liver.

The heart was also enlarged, with the left side close to the aortic lunette and with a firm nodule, 0.1 cm in diameter, yellowish, in addition to a dilated vena cava. In the lungs, intense pulmonary edema, with congestion and hemorrhage, affected approximately 80% of the organ. The right renal capsule was adherent, and the consistency of both kidneys was soft to the touch. Brain was hemolyzed and congested and there was bloody fluid between the meninges with focal regions of ischemic and hemorrhagic necrosis.

The anatomopathological findings were consistent with the myonecrotic and hemorrhagic action of the brown spider venom.

DISCUSSION

There are 2 clinical forms of loxoscelism: the cutaneous and viscerocutaneous [13]. At the site of the bite, there is little or no pain at first, developing itching, pain, swelling, and target damage within 3 to 8 h and turning into a necrotic area within [10] with an eschar covering a deep ulcerated wound that heals slowly [13]. This is the common presentation (cutaneous form) and secondary infections may occur [13].

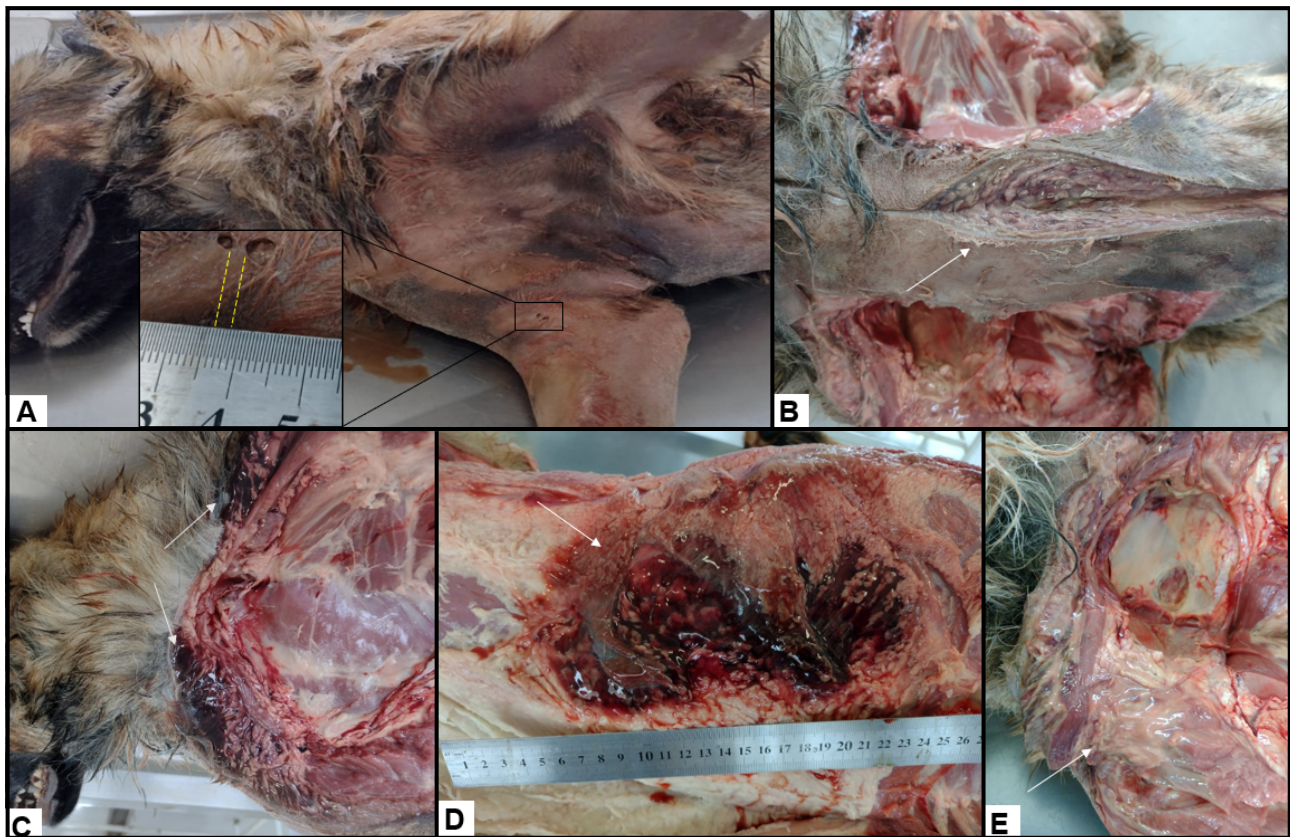


Figure 2. Necropsy of a bitch German shepherd with suspected envenomation by a brown spider bite (*Loxosceles* sp.), due to the presence of a small double cutaneous perforation (~0.3 cm = 3 mm) in the radio-ulnar region of the right forelimb (A, enlarged detail), characteristic of chelicerae inoculation in spiders, in addition to dark areas on the right and left forelimbs. Large tracts of muscle tissue (B) with necrosis and hemorrhage (C and D), as well as cellulitis (E), were characteristic of necrohemorrhagic myositis and necrotizing dermatitis, respectively. These findings were consistent with myonecrotic, and hemorrhagic action triggered by toxins present in brown spider venom, evidencing the suspicion of loxoscelism.

However, when systemic reactions occur within 6 to 24 h, such as severe hemolytic anemia, hemoglobinuria, hematuria, thrombocytopenia, leading to generalized intravascular coagulation and systemic organ failure, as renal failure [14], this form is aggressive and fatal (viscero-cutaneous form) [13], which it was noted in the reported animal. The bitch presented leukocytosis, platelet aggregation, thrombocytopenia, proteinuria, and occult blood in urine, besides necrotic areas in the forelimb and ventral abdomen. Considering that the swelling in the forelimb was noticed by the owner for more than a week and that the bitch was belatedly taken to the veterinary hospital, its clinical condition has worsened, compromising the systemic organs.

Loxosceles sp. venom inactivate the serum hemolytic complement, inducing rapid coagulation and occlusion of small capillaries, and subsequent tissue necrosis [14]. The coagulation profile (prothrombin time, partial thromboplastin time, platelet count, and fibrinogen) is important to assess whether there is an extension of the cutoff time [13], but it was not possible

to carry it out. Necrotic signs are mainly caused by proteins belonging to the phospholipase D family, popularly known as “dermonecrotic toxins”, due to the induction of an inflammatory response, dermonecrosis, hemolysis, thrombocytopenia, renal failure [8], causing systemic effects and death, beyond edema and local tissue inflammation [13].

The uremia (70.65 mg/dL) indicated kidney injury, but this is not a specific marker. When analyzing together with urinalysis [proteinuria (+), hematuria (++) and high urinary protein-creatinine ratio (2.75)], the acute kidney failure was recognized. Intravascular hemolysis developed in the patient’s kidneys led to inflammation and adhesion of the renal capsule during the release of necrotic cells into the tubular lumen [9], which had amorphous reddish material intratubular and in Bowman’s space. When evolve into acute renal failure, this is the main cause of death by loxoscelism [13].

Due to skin changes and extensive local tissue necrosis, mycobacterial infections, decubitus ulcers, 3rd-degree burns and pyoderma are conditions

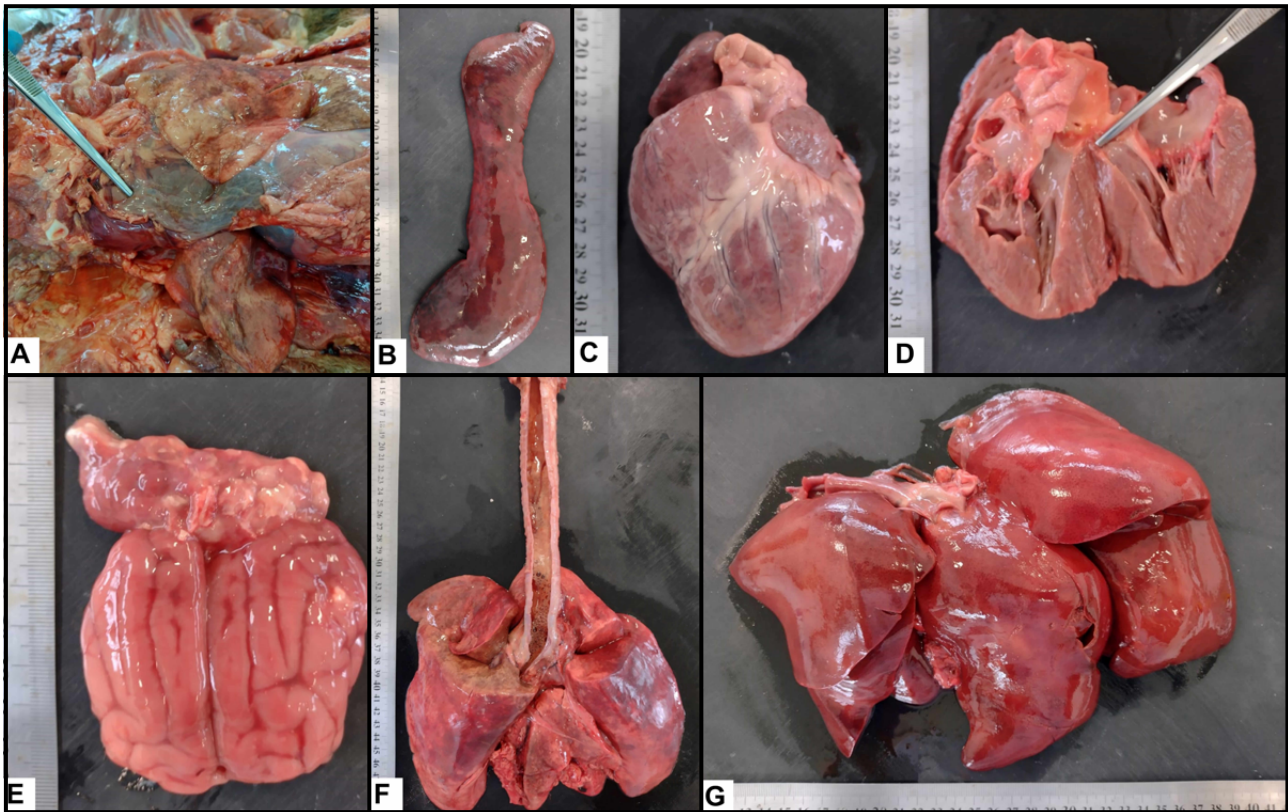


Figure 3. Pathologic findings of systemic organs in a bitch German shepherd with suspected accidental brown spider (*Loxosceles* sp.) bite. Presence of hemoperitoneum (A), enlarged spleen (B), and globular heart (C) which, when opened, revealed the presence of a firm, yellowish nodule, and dilated vena cava (D), indicating infarction. In the brain (E), the presence of bloody fluid content and a congested brain suggested stroke. In the lung (F), there was severe pulmonary edema with congestion and hemorrhage, in addition to hepatic necrosis (G).

that should be considered as a differential diagnosis [14]. Systemic signs must be distinguished from other disorders that cause hemolytic anemia (such as immune-mediated anemia, zinc, onions, or acetaminophen poisoning), snake bites, or parasitic infections [13]. The presumptive diagnosis hemoparasitosis was discarded after a negative result in the blood exam, and the presence of small double perforation in the forelimb, allied to the edematous and necrotic lesion, were strongly suggestive on brown spider bite. Due to the extent of the lesions and the delay in obtaining veterinary intervention, the bitch unfortunately died, so not enough time could be provided to initiate any specific treatment. Although antiloxoscelic serum is used to neutralize toxins in humans, there is no specific antidote for veterinary use in Brazil [9].

Therapy is based on several daily cleanings with hydrogen peroxide [14] or soap and water, preventing secondary infection [13] and some debridement [14]. Fluid therapy with Ringer Lactate, broad-spectrum antibiotics, opioids, corticosteroids, and antipyretic and analgesic agents can be useful [14]. The

wound must be cleaned, and cold compresses should be applied to reduce pain and swelling, in addition to the application of ointments for healing [6]. In humans, tetracycline reduces kidney damage [12] and plasma exchange improved the clinical condition for systemic form [1] and can be valid in veterinaries cases.

Although surgical incision was recommended in the past, this method is no longer indicated due to postoperative complications [14]. Nowadays, studies involving recombinant toxins for generates neutralizing antibodies [11] and immunization protocol with synthetic antigenic determinants [6] are promising for therapy. These findings may represent a new path for developing antivenom manufacture, as well as better support for diagnosis and treatment.

Due to delayed veterinary intervention and systemic complications, the animal died. Although there are no definitive systemic or histologic lesions in dogs and cats victims of accidents with brown spiders [14], the necropsy showed intense necrosis at the muscular level and in systemic organs, as noted in the right forelimb, kidneys, liver, brain, and heart.

The enlargement of the spleen happened due to severe hemorrhage and congestion that distorted the architecture of the organ [7], whereas the enlargement of the heart and vena cava happened due to necrosis of cardiomyocytes and endothelium [7,9], with the left side of the heart approaching the aortic lunates. In the remaining organs, the massive hemorrhagic necrosis found in liver, lungs, stomach, duodenum, pancreas and brain were consequence of the lytic activities of the toxic enzymes present in the brown spider venom, as platelet aggregation, local ischemia, followed by necrosis [8,14]. The pathological findings were compatible with accidents with poisonous animals in which their toxins have myonecrotic and hemorrhagic action. Together with the presence of small double perforation in the forelimb, suggestive of inoculation by spider chelicerae, the clinical diagnosis was concluded.

The present case reported a fatal accident in a bitch caused by the venom of Brown Spider (*Loxosceles* sp.). Although the tutor did not see the brown spider, the presence of 2 small perforations on the right limb was compatible with inoculation by spider chelicerae. Symptoms such as edema, bruises, and necrosis in the right forelimb for about a week, in addition to systemic

involvement, reinforced the suspicion of loxoscelism. However, the delay in receiving suitable treatment and the clinical condition of the patient led to death.

The anatomopathological findings were consistent with the myonecrotic and hemorrhagic action of the brown spider venom. This case reinforces the importance of prompt treatment and thorough clinical inspection for the accurate diagnosis of loxoscelism.

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