Lactrodectism with Cardiac Involvement

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Abstract

Bite caused by arachnids form the genus Latrodectus is one of the most common worldwide. Mainly, it is associated with nervous system involvement and cardiovascular compromise, especially myocardic, is rare. We present the case of a 21 year old patient that was bitten by a Latrodectus mactans spider, who developed neurologic compromise and later presenting severe acute heart failure. After 10 days of treatment, the patient recovered without sequelae.

Keywords: Latrodectus; Myocarditis; Acute heart failure

Introduction

Lactrodectism is a clinical entity with characteristic symptoms and signs caused by the bite from arachnids of the genus Latrodectus with compromise of several organs, specially nervous and cardiovascular systems. Among cardiovascular symptoms, arterial hypertension and brady-tachycardia are common in the first hours. Secondary acute myocardial compromise is rare and the mechanisms of myocardial damage as well as the prognosis of this complication have not been well defined [1,2].

Electrocardiographic alterations could be explained by the effect of alpha-latroxin, which is the most active component of this venom. This toxin causes neurotransmitter, specially acetylcholine and noradrenaline, liberation and depletion form synaptic terminals and inhibiting their posterior uptake [3].

Actual therapy is based mainly in supportive measures and symptoms relief. Antivenom is the only available therapy which has been proved effective but with a brief therapeutic window and secondary and a wide range of described allergic reactions in diverse series [4].

We present the uncommon case of myocarditis caused by Latrodectus mactans bite, with an updated literature review of this clinical entity.

Case Presentation

A male 21 year old patient, with no previous medical history or cardiovascular symptoms. He refers to be bitten in his right scapular region by a black spider with red abdomen, while he was performing his job spraying plaguicide with adequate protection of hands and arms. After 20 min he describes intense pain and pruritus over the bite zone. On the skin, an intense erythematic lesion with a diameter of 10 cm appeared which, after two hours, presented marked edema. He presented concomitant malaise and diffuse myalgia. He was admitted in the emergency department after 4 h of the event, febrile, tachycardic, polypneic, diaphoretic and with diffuse erythema. The electrocardiogram showed only sinus tachycardia (Figure 1). He was transferred to the intermediate care unit where supportive care was initiated and intravenous corticoids, antiallergics, calcium gluconate and opioids were administered.

Following advice of the local Toxicology Center, therapy with antivenom was not administered because a high risk of anaphylactic reaction. After 24 h, the patient developed progressive dyspnea and oxygen desaturation. He was severely hypertense (220/110 mmHg), with a heart rate of 140 bpm, febrile and with intense myalgias and shivering. Physical exam revealed rales on both lung fields which were corroborated by chest X-ray were the appearance of bilateral interstitial infiltrates was observed (Figure 2) compatible with acute pulmonary edema. Severe hypoxemia was documented with a PaO₂/FiO₂ of 156 and levels of ultra sensitive Troponin T (usTnT) were 4.74 ng/mL (normal value <0.16 ng/mL).
The patient was treated with intravenous furosemide and nitroglycerin infusion, achieving blood pressure control and negative hydric balance. Transthoracic echocardiogram evidenced mild LV dilatation with global hypokinesia that determined a LVEF of 29% and a suspicious image of apical ballooning. Mild regurgitation of mitral and aortic valves was observed (Figure 3). Dobutamine infusion was started at a dose of 1 mcg/kg/min without clinical response. The patient developed a new episode of intense desaturation and atrial tachycardia with need or orotracheal intubation and connection to invasive mechanical ventilation. The patient was then derived to our center after 48 h of therapy.

On physical exam a decreased peripheral perfusion was noted, with a third heart sound and pulmonary rales. Laboratory showed leukocytosis (15,000 x mm$^3$, 70% polymorphonuclear), usTnT of 128 pg/mL, CK 123 U/L, CKmb 26 U/L, Lactate 1.3 mmol/L (normal value <1.7) and creatinine of 0.87 mg/dL. On electrocardiogram, atrial tachycardia was seen, with a diffuse PR depression, rS from V1 to V3 and diffuse ST elevation and T wave inversion T seen in I, aVL, V5 and V6 (Figure 4). A new echocardiogram corroborated a LVEF of 35% with a LV of normal diameters, diffuse hypokinesia more pronounced in anterior and anteroseptal basal and medial segments. RV presented a preserved systolic function without pulmonary hypertension. QUE TERAPIA SE DEJO??

The patient evolved with progressive improvement in oxygen requirements and resolution of lung infiltrates (Figure 5). After four days of treatment, inotropes were suspended and a new echocardiogram showed a LVEF of 45%. usTnT 98 pg/mL. The patient was successfully extubated.

Vasodilator therapy with captopril, spironolactone, amlodipine
and carvediol was adjusted. Subsequent electrocardiograms showed intermittent ectopic atrial rhythm and ST elevation resolution with a profound T wave inversion in I, II, aVL and V1 to V6 (Figure 6) with posterior normalization (Figure 7).

Echocardiogram after eleven days of therapy denoted a complete recovery of LV systolic function. Patient was discharged after twelve day with the following therapy: Enalapril 5 mg bid and Carvedilol 12.5 mg bid. After XXXX months, the subject remains asymptomatic with a normal echocardiogram.

**Discussion**

Bite from arachnids from the genus Latrodectus is one of the most common worldwide [5] and *L. mactans, L. tredecimguttatus* and *L. hasseelti* are the principal species of this genus. In Chile, the bite from *L. mactans* is described since 1852, generating seasonal epidemics depending on temperatures and agricultural activities [6]. Commonly named “black widow” or “wheat spider”, it has a black color with characteristic red stains in the ventral side of its globular abdomen. Female spiders are bigger and have a more potent venom. It has daily habits and it is found more commonly in rural areas. The higher rate of bites is registered during agriculture task hours (between 10 h and 19 h).

The most important component of the venom is α-Latrotoxin (α-LTX), a protein that consists in two polypeptides of 8 and 130 kD, the last of them with biologic activity [7]. This toxin produces massive exocytosis of neurotransmitters from neurosecretory cells, predominantly acetylcholine and noradrenalin, into motor synapses. This secretion produces synaptic terminal depletion with neurotransmission blockade deriving into paralysis. Three physiopathologic mechanisms have been described to explain this effect:

1. **Massive influx of calcium through de novo formed transcellular pores and preexistent channel opening:**

2. **The action Neurexins:** Transmembrane proteins that bind to α-LTX in presence of extracellular calcium, triggering exocytosis directly through Synaptotagmin;

3. **G-Protein binded receptor, calcium independent, called Latrophilin.** The mechanisms of toxicity that predominate are different in every organ, with no available evidence about the direct effects of this toxin over cardiac tissue.

In the typical clinical scenario, local reaction to the bite predominates, with pain and edema on the site of inoculation [6,8]. In 25% to 60% of patients remote symptoms develop, characterized by generalized pain, diaphoresis, muscular spasms, nausea, vomits, tremor, photophobia and dyspnea [4-6,8]. Cases of renal failure, rhabdomyolysis, compartment syndrome, ileus and seizures [9]. Laboratory findings are nonspecific, with elevation of AST, ALT, LDH, CK and leukocytes. Reported mortality of Latrodectism varies from 0% to 10% [4-6], with higher levels in undeveloped regions.

Cardiovascular manifestations are frequent, with 30% of patients presenting systemic arterial hypertension and tachycardia [1,9]. Literature describes secondary myocarditis as a rare phenomenon [9,10]. Typically, myocardial involvement is suspected through elevated Troponin levels and electrocardiographic abnormalities such as: ectopic rhythm [1], atrial fibrillation and ST deviation [11,12]. QRS alterations, QT prolongation and evolutive T wave changes are also described [1]. Contractile alterations are described such as diffuse hypokinesia and occasional segmental abnormalities, mainly in the anterior wall [1,9,11]. These changes are characteristically reversible within approximately 7 days. In this case, the patient presented with severe transient systolic dysfunction associated with marked electrocardiographic changes in PR and ST segments and T wave inversion.

Therapy is based mainly on supportive measures. Due to the physiopathological evidence of intracellular calcium abnormalities, calcium gluconate infusion has been described as an additional treatment in the first hours; nevertheless, different series have not demonstrated benefits in terms of duration or severity of the disease [4]. Neostigmine in doses of 0.5 mg to 1.0 mg tid has been proven effective in small series and reviews, specially related to neurologic symptoms [6,13]. Administration of Benzodiazepines and opioids were proven effective in symptom control but not in the duration of the disease [4,14].

The only therapy that has demonstrated to reduce the symptomatic period is the Antivenom [4,8,14]. This substance is obtained though derivate of Immunoglobulin G synthesized from different Latrodectus species. In animal models, extracts from one species are effective in counteracting venom from other types of Latrodectus [15]. Main concern about this substance are allergic reactions, reporting variable degrees of intensity [5,16] with cases of anaphylactic shock and even death. In review of the cases from Australia and United States, there is a marked difference in the reported adverse effects which vary from 0.5 to 0.8 in the Australian versus 9% to 80% in...
the North American series [5]. These differences are thought to be explained by the administration route: Intramuscular in the Australian and intravenous in the North American cohort. Besides, in the latter, allergies obtained in cutaneous tests were described as adverse reactions, which could increase the number of reported complications. Studies have compared the administration of the Antivenom through intravenous versus intramuscular route, with faster onset of action using intravenous route without increasing adverse effects [17]. The administration of Antivenom remains underutilized because of concerns of adverse reactions [4,5] reserving it only for severe cases, but in recent experiences the rate of severe adverse effects is low [16]. Newer therapies are being developed, a fragment of purified F(ab)2 has been described to produce the same benefits with fewer adverse reactions that could increase the use of the antidote [14].

References