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Challenges in the diagnosis and management of brown widow spider (*Latrodectus geometricus*) envenomation in dogs

Desafios no diagnóstico e manejo do envenenamento por aranha viúva marrom (*Latrodectus geometricus*) em cães

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Willer Alves Santana
ORCID: https://orcid.org/0009-0005-6738-6934
Universidade de Uberaba (UNIUBE) – Uberaba, MG
E-mail: willer.veterinario@gmail.com
Isabel Rodrigues Rosado
ORCID: https://orcid.org/0000-0001-7819-4253
Universidade de Uberaba (UNIUBE) – Uberaba, MG
E-mail: isabel.rosado@uniube.br
Marina Cazarini Madeira
ORCID: https://orcid.org/0000-0002-0096-2360
Universidade de Uberaba (UNIUBE) – Uberaba, MG
E-mail: marinacazarinimadeira@gmail.com
Marcus Vinícius Caetano de Sousa
ORCID: https://orcid.org/0009-0007-0512-7579
Clínica pulo do Gato Atendimento Veterinário Especializado, Uberaba, MG
E-mail: sousa.marcusviniciusmvet@hotmail.com
Ian Martin
ORCID: https://orcid.org/0000-0001-6934-8257
Universidade de Uberaba (UNIUBE) – Uberaba MGE-mail: ian.martin@uniube.br
Endrigo Gabellini Leonel Alves
ORCID: https://orcid.org/0000-0001-8524-3949
Universidade de Uberaba (UNIUBE) – Uberaba MG
E-mail: endrigoglalves@gmail.com

ABSTRACT

This study reports two cases of araneism in dogs caused by the bite of the brown widow spider (*Latrodectus geometricus*), one of which resulted in death. The first case presented mild signs, successfully treated with medication and ice packs. The second case, more severe, involved exacerbated local signs such as extensive edema and ecchymosis, and diffuse cutaneous hemorrhage in the affected limb, as well as systemic signs, including vomiting, tetraparesis, ataxia, and epileptic seizure, culminating in renal and hepatic failure, circulatory collapse, and death. The treatments employed were based on the symptoms and included the use of analgesics and anti-inflammatories. The study highlights the importance of early diagnosis and appropriate treatment, including the use of specific antivenoms in more severe cases. It emphasizes the importance of preventive measures, such as the use of insecticides, to prevent future accidents. Awareness of the clinical signs of poisoning and the available treatment options is crucial for healthcare professionals and veterinarians to ensure proper management of these incidents and minimize their consequences.

Keywords: Latrodectism; Araneism; Poisoning; Toxicology; Venomous animals

RESUMO

Este estudo relata dois casos de araneísmo em cães causados pela picada da aranha viúva-marrom (*Latrodectus geometricus*), um dos quais resultou em óbito. O primeiro caso apresentou sinais leves, tratados com sucesso através de medicamentos e compressas de gelo. O segundo caso, mais grave, envolveu sinais locais exacerbados, como edema e equimose extensos, e hemorragia cutânea difusa no membro acometido, além de sinais sistêmicos, incluindo vômito, tetraparesia, ataxia e crise epilética, culminando em falência renal e hepática, colapso circulatório e morte. Os tratamentos empregados foram baseados nos sintomas e incluíram o uso de analgésicos e anti-inflamatórios. O estudo destaca a importância do diagnóstico precoce e do tratamento adequado, incluindo o uso de antivenenos específicos em casos mais graves. Ressalta-se a importância de medidas preventivas, como o uso de inseticidas, para evitar futuros acidentes. A conscientização sobre os sinais clínicos do envenenamento e as opções de tratamento disponíveis é crucial para profissionais de saúde e veterinários, a fim de garantir um manejo adequado desses acidentes e minimizar suas consequências.

Palavras-chave: Lactrodectismo; Araneísmo; Envenenamento; Toxicologia; Animais peçonhentos

INTRODUCTION

The brown widow spider (*Latrodectus geometricus*) is one of the thirty-one species of the genus Latrodectus and has gained notoriety due to its potential for envenomation in both humans and animals (Kiriakos et al., 2008; Mokhtar et al., 2021). Although less known in the veterinary field compared to its more famous relative, the black widow (*Latrodectus mactans*), whose venom is more potent, the brown widow still poses a significant risk (Isbister et al., 2003). This species, belonging to the Theridiidae family, has a wide geographical distribution, covering temperate and pantropical ecosystems around the world (Brown, Necaise, Goddard, 2008).

Envenomation caused by *Latrodectus geometricus*, known as latrodectism, is characterized by local and systemic symptoms that range from mild to severe, including acute pain, erythema, and edema at the bite site, as well as systemic manifestations such as cramps, severe muscle pain, nausea, vomiting, and hypertension (Caruso et al., 2021). Although fatal cases in humans are rare, they have been documented, highlighting the importance of recognizing and properly treating these accidents (Keyler et al. 2020). In veterinary medicine, reports of *Latrodectus geometricus* envenomation in domestic animals are even rarer, and fatal cases have not yet been documented (Reyes-Lugo et al., 2009). Early diagnosis and appropriate treatment are essential to prevent fatal outcomes, which include the use of specific antivenom in severe cases (Isbister et al., 2003).

In addition to the direct toxic effects, the venom of *Latrodectus geometricus* contains metalloproteinases that can degrade components of the extracellular matrix, such as fibronectin, laminin, and collagen, contributing to the severity of the symptoms (Guerrero et al., 2010). Knowledge of the venom composition and mechanisms of action is fundamental for the development of effective therapeutic strategies.

Latrodectus geometricus envenomation represents an emerging risk to public and animal health. Awareness of the species' geographical distribution, clinical signs of envenomation, and available treatment options is crucial for health professionals and veterinarians to ensure proper management of these incidents and minimize their consequences. In this context, the present work aims to report and discuss two cases of lactrodectism in dogs, one of which resulted in a fatal outcome, highlighting the importance of veterinary attention to these events and contributing to the knowledge about the clinical management of these cases.

CASE REPORTS

Geographical location characterization of the accidents

Uberaba is a municipality located in the state of Minas Gerais, in southeastern Brazil. The city is situated in the Triângulo Mineiro region, an area known for its economic importance, especially in agriculture and livestock. Uberaba's climate is classified as tropical, characterized by hot and humid summers and dry and relatively cold winters. Temperatures vary throughout the year, with averages ranging from 15°C to 30°C. Summers are hot, with temperatures often exceeding 30°C, while winters are milder, with averages around 15°C to 20°C. The city has a well-defined rainy season, which occurs mainly between October and April. The dry season takes place between May and September, with scarcer precipitation. The relative humidity of the air varies throughout the year, being higher during the rainy season and lower in the dry season. Uberaba is located in a plateau region, with altitudes ranging between 800 and 1,000 meters above sea level. The city is crossed by the Uberaba River and has a landscape marked by cerrado areas and pastures.

Case of Kira: mild araneism manifestation in canine

A canine, American Pit Bull Terrier, female, spayed, 7 years old, and weighing 30 kg, presented to the veterinary clinic with an erythematous and edematous skin lesion in the cervical region. The patient was up-to-date with her vaccination schedule and had undergone a unilateral mastectomy due to a mammary nodule approximately 30 days prior, from which she had satisfactorily recovered. According to the owners, the animal resided in a yard with grass and concrete areas, and had not shown recent signs of vomiting, diarrhea, or inappetence.

The clinical examination revealed a dermonecrotic area of approximately 5 cm in diameter, surrounded by a reddish halo, suggesting possible araneism. The animal's vital signs were within normal parameters, and no other clinical symptoms were observed. A complete laboratory profile, including complete blood count, glucose, urea, creatinine, transaminases (oxaloacetic and pyruvic), alkaline phosphatase, gamma-glutamyl transferase, lipidogram, and total proteins and fractions, showed no abnormalities.

Given the suspicion of a spider bite, symptomatic treatment was instituted with enrofloxacin (5 mg/kg, SID), tramadol hydrochloride (4 mg/kg, BID), dipyrone (25 mg/kg, BID), meloxicam (0.1 mg/kg, SID), and application of ice packs for 15 minutes, four times a day. The treatment was successful, and the episode did not result in major complications for the animal. The owners were advised to immediately carry out pest control in the residence to prevent new incidents.

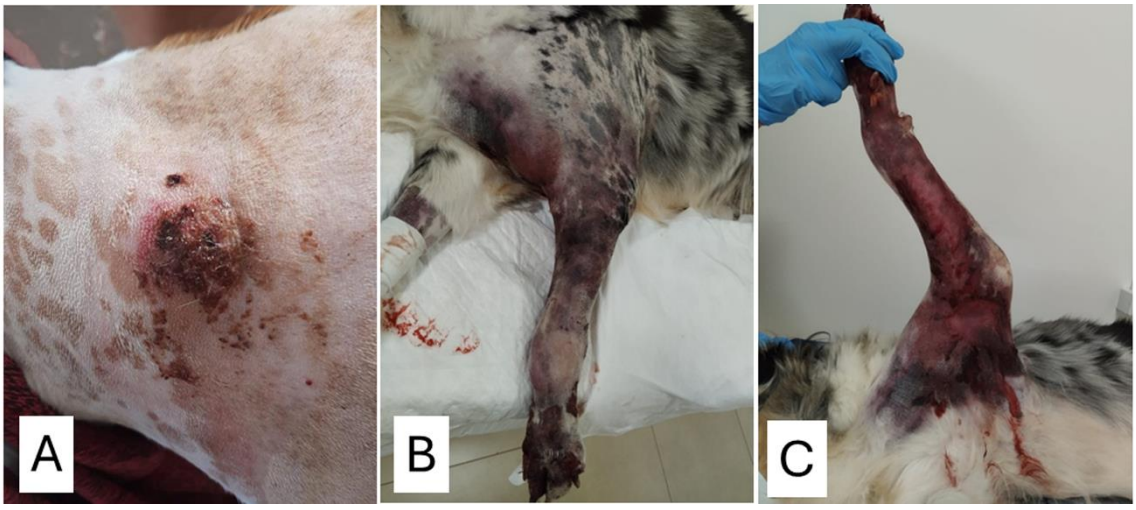
Case of Troya: Severe araneism manifestation in canine

A Border Collie, female, fertile, 4 years old, and weighing 30.1 kg, was evaluated due to lameness and discomfort in the left thoracic limb. The animal had an uneventful clinical history, with up-to-date vaccinations, residing in a domestic environment with a mixed outdoor space, grassy and cemented, sharing the area with other dogs, including the one from the previously described case.

On the eve of the consultation, the dog had been sedated for blood collection from the jugular vein, with multiple attempts at puncturing the cephalic vein and suspicion of propofol extravasation into the subcutaneous tissue. Consequently, topical treatment with an anti-inflammatory gel containing dimethyl sulfoxide (DMSO), dexamethasone, and lidocaine (DM-gel, Vetnil, São Paulo, Brazil) was prescribed for relief of inflammation and discomfort.

Physical evaluation revealed pain, edema, and hyperthermia in the affected limb. Initially, phlebitis was suspected due to the punctures and possible extravasation of propofol. The patient was hospitalized for observation and treatment, which included dipyrone (25 mg/kg, IM, Dipirona Ibasa, Rio Grande do Sul, Brazil), meloxicam (0.1 mg/kg, IM, Maxicam Injectable Solution 0.2%, São Paulo, Brazil), methadone (0.3 mg/kg, IM, Mytedon, Cristália, São Paulo, Brazil), and amoxicillin with clavulanate (15 mg/kg, Eurofarma, São Paulo, Brazil), in addition to maintenance fluid therapy with Ringer's Lactate (Isofarma, Ceará, Brazil). Blood tests [Complete Blood Count, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Gamma Glutamyl Transferase (GGT), Total Proteins and Fractions, Glucose, Cholesterol and Fractions] showed no abnormalities.

Figure 1: Lesions in two dogs after bites from brown widow spiders (*Latrodectus geometricus*). (A) Dermonecrotic lesion of approximately 5 cm in diameter with a reddish halo on the left lateral cervical region (patient Kira). (B) Left thoracic limb with edema, ecchymosis, and diffuse cutaneous bleeding (lateral view). (C) Detail of the lesions in the same region (medial view).

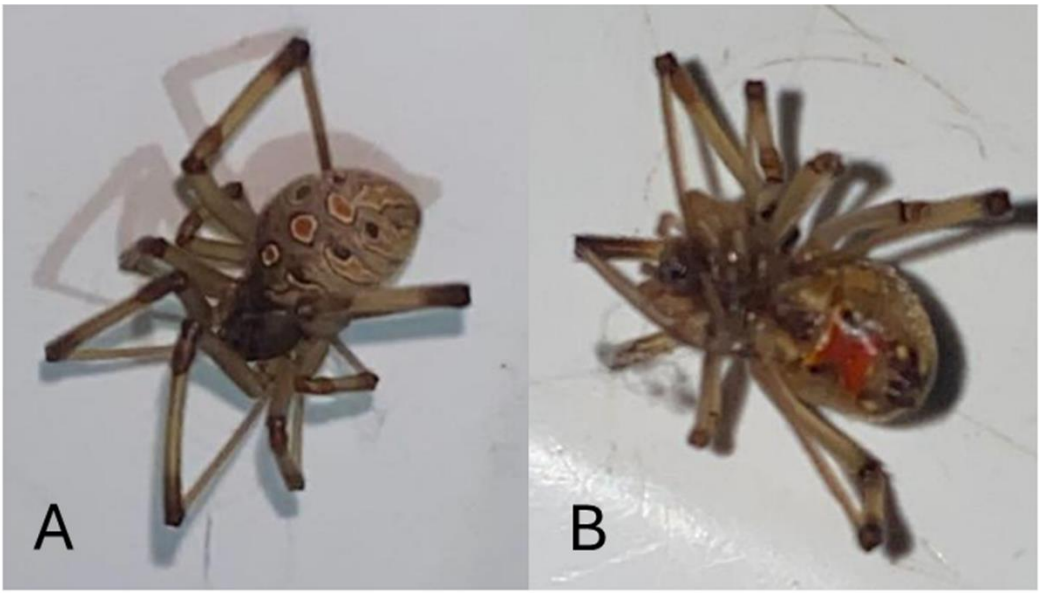


After 6 hours of hospitalization, the patient showed worsening of the clinical condition with an increase in the swollen area, appearance of ecchymosis in the left thoracic limb, and acute vomiting. The treatment administered was maropitant citrate (1mg/kg, SC, Cerenia, Pfizer, France) and omeprazole (1mg/kg, IV, Cristália, São Paulo, Brazil). At this point, araneism was suspected, the topical treatment with DMgel was discontinued, and the application of ice packs was initiated.

Approximately 12 hours after hospitalization, the clinical condition further deteriorated, with edema, ecchymosis, and diffuse cutaneous bleeding throughout the left thoracic limb. In addition, ambulatory tetraparesis, ataxia, and an episode of epileptic seizure were observed. All blood tests were repeated and showed thrombocytopenia (79,000/mm³ platelets), left shift (3,007/mm³ bands, relative value of 31%), acute hepatic injury (AST 191.0 U/L; ALT 244.0 U/L; ALP 187.0 mg/dL and GGT 66.0U/L), and also acute renal injury (Urea 183.0 mg/dL and Creatinine 3.6 mg/dL).

In the following four hours, the patient developed anuria and hypothermia, with the rectal temperature dropping to 35.4°C. Additionally, hypotension was observed, with blood pressure difficult to measure, remaining around 55 mmHg. Measures were taken to warm the patient using thermal bags, and a fluid challenge was conducted with the administration of Ringer's Lactate (Isofarma, Ceará, Brazil) at an infusion rate of 15 ml/kg for 15 minutes, but without success. Subsequently, continuous infusion of norepinephrine at a dosage of 0.05 g/kg/min (Hypofarma, Minas Gerais, Brazil) was initiated in an attempt to reverse the hypotension, but all attempts were futile. Unfortunately, the patient died approximately 19 hours after the initial consultation. Due to the distress caused by the situation, the owners opted not to authorize the necropsy

Figure 2: Brown widow spider (*Latrodectus geometricus*) specimen found in the yard of the reported patients' residence, where they spent most of their time. (A) Dorsal view, highlighting the light brown to grayish coloration and circular black and orange spots. (B) Ventral view, showing the characteristic orange hourglass-shaped mark on the lower abdomen.



The suspicion of arachnism led the owners to hire a specialized company to apply insecticide in the residence and yard where the dogs spent most of their time. Approximately 15 hours after the initial treatment, two spiders were found in the area where the dogs used to stay. The spiders had a light brown-grayish color with circular black and orange spots on the dorsal region, and an hourglass-shaped spot on the lower abdomen in orange color. The body length was 12 mm (Figure 2).

DISCUSSION

The importance of studying araneism caused by the brown widow spider (*Latrodectus geometricus*) is evidenced by its global distribution (Brown, Necaise, Goddard, 2008; Vetter et al., 2012; Muslimin et al., 2015; Keyler et al., 2020; Khamtorn et al., 2020; Caruso et al., 2021) and reports of human envenomation (Goddard et al., 2008; Kiriakos et al., 2008; Almeida et al., 2009; Monte, Bucher-Bartelson, Heard, 2011; Earwood, Ladde, Giordano, 2020; Mokhtar et al., 2021). The presence of the brown widow has been confirmed in almost all countries of the Americas, including Brazil, indicating its wide distribution and potential to cause accidents in various regions. The recent introduction of this species into new territories underscores the importance of monitoring its spread and impact on public health (Caruso et al., 2021).

This study is one of the first reports of an accident involving brown widow spiders in animals and the first with a fatal outcome in dogs, considering the databases consulted (PubMed, Scopus, Web of Science, Science Direct; Google Scholar). Death from araneism related to an accident involving the black widow spider (*Latrodectus mactans*) has been reported in humans and was associated with an anaphylactic reaction related to the use of antivenom (Isbister et al., 2003; Caruso et al., 2021). It is believed that accidents involving brown widow spiders in animals are more common than scientific evidence suggests, as the diagnosis is difficult because the spider bite is rarely witnessed by a human. Diagnosis is often based on clinical signs and the presence of the spider in the animal's habitat.

The spiders found in the report exhibit morphological and coloration characteristics typical of the species *Latrodectus geometricus*, known as the brown widow. These spiders have a body color ranging from light brown to dark brown, which aids in camouflage in various environments. A distinctive feature is the presence of a distinctive hourglass or diamond-shaped pattern on the underside of the abdomen, which

is a clear indicator of the species. The females, which are typically larger than the males, can vary in length from 6 to 20 mm (Earwood, Ladde, Giordano, 2020; Khamtorn et al., 2020; Khamtorn et al., 2021; Mokhtar et al., 2021). These morphological and coloration characteristics are consistent with the descriptions of *Latrodectus geometricus* in the scientific literature.

The differential diagnosis for the reported cases of brown widow poisoning includes various conditions that can present similar symptoms. Among them are the bite of other cytotoxic spiders, which can cause similar local lesions; the scorpion sting, which can cause intense pain and systemic symptoms; and the snake bite, which can lead to neurological and hemorrhagic manifestations (Almeida et al., 2009).

The geographical location and climate are factors that can influence the distribution and behavior of spiders of the genus Latrodectus, including the brown widow (Vetter et al., 2012). The tropical climate, with periods of rain and heat, favors the proliferation of insects, which are potential prey for spiders. Additionally, cerrado and pasture areas provide natural shelters for these arachnids. The occurrence of accidents with brown widows in urban and rural areas of Uberaba may be associated with the adaptation of these spiders to environments modified by humans, including backyards, gardens, and residences. It is important to highlight that knowledge about the geographical distribution and ecological aspects of brown widow spiders in Brazil is still limited. The presence of *Latrodectus geometricus* and lactrodectism had not yet been documented in the municipality of Uberaba. Additional studies are needed to better understand the relationship between environmental characteristics, such as climate and habitat, and the presence of these spiders in different regions of the country.

The venom of the brown widow contains a variety of bioactive components, including latrotoxins, apolipophorins, hemocyanins, chitinases, arginine kinase, allergen antigen 5-like protein, astacin-like metalloproteinases, and serine proteases, which are responsible for a range of high morbidity symptoms (Khamtorn et al., 2020), being compatible with the findings of the cases reported here.

Local signs, such as edema, erythema, and pain, observed in both canine patients of this report, are commonly reported in cases of araneism by brown widow in humans (Goddard et al., 2008; Almeida et al., 2009; Monte, Bucher-Bartelson, Heard, 2011; Earwood, Ladde, Giordano, 2020; Mokhtar et al., 2021). Although the neurotoxic fraction of the brown widow venom is more studied, it is known that the metalloproteinases present in the spider's venom are also important and contribute to dermonecrosis, as

observed in the first case described in this study (Kira). The dissemination capability of these enzymes is not yet fully understood, but it is believed that collagen degradation compromises the integrity of the extracellular matrix of capillary vessels. This process may facilitate and potentiate the rapid dispersal of toxins to the target tissues during spider envenomation, increasing the severity of the clinical picture as observed in the second case described (Troya). The ecchymosis and diffuse cutaneous bleeding observed in the left thoracic limb of this patient are more concerning and had not yet been reported in cases of accidental latrodectism. It is plausible to consider that these symptoms are related both to the uniqueness of the individual reaction of the patient Troya and the specificities of the envenomation process, such as the composition and amount of venom inoculated by the spider. Furthermore, the influence of the DMgel medication on the worsening of the case is undeniable, as the dimethyl sulfoxide present in the medication is a potent carrier and certainly contributed to the greater distribution and rapid spreading of the venom.

Intense and burning local pain is a common characteristic of latrodectism and is often the first symptom to be noticed after the bite. The pain is caused by the release of neurotransmitters, such as acetylcholine and norepinephrine, induced by the venom, leading to excessive stimulation of sensory nerve endings (Caruso et al., 2021). The observed swelling may be the result of vasodilation and increased vascular permeability induced by inflammatory mediators released in response to the venom. These mediators, including histamine, serotonin, and bradykinin, can cause the leakage of fluids from blood vessels into the surrounding tissue, leading to swelling (Reyes-Lugo et al., 2009). The bruising, ecchymosis, and diffuse cutaneous bleeding observed in the left thoracic limb of the dog Troya can be explained by the combination of vasodilation, increased vascular permeability, and effects on blood coagulation. Additionally, the venom of the brown widow spider can cause direct damage to the endothelial cells of blood vessels, exacerbating the bleeding (Guerrero et al., 2010).

The systemic symptoms observed in the patient Troya, such as vomiting, ambulatory tetraparesis, and ataxia, have already been documented in reports of accidental envenomation by brown widow spiders in humans (Goddard et al., 2008; Kiriakos et al., 2008; Almeida et al., 2009; Monte, Bucher-Bartelson, Heard, 2011; Earwood, Ladde, Giordano, 2020; Mokhtar et al., 2021) and in experimental studies with mice (Reyes-Lugo et al., 2009). However, the occurrence of epileptic seizures and renal and hepatic failure, followed by circulatory collapse, represents more severe

manifestations that had not yet been described in works related to human envenomation. The systemic manifestations can be attributed to a series of pathophysiological mechanisms triggered by the toxins present in the venom. Seizures may occur due to excessive release of neurotransmitters, such as glutamate and aspartate, which are excitatory mediators of the central nervous system. α-Latrotoxin, one of the main toxins of Latrodectus venom, induces the massive release of these neurotransmitters, leading to neuronal hyperexcitation and potentially to convulsive crises (Caruso et al., 2021). Acute renal injury may be the result of rhabdomyolysis, a condition in which there is skeletal muscle injury with the release of myoglobin into the circulation, which can lead to tubular obstruction and renal damage (Monte, Bucher-Bartelson, Heard, 2011). In addition, dehydration resulting from vomiting can contribute to the reduction of renal blood flow and aggravate the injury.

Renal and hepatic injuries may be correlated with the direct effects of components of the brown widow spider venom on these organs. The venom has demonstrated proteolytic activities that degrade extracellular matrix proteins, such as fibronectin, laminin, and collagen, which are essential for tissue integrity. The degradation of these proteins can induce inflammatory processes, contributing to injuries in distant organs, including kidneys and liver. Furthermore, the fibrinogenolytic activities of the venom can affect hemostasis, leading to hemorrhagic syndromes that exacerbate organ damage (Guerrero et al., 2010). In addition, the hypoxia resulting from hemodynamic changes and the pro-inflammatory state triggered by the venom can contribute to the injuries.

In addition to its neurotoxic, proteolytic, and hemorrhagic effects, the venom of the brown widow spider is capable of causing acute adrenal insufficiency, which may have been a critical factor in the death resulting from the poisoning of the second patient in this report (Troya). The lesions observed in the adrenal cortex, especially in the endothelial capillaries and mitochondrial membranes, can induce acute adrenocortical failure, clinically manifested by circulatory collapse, severe hypotension, and neurological changes. These alterations suggest severe adrenal dysfunction, which, together with hemostatic disorders and the degradation of extracellular matrix proteins (Guerrero et al., 2010).

It is believed that the death of the reported patient may have been influenced by all the factors discussed, but the delay in diagnosing brown widow spider envenomation and the unavailability of antivenom were the most critical points. The suspicion of envenomation only arose after the discovery of two brown widow specimens, several

hours after the event, when the patient had already been treated with DMgel and presented a severe clinical picture. Systemic complications, including renal and hepatic dysfunction, cardiovascular changes, and severe neurological disorders, were already established at the time of diagnosis and contributed to the fatal outcome.

The treatments performed on the dogs in the reported case of *Latrodectus geometricus* poisoning were based on the symptoms presented and involved the use of antibiotics, analgesics, anti-inflammatories, and ice packs. This approach was effective in the less severe case (Kira). These approaches are similar to those described in other studies for managing latrodectism in humans. Most cases of latrodectism from brown widow spiders in humans have presented with mild clinical features, predominantly local signs, and have been treated symptomatically (Almeida et al., 2009; Monte, Bucher-Bartelson, Heard, 2011; Mokhtar et al., 2021). The most commonly used treatments include muscle relaxants, opioids, benzodiazepines, calcium gluconate, and non-steroidal anti-inflammatory drugs (Kiriakos et al., 2008; Almeida et al., 2009; Monte, Bucher-Bartelson, Heard, 2011; Mokhtar et al., 2021), although the efficacy of some of these treatments is questionable as they do not neutralize the effects of the venom (Goddard et al., 2008; Earwood, Ladde, Giordano, 2020).

The most severe case (patient Troya) would certainly have benefited from the use of antivenom, which was not available. Antivenom for Latrodectus is rarely used, with usage rates in the United States ranging from 2.2 to 3.8%. Concerns about its use in less severe cases increased after reports of deaths from anaphylactic reactions (Isbister et al., 2003; Keyler et al., 2020; Caruso et al., 2021). Antivenom is recommended for severe cases, with positive outcomes in quickly resolving acute pain and discomfort symptoms (Isbister et al., 2003; Keyler et al., 2020). However, there is no specific antivenom for *Latrodectus geometricus*, but this is not a problem as studies have shown cross-reactivity, meaning that any anti-Latrodectus serum can be effective in treating envenomations by different species of Latrodectus and other spiders of the family Theridiidae. The antivenom produced by the Vital Brazil Institute against the venom of *Latrodectus curacaviensis* may be a safe option for treating black widow envenomation in Brazilian territory (Caruso et al., 2021). Species identification is not clinically relevant, as all patients tend to respond well to antivenom. Antivenom use is recommended, especially in severe cases, and outcomes are generally very good.

Another possible treatment that was not used in the reported cases is the use of calcium channel blockers. Since Latrodectus venom causes massive release of

neurotransmitters through activation of presynaptic calcium channels, the use of blockers of these channels may help attenuate the neurotoxic effects of the venom. This approach is still under investigation, but preliminary studies suggest it may be a promising strategy for managing latrodectism (Isbister et al., 2003). Although these innovative treatments offer potential for managing latrodectism, it is important to emphasize that the choice of treatment should be based on a careful assessment of symptoms and the severity of the poisoning, as well as the availability of therapeutic resources. Continuous monitoring and veterinary follow-up are essential to ensure the effective recovery of the affected animal.

Prevention and control of arachnidism, especially in areas where the species *Latrodectus geometricus* is prevalent, are crucial to avoid future spider envenomation cases. One of the most effective measures in this regard is pest control, which involves the application of specific chemical products to eliminate spiders and other arthropods in domestic environments and surrounding areas. The use of pyrethroid insecticides has been effective against adult spiders. However, Hayasaka, Numa, and Sawahata (2021) highlight that chemical control becomes costly and unsustainable for eradication, as populations tend to recover. An alternative is the use of fipronil, which has shown less impact on non-target spider communities. Exposure to dry heat for a short period may be an effective strategy to exterminate Latrodectus spiders. Hayasaka et al. (2021) demonstrated that exposure to temperatures of 55°C and above for 10 minutes completely prevents the hatching of eggs inside the egg sacs of these spiders. Additionally, an integrated pest management program is important, which also includes prevention measures such as maintaining cleanliness and eliminating potential shelters and food sources for the spiders. Furthermore, raising awareness about the preferred habitats of Latrodectus spiders and the signs of infestation can help people avoid contact and identify problems before they become serious.

CONCLUSION

Arachnism, caused by bites from spiders such as the brown widow (*Latrodectus geometricus*), is a condition that requires immediate veterinary attention. Although less well-known than the black widow, the brown widow still poses a significant risk of poisoning to both humans and animals. Proper management of these cases is essential to prevent fatal outcomes. Treatments such as administering analgesics, anti-inflammatories, and, in more severe cases, the use of specific antivenoms, are

fundamental for relieving symptoms and promoting the animal's recovery. Additionally, preventive measures such as regular pest control in areas where the species is prevalent can help reduce the risk of future accidents. Awareness of the clinical signs of poisoning and available treatment options is crucial for healthcare professionals and veterinarians to ensure proper management of these accidents and minimize their consequences.

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