Case study

Lymphedema as consequence of Loxosceles Brown Spider Bite: A Case Report and a Literature Review

ABSTRACT

Introduction: Secondary lymphedema is defined as a chronic-progressive disease which causes a rich protein edema of the limbs, this may be caused due to the damage or obstruction of lymphatic structures; complications associated to loxosceles spider bite may cause damage of lymphatic system.

Objective: To describe a clinical case of a patient with lower extremity lymphedema secondary to loxosceles' spider bite complications and to present a review of literature about the topic.

Case Presentation: A 24-year-old man received previous medical attention between 2020-2021 due to complications of loxosceles spider bite; the patient was bitten in the medial third of his left leg. He arrived at our facilities in January 2022 to assess his case due to increased left leg volume related to progressive edema and a chronic wound in the bitten site; situation that did not ended to improve with time, rest, simple cleaning, elevation and began to limit his ability to walk and work. Spider bite caused local soft tissue destruction and dermonecrosis due to local loxoscelism in August 2020. Patient had no history of lymphedema nor other venous or lymphatic disease. Other comorbidities were discarded by clinical assessment, radiography, MRI of the limb and ultrasound of leg's venous system. Patient identified a worsening tendency of limb volume in time along recurrent local lymphangitis infections. After clinical history analysis, physical examination and near-infrarred lymphography study of the leg, damage of lymphatic structures was identified due to local destruction of lymph vessels in the affected area; secondary lymphedema was confirmed. With treatment consisting in multilayered compression therapy, exercise and wound care based on TIME acronym patient reversed and controlled lymphedema volume and ulcer evolved to complete closure. It was decided to present the case along a literature review on the topic.

Conclusion: It was presented a case of lymphedema associated to loxosceles spider bite that was solved successfully. Lymphedema related to loxosceles spider bite and its complications is a clinical reality that might be underrecognized by scientific literature and clinicians; this condition should be properly studied and considered with the adequate assessment strategies in patients after suffering the spider bite in extremities, especially in the mid and long-term.

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Keywords: lymphedema, secondary lymphedema, loxosceles bite, near-infrared lymphatic imaging, NIR lymphography, brown spider, violinist spider

1. INTRODUCTION

Lymphedema is a chronic-progressive disease that causes rich protein edema in a body's segment, it occurs due to the obstruction of lymph vessels, lymph nodes or lymphatic function disorders, according to Pubmed's MeSH database and the International Society of Lymphology [1,2]. Lymphedema produces progressive limb growth due to lymph stasis, chronic fibrosclerotic changes in tissues and a chronic inflammatory response [3], its progression affects the quality of life [4] the social context and economy of patients [5], affecting more than 250 million people worldwide [6] and an estimated of 5 million in Mexico [7].

Lymphedema is classified mainly into primary and secondary, the first is related to congenital anomalies of lymphatic structure and function [7] while secondary lymphedema is commonly caused by events that affect lymphatic structures and function such as: neoplasm, cancer related treatments like lymph node removal surgeries, radiotherapy, central venous catheter complications, direct trauma, chronic infection, or any factor that affect lymphatic structure integrity like obesity and venous disease. [7-11] 25.01% of cases of secondary lymphedema are not related to cancer in Mexico. [6]

Sometimes animals play a role in some types of lymphedema, for example, it is known that mosquito bite is the vector that transmits lymphatic filariasis infection, one of the predominant causes of secondary lymphedema worldwide [13]; some insect bites have been reported as cause of chronic infections, wounds, and later onset lymphedema as a complication [14-16] this may be explained due to the toxicity of the poison that destroys subcutaneous structures in some cases but also the exposure to the chronic related infections; when lymphedema is not directly caused by the complications of bite, the process well may make evident an underlying primary lymphedema [17].

The violinist spiders are venomous arthropods that belong to loxosceles genus, these spiders are endemic from South America, but they are spreading worldwide due to their high adaptability, there are 140 species identified as loxosceles, violinist or brown spider corresponds to the loxosceles laeta one. [18,19]. The spider uses their venom for predation and defense, however when this spider bite humans it provokes local and systemic toxicity; local toxicity includes dermonecrosis, subcutaneous tissue destruction, with gravitational spread of lesions while systemic toxicity may cause hematological abnormalities and impaired renal function. The signs and symptoms observed following a loxosceles spider bite are called loxoscelism and in some cases may result in patient's death, amputation of affected limb or a broad variety mid-term complication like recurrent cellulite, lymphangitis, chronic ulcers, swelling and disability among others. [19, 20].

It is presented a case of secondary lower extremity lymphedema in clinical stage II, according to the ISL lymphedema clinical staging system, lymphatic damage confirmed by near infrared lymphatic imaging, related to loxosceles laeta spider bite complications.

Due to the lack of reports about peripheral lymphedema described as a complication of loxosceles spider bite, we decided to perform a literature review about the topic.

Objective: The objective of this study is to describe a clinical case of lower extremity lymphedema as a loxosceles' spider bite complication and to present a review of literature of lymphedema and complications related to integrity of lymphatic system after loxosceles spider bite and a literature review on the topic.

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2. CASE PRESENTATION

A 24-year-old white man, height 1.87 m, 119 kg weight, normal heart rate and respiratory frequency, 120/80 arterial tension, without comorbidities referred and other possible comorbidities not identified without relevant familial health antecedents. The patient lives in a rural environment, he is an active farmer but sedentary lifestyle, single. The patient received previous medical attention in public and private health services due to loxosceles spider bite in the medial third of his left leg between August 2020 and December 2021; this bite caused local loxoscelism, same conditioned chronic local inflammation process, increased edema volume, dermonecrosis, subcutaneous soft tissue destruction and a chronic wound in the bite site. **(Fig 1)**

Fig 1. Three months after spider bite

Bony, muscle and deep vascular damage was discarded with radiography, MRI and ultrasound duplex of affected leg.

Previous treatments consisted only in local simple clean of wound with surgical soap, gauze, and long stretch cotton bandaging for leg as wound control; diuretics, rest, same bandage, and leg elevation for edema reduction; oral antibiotics for recurrent lymphangitis, and thromboprophylaxis with acetylsalicylic acid. All this care provided poor results for managing wound and leg volume.

6 months after the spider bite and treatment beginning, patient noted edema volume worsening that did not improved with time and despite his treatment, notwithstanding this, wound improved but not completely, patient began to present lymphorrhagia of leg.

The patient arrived at our center Fi Fisioterapia Integral S.C. located in Zapopan, México, in January 2022 to receive attention and to assess his case due to increased leg volume related to progressive edema and a chronic wound that didn't improve with previous treatments; the situation began to affect movements and basic activities that demanded continuous efforts, like walking, working, and completing house chores.

The patient identified a faster worsening tendency of volume in time since November 2021; noteworthy, he presented a frequent lymphangitis rate that began 6 moths after spider bite, being at least 4 lymphangitis episodes since last year until his assessment date in January 2022.

Medical file included radiography and MRI performed in February 2021, studies helped to discard any bony or muscular damage of the leg, and a venous duplex ultrasound study performed in September 2021 in which is showed normal integrity of superficial and deep veins, normal behavior of mechanical characteristics of venous system and an absence thrombosis of any vein of his left lower limb.

After exploration of left leg of the patient presented positive godet sign from knee to foot, thicker skin panicles than his right leg due to the presence of edema (positive Stemmer sign), chronic inflammatory changes in the skin and concentric fibrosclerotic tissue around the wound, wound located in the epicenter of spider bite. **(Fig 2)**

Fig. 2 Leg after 14 months of spider bite, during at-clinic assessment

The wound dimensions were 3cm x 2cm, 3mm deep, moderately exudative, with a high amount of necrotic tissue and superficial bacterial burden. **(Fig. 3)** However, after eliminating the superficial devitalized tissue rings around the wound epicenter, it was noticed epidermolysis underneath. Wound extension was still 10cmx10cm.

Fig. 3 Wound detail, note the broad rings of fibrous and devitalized tissue as well as the epicenter of the wound with a high necrotic and bacterial burden.

Comparative anthropometric circumferential measurements were performed for lower limbs: knees, 10cm and 20 cm below, ankle and foot. Circumferential measures showed a significant circumferential mean difference of 2.7cm **(Table 1).**

Circumferences	Right leg (cm)	Left leg (cm)	Difference (cm)
Knee	47	47	0
10cm below knee	42.5	44.5	2
20cm below knee	41	46.5	5.5
Ankle	31	36.5	5.5
Foot	27.5	27.5	0.5
		Average	2.7

Table 1. Circumferential measurements

Clinically it is suspected a case of secondary lymphedema due to lymphatic injury as complication of three important factors that may correlate to lymphatic structure damage:

The first is the acute loxcescelism process that may have conditioned the partial destruction of important superficial lymphatics of the leg and subcutaneous soft tissue; the second, the recurrent lymphangitis; and the third, the exposure of superficial lymphatics to the chronic inflammatory regional process.

Anatomically, most of peripheral superficial lymphatic vessels of lower leg run along the way of the medial face of the limb, parallel to superficial great saphenous vein [21] damage, chronic inflammation and trauma to this specific anatomic area contribute to the development of secondary lower limb lymphedema [22-26]. This site was exactly the spider bite site, where local loxoscelism was developed, where the skin and soft tissue destruction happened to be; the epicenter of the chronic inflammatory process caused by the wound and where recurrent lymphangitis originated.

It was decided to perform an ICG Near-Infrared Lymphatic Imaging Lymphography study in the affected leg; this study allows an economic, ambulatory, and secure assessment of the superficial lymphatic system with exquisite detail, which allows the identification of any impairment, disfunction or damage of superficial lymphatic structures. [27] employing our low-cost NIR lymphatic imaging device [28] which have helped before to identify secondary lymphedema [29]; 0.5 mg of indocyanine green (ICG) was administered into interdigital spaces of foot. Four sequential images of leg were attained and then integrated to get a sole image of the limb.

NIR imaging test allowed good visibility of superficial lymphatic vessels of the leg and different patterns described in literature. [30-33]. Left leg showed an initial normal Linear Pattern (LP) of foot and distal leg; as long as we screened medial region following this lymphatic pathway it was identified an interruption of flux and a Stardust Pattern (StP) that made evident an abnormal lymphatic function with no clear definition of lymphatic vessels pathway; this site happened to be the bite and wound site; noteworthy that following this interruption, the lymphatic vessels appeared again in its normal path without any other abnormality identified. **(Fig. 4).**

Fig. 4 NIR lymphatic imaging test sequence. Note the medial interruption accompanied with stardust local pattern.

These findings, the clinical history and the clinical examination confirmed secondary lymphedema in clinical stage II, according to ISL staging system, the lymphatic involvement was confirmed with the NIR-ICG pattern; this imaging pattern shows a lymphatic injury and a decaying peripheral lymphatic function; this lymphedema was onset as late consequence of loxosceles spider bite and its related complications, like infection and a chronic wound.

The patient underwent treatment in our facilities, based on rehabilitation and proper wound care employing TIME acronym (tissue debridement, infection control, moisture control, edema control), 24/7 short-stretch multilayered bandaging compression, daily strength and resistance functional exercises to retrieve physical capacities, weight control and education on selfcare and risk reduction habits to avoid associated complications and progression of limb volume during 5 weeks and a frequency of 3 sessions per week. Treatment resulted in a successful and complete wound healing and a total lymphedema volume reduction, to be later controlled only with a 30-40mmHg compression stocking to use only along the day. Patient was re-assessed after 3 weeks of finishing treatment completion with stable and good results. Patient will continue to use compression stocking long-life. **(Fig. 5)**

Fig. 5. Patient's leg after 8 weeks, during control assessment.

Due to the rare case, it was decided to perform a literature review of lymphedema related to loxosceles spider bite complication.

3. LITERATURE REVIEW

It was performed a research of similar cases in scientific literature, but it was found a total absence of reports of explicit lymphedema or lymphatic injury related to brown spider bite; the aim of this literature review was to analyze the reports of lymphedema, or sign and symptoms associated to lymphatic injury as a complication related to brown spider bite.

Mesh terms, keywords and phrases in English and Spanish were employed in medical scientific search engines such as PubMed, Cochrane, Cinhal, Scielo, Scopus, Researchgate and Google Scholar. Phrases and keywords included "lymphedema", "lymphatic", "lymphoedema", "lymphatic injury", "secondary lymphedema" plus "loxosceles bite", "loxosceles spider", "violinist spider", "brown spider", "loxosceles laeta" and "loxsoceles". Surprisingly no results were found with this keyword and phrases combination; it was decided to do a broader research substituting the first keywords by

"secondary effects", and "consequences" reported due to this spider bite to identify those cases, reports, and studies in which lymphatic involvement could have been present without being directly reported like: dermonecrosis, wounds, lymphangitis, cellulitis, edema, and limb swelling that might have been present.

116 studies were reviewed and considered to analyze during the research with a total of 257 patients;

The first report was made by Sanchez M, et al. in 2011 [34] about a patient with classical initial evolution of brown spider bite in the forearm and leg and a follow-up of 1 week; however, it is not stated if there was an evolution to lymphedema due to the lack of medium- and long-term follow-up nor received any lymphatic assessment or screening.

In 2012, Baldovino R et al. [35] presented the case of a child (19 months old) in which loxescelism characteristics were present after the spider bite in his leg; the initial carachteristics are very similar to our case study presented, but the follow-up is only about 23 days.

Harz-Fresno et.al [36] reported in 2014 another interesting case in which might have been development of lymphedema due to location of loxoscelism, this time in the forearm; unluckily the patient fled and only was possible 32 hours follow-up.

Another case was presented by Pezzi et. al [37] in 2016; a 65-year-old woman suffered a bite in the third finger of his hand and experienced an extremely aggressive local response that affected her whole hand; patient died so it was not possible any further evolution tracking.

Probably Cachia et.al [38] in 2016 and Köse et.al [39] in 2020 reported the most similar case to ours, at least in location and initial local loxoscelism responses and complications. The first patient was a female with a bite in his thigh; she had a 2 month follow-up and it is evidenced the chronic complication of a local wound and dermatological management in the future, but there was no further report on its evolution. In Köse's report, the patient was bitten in his left thigh near the knee, but only underwent a 33 day follow-up, they treated the ulcer with plastic surgery there is no report of success in the mid-term or long-term, and as in the rest of cases there is only a short term follow-up.

Fernandez et.al [40] in 2018 reported a very severe case of loxoscelism and complications in the arm of an elderly patient in which was necessary, first, a partial amputation of the arm and later a shoulder disarticulation. This was patient with the longest follow-up with 10 months. In the end patient died due to cancer, but there were no reports of any potential lymphatic complication once the last amputation occurred.

The time span between these studies was 9 years, 2011 to 2020; a total of 7 case reports and 7 patients. Out of 257 patients reports only 7 (2.7%) reported some relevant data that could be associated to lymphatic injury in the future, such as dermonecrosis, edema, lymphangitis, cellulitis, ulcers, and wounds. There was no reported lymphedema in any of them. It should be noted that 57% of these studies reported follow-up of less than a month, 28% of the studies reported a follow-up between 1-2 months, 14% up-to 10 months and the rest did not report a follow-up time.

Table 2. Reports about lymphedema or complications potentially related to lymphedema development as consequence of brown spider bite

Author	Date	Study	Patient characteristics	Initial signs/ and symptoms	Tracking time	Clinical outcome
Sanchez M., et al. [34]	2011	Case report	A 28-year-old male patient with no family or personal history record.	Skin injury on the left forearm, with pain, and local inflammation, with a violaceous appearance, scaling and transudate, which evolved into a necrotic eschar. He then presented two injuries with the same characteristics, located on the back of	1 week	First injury queloid scar. The other two injuries not reported.

				the left leg.		
Baldovino R, et al. [35]	2012	Case report	Female patient aged 1 year 7 months with no family or personal history to highlight.	Necrotic eschar, lower limb edema, pain, perilesional erythema, exudate.	23 days	Autograft surgery and supervision.
Harz-Fresnol, et.al. [36]	2014	Case report	27 years old male patient, consulted the emergency department for a skin injury of 20 hours of evolution, secondary to a spider bite in the proximal third of the right forearm, ventral side.	Central violaceous plaque associated with edema, erythema, and pain. 4mm skin ulcer with signs of necrosis on the forearm. At 32 hours of evolution, he presented macroscopic hematuria and an increase in edema with the appearance of a blister of approximately 6 mm in diameter at the site of the injury.	32 hours	The patient abandoned treatment, so it was not possible to document the final situation of his case.
Pezzi M, et al. [37]	2016	Case report	65-year-old woman, obese, with no history of diabetes and allergies but with a mild form of myasthenia gravis.	Circular necrotic skin lesion on the middle phalanx of the third finger of her right hand with erythroderma and oedema of the hand which partially affected the forearm, with strong pain symptoms.	Not reported.	Patient died
Cachia M, et al. [38]	2016	Case report	Female patient with no recorded personal and family history.	He presented pain, erythema, ulcer, and necrosis in the left thigh.	2 months	Conservative local wound care with povidone-iodine dressings and dermatological follow-up. The study doesn't mention a long-term solution.
Fernandez E, et. Al [40]	2018	Case report	71 years old man with a history of colon adenocarcinoma in complete remission. 3 days after the spider bite, the patient presented to the hospital.	Blistering, violaceous mass with surrounding erythema and dema of the forearm, associated with severe pain. Compartment syndrome, after 2 surgical debridements with poor response, amputation above the elbow was chosen, and later a shoulder disarticulation.	10 months	Patient died at 1 year due to colon cancer recurrence.
Köse A.,et. al[39]	2020	Case report	A 29 year-old female patient who had no history of illness was admitted to the emergency department. The patient reported that she had been bitten by a brown spider on the upper part of her left knee 6 days earlier.	Lymphangitis; erythematous surface on the trunk and arms. Local necrotic arachnidism (skin ulcer), urticaria and cellulitis.	33 days	The necrotic area was debrided through plastic surgery and a flap was implanted in that area.

4. DISCUSSION

It is relevant to put special attention to the fact that patient suffered in the mid-term and long-term a bad management due to the lack of a precise early diagnosis and the specific treatment for the conditions that were chronic after the acute spider bite complications, such as the wound and the lymphedema.

It is important to note that the clinical evolution of this patient's case was solved with conservative management based in physiotherapy and advanced wound care in a short time and a relatively low cost (approximately $400USD) that made possible the patient to work again. This cost is estimated lower than the economic impact of treating the frequent infections for the last year ($200USD), the ineffective previous treatments ($500USD) and the patients disability to work caused by the condition,

the prognosis of this burden in the future tends to be worse considering the risk of this health condition being each time more severe and expensive to treat in time.

Lymphedema as complication of loxosceles spider bite should be considered as a rare entity but not an impossible condition that might happen in the long term after loxoscelism in extremities; specially when it occurs in critical anatomic areas that compromise importan venous and lymphatic structures.

This patient had in common something with the reviewed cases in literature; all of them had a lack of follow-up in the long term. It is suspected that many patients do not receive the control, treatment or supervision they need in the long term, and this may represent the reason there are only few cases reported in literature with long term consequences of loxosceles spider bite, being this the only one reporting a condition like lymphedema.

It might be possible, according to the reviewed data, a prevalence of lymphedema after loxosceles Spider bit of 0.82% in a span of 11 years and a population of 257 patients, which is a small rate. However, this number might increase if more reports of loxosceles spiders' bites complications were published, and especially if they had a long-term follow-up. We encourage clinicians and researchers to study and report more cases and long-term data about this population, which seems to be necessary to solve more efficiently these clinical scenarios.

From this research it was identified that this is the only review and case addressing this clinical problem considering available literature and scientific reports.

It is suspected that peripheral lymphedema related to loxosceles spider bite and its complications may be an underdiagnosed, underreported, and underrated entity probably due to different factors, such as:

1- Follow-up time for patients that suffered this spider's bite: this, considering that largest follow-up in similar and relevant clinical case was up-to 10 months. We suggest clinical prospective studies with long-term follow-ups; however, it is logic the difficulty to perform this kind of studies.

2- Clinical skills to identify and diagnose lymphedema in clinical practice. We suggest clinicians to become familiar with lymphatic pathology.

3- Lack of precise and accessible diagnostic tools for lymphatic function such as NIR lymphatic imaging to identify differential causes of "edema" additional to only clinical presentation; this lack of tools may be leading to inaccurate reports of "chronic edema", unspecific "edema" or the assumption that it has a venous origin with no clear definition of etiology. We suggest the use of NIR lymphatic imaging as a tool for clinical practice, as it is easy to use, ambulatory, economic, secure, and easy to develop imaging technique, with high sensitivity and specificity to assess peripheral lymphatic function.

4- Poor- and low-quality evidence reporting this complication; most reports are based on highly heterogeneous populations and case reports, only estimations can be done regarding epidemiology of this situation. We suggest developing new studies considering strategies to identify lymphedema along other complications after loxosceles spider bite, not only in the short term but also in the mid and long-term.

5. CONCLUSION

It was presented a case of lymphedema associated to loxosceles spider bite that was solved successfully. Lymphedema related to loxosceles spider bite and its complications is a clinical reality that might be underrecognized by scientific literature and clinicians; this condition should be properly studied and considered with the adequate assessment strategies in patients after suffering the spider bite in extremities specially in the mid and long-term.

CONSENT

Authors declare that written informed consent was obtained from the participant for publication of this study and accompanying images.

ETHICAL APPROVAL

Hereby, all authors declare that all interventions have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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