

Gnathostomiasis and cutaneous leishmaniasis: a possible co-infection

Gnatostomíase e leishmaniose cutânea: uma coinfeção possível



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ABSTRACT

Gnathostomiasis is a zoonosis transmitted to humans by eating raw or undercooked foods contaminated with the larvae of *Gnathostoma* sp. The clinical manifestations of gnathostomiasis vary according to the species, parasite load and affected tissues. Skin lesions are mainly characterized by nodules or areas of edema that affect any topography of the body. Cutaneous leishmaniasis is mainly characterized by a single ulcerated skin lesion caused by different species of *Leishmania*. In this article we present a case report of *Gnathostoma* and *Leishmania* co-infection, with clinical presentation of an ulcerated skin lesion in the triceps region of the right upper limb that appeared during a trip to Peru. A diagnosis of leishmaniasis was made by detection of amastigotes and at the beginning of treatment, there was an exit of helminth characterized with *Gnathostoma* by stereomicroscope. He received treatment with albendazole, and the lesion healed. This is the first report of *Gnathostoma* and *Leishmania* co-infection described in the literature.

Headings: Leishmaniasis; Cutaneous; Helminths; Skin Ulcer.

RESUMO

Gnatostomíase é uma helmintose transmitida ao homem por ingestão de alimentos crus ou malcozidos, contaminados com larvas de *Gnathostoma* sp. As manifestações clínicas da gnatostomíase variam de acordo com a espécie, carga parasitária e tecidos acometidos. As lesões cutâneas são caracterizadas, principalmente, por nodulações ou áreas de edema que acometem qualquer topografia do corpo. Já a leishmaniose cutânea se caracteriza, principalmente, por lesão cutânea ulcerada única, causada por diferentes espécies de *Leishmania*. Neste artigo, apresentamos um relato de caso de coinfeção de *Gnathostoma* e *Leishmania*, com apresentação clínica de lesão cutânea ulcerada em região tricípital de membro superior direito que surgiu durante viagem ao Peru. Inicialmente foi feito o diagnóstico de leishmaniose por detecção de amastigotas, mas quando do início do tratamento, houve saída de helminto caracterizado com *Gnathostoma* por esteromicroscópio. Paciente recebeu tratamento com albendazol, tendo apresentado cicatrização da lesão. Esse é o primeiro relato de coinfeção *Gnathostoma* e *Leishmania* descrito na literatura.

Descritores: Gnatostomíase; Leishmaniose cutânea; Coinfeção; Albendazol; Antimonial pentavalente.

INTRODUCTION

Gnathostomiasis is a zoonosis caused by the nematode helminth and is transmitted to humans by accidental ingestion of raw or undercooked aquatic animals contaminated with *Gnathostoma* ssp¹ larvae. The disease has been described mainly in Southeast Asia, especially in Thailand and China¹. In Latin America, the first record of gnathostomiasis occurred in Mexico in 1970², and in South America, the first report was in Ecuador

in 1984³, in a series of migratory nodular eosinophilic panniculitis cases. Between 1987 and 1999, four cases of gnathostomiasis in Peru were described as being related to raw fish intake⁴. The first case report in Brazil occurred in 2009⁵ in a Peruvian patient, but the first autochthonous report occurred in 2012 in a patient from the country's northern region⁶. Recently, two other cases from the Brazilian Amazon region have been reported⁷.

The genus *Gnathostoma* comprises 13 different species, of which six have been described to date as causing disease in humans: *G. spinigerum*, *G. hispidum*, *G. binucleatum*, *G. malaysiae*, *G. doloresi* and *G. nipponicum*⁸. The life cycle is metaxenic, developing in intermediate hosts (crustaceans and freshwater and saltwater fish) and having domestic and wild mammals as definitive hosts. Paratenic hosts, including, humans, reptiles and birds are also noted¹.

Gnathostomiasis clinical manifestations in humans vary depending on species, parasitic load and affected tissues, and there may be visceral or cutaneous manifestations¹. Skin lesions are characterized mainly by nodulations or areas of edema that affect any topography of the body, with associated infiltration and erythema, which can be painful and pruriginous. Central nervous system involvement is rare, but this is the most severe form of the disease⁹.

Depending on the clinical presentation, the cutaneous manifestation of gnathostomiasis may be confused with different skin disorders¹⁰. Bacterial infections are the most frequent differential diagnosis; however, cutaneous leishmaniasis with ulcerated presentation may also be confused with gnathostomiasis.

The cutaneous manifestation of leishmaniasis is quite varied. Although, the unique ulcerated lesion is its main clinical form and it also may be confused with other diseases caused by different etiological agents¹¹. Leishmaniasis co-infection with other diseases is not common. Moreover, co-infection of gnathostomiasis with other parasitic diseases is very rare. In this paper, we report a clinical case of co-infection involving gnathostomiasis and cutaneous leishmaniasis.

CLINICAL CASE

A 27-year-old woman, previously healthy, coming from France, sought health services in Sao Paulo due to a skin injury that arose during a trip to Peru, where she consumed ceviche on several occasions. She reported the appearance of an ulcerated skin lesion within 45 days of its evolution in the tricipital region of the right upper limb and was initially treated with enteral antibiotic therapy. When the patient sought medical attention in that country,

she was diagnosed with cutaneous leishmaniasis, which was confirmed by the presence of amastigote forms in scraped lesions. Therefore, she was instructed to start treatment as soon as staying long enough in a same city during her trip, which happened to be in Brazil.

Laboratory tests showed no alterations, and the patient did not have eosinophilia. Initial physical examination showed a shallow, ulcerated cutaneous lesion with a subcutaneous nodule and a serous secretion discharge (Figure 1A). Treatment with intralesional pentavalent antimony was initiated, with local itching and the exit of a larva being reported six days after the first dose. The patient saved the larva (Figure 1B), which was stored in formaldehyde and was sent for taxonomic analysis at the Adolfo Lutz Institute (Figure 1C and 1D). She received treatment with 12 mg/day of ivermectin for two days for empirical treatment of myiasis, and three sequential stool samples were requested, which tested negative for verminosis research. Ultrasound of the skin and soft tissues in the topography of the lesion revealed the presence of a small collection and a part of a dead larva. Treatment of leishmaniasis was completed without complications (three doses of intralesional antimony).

Parasitological examination of the larva identified it as *Gnathostoma* sp. Treatment of albendazole (800 mg/day) was then performed for 21 days, with no adverse events. There was an important improvement in the ulcerated lesion, which showed complete healing, no nodulation, and no secretion discharge at the end of the treatment. The patient then returned to her home country.

DISCUSSION

Gnathostomiasis is a neglected zoonosis transmitted to humans by ingesting raw aquatic animals infected with a third-stage development larva¹. Considered endemic in Latin America¹², more than 10,000 cases in Mexico and more than 2000 cases in Ecuador were described between 1986 and 2015¹³. This is the sixth case described in Brazil, not autochthonous to Peru, and is related to the ingestion of raw fish (ceviche).

The presence of amastigote forms of *Leishmania* in the scraped lesion allowed the diagnosis of cutaneous leishmaniasis (CL), which should not be confused with gnathostomiasis. It is the fact that there was larval exit after the treatment for CL was started, which is apparently the first description of *Gnathostoma* and *Leishmania* co-infection in the literature.

One of the main factors related to *Gnathostoma* infestation is eating habits, mainly the intake of raw fish associated with the presence of intermediate hosts¹³. The patient traveled through a CL transmission area (Peruvian

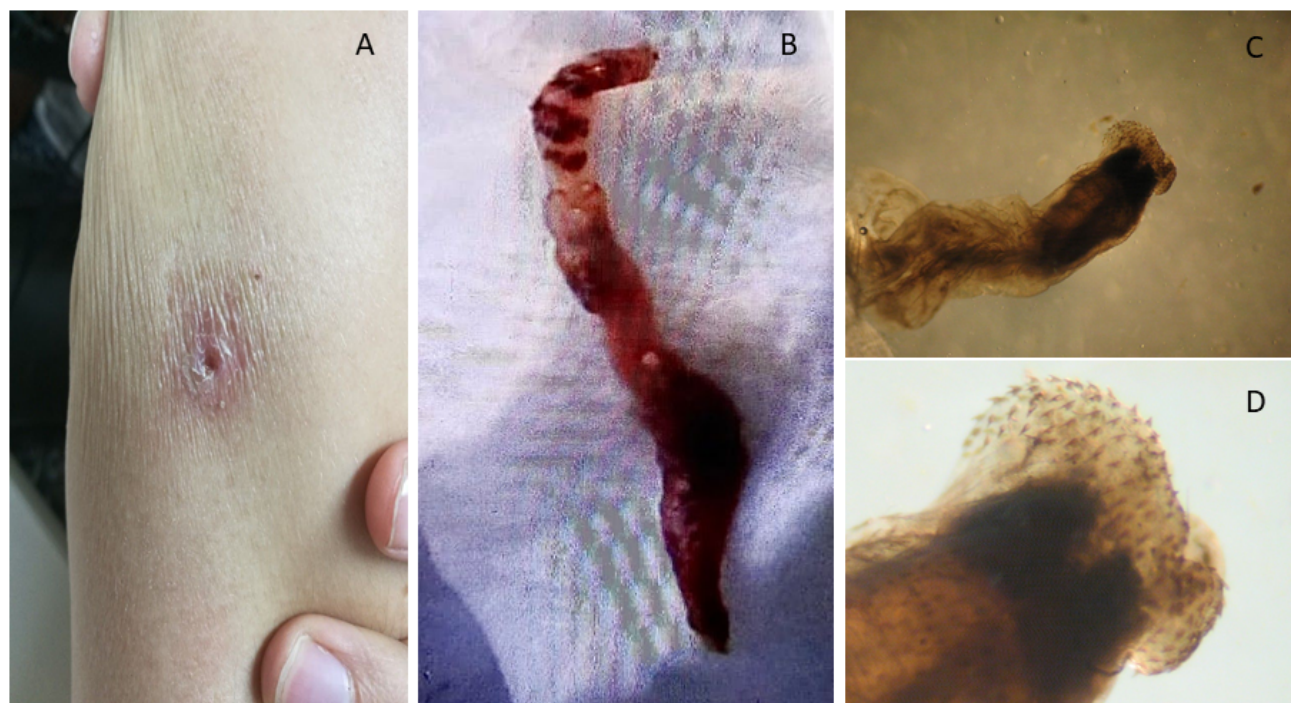


Figure 1. Lesion photograph and photomicrograph of etiological agent. **A:** A shallow, ulcerated skin lesion, about 1 cm in diameter; **B:** A 35-mm cylindrical structure removed from the skin lesion, identified as a *Gnathostoma*; **C:** Adult worm with cephalic bulb visualization, typical of the genus *Gnathostoma*, observed in a stereomicroscope with a magnification of 20X; **D:** View of the cephalic bulb surrounded by thorns, through a stereomicroscope at 40X magnification.

Amazon and Bolivia), and ingested raw fish. These two epidemiological antecedents, associated with the findings of amastigote forms of *Leishmania* and the detection of *Gnathostoma* sp. adult worms, confirm the report of co-infection. Both infections have been reported in the natives of endemic areas and travelers. In this particular case, both gnathostomiasis and leishmaniasis should be considered in the context tropical diseases of the travelers.

The clinical manifestation of gnathostomiasis is classically characterized by nodular migratory panniculitis and eosinophilia due to the migration of the larva through the epidermis, dermis, and subcutaneous tissue. Although, the disease may also manifest as rash, abscess, and isolated nodules. The description of ulcerated lesions is rare¹⁰. The cutaneous manifestation of our report was a shallow, ulcerated cutaneous lesion, with a subcutaneous nodule, serous secretion discharge, and an absence of eosinophilia. This was an atypical manifestation, unlike most descriptions in the literature. A possible explanation for this presentation may be the co-infection with *Leishmania* itself, as it manifests more commonly as a single ulcerated lesion in an exposed area, secondary to a phlebotomine fly bite¹¹. It is known that localized cutaneous leishmaniasis leads to a cell-type immune response pole where there is no eosinophil (TH1)

activation¹⁵, while diseases caused by helminths induce a TH2 response pole, characterized by humoral immune response and activation of eosinophils¹⁶. Therefore the immune response induced by localized CL may have contributed to the absence of eosinophilia that could have been induced by gnathostomiasis.

The diagnosis of CL and gnathostomiasis is mainly based on clinical and epidemiological criteria, while the confirmation of the diseases is made by laboratory, through the detection of amastigote forms and larvae, respectively, at the site of injury^{1,13}. It is noteworthy to highlight the ultrasound discovery of a part of dead larva in a subcutaneous collection in this case, which is not commonly described in the literature¹.

Gnathostomiasis is treated with ivermectin or albendazole¹⁷. In this case, the patient was first treated with ivermectin due to the initial diagnostic hypothesis of myiasis, but after confirmation of *Gnathostoma* sp., we switched to albendazole treatment for 21 days, due to the risk of the occurrence of a severe visceral form (CNS gnathostomiasis). The patient had an excellent response to the treatment. CL can be treated with systemic or intralesional medication¹⁴. In this case, due to the small ulcerated lesion, treatment with intralesional antimony (3 doses) was chosen and also showed an excellent therapeutic response.

CONCLUSION

We reported the first case of gnathostomiasis and cutaneous leishmaniasis co-infection with atypical presentation of a shallow ulcer and absence of eosinophilia, in which the patient evolved with excellent therapeutic response to both diseases. It is important to highlight that there was a delay in the diagnosis of gnathostomiasis due to ignorance on the part of healthcare professionals, the atypical presentation form and the finding of amastigote forms of *Leishmania* sp.

"This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies. This Open Access article is distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work and authorship are properly cited."

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