# Localized Lymphadenopathy Due to Leishmanial Infection

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#### **Abstract**

A 25-year-old female patient presented with an isolated cervical lymph node enlargement several months after having returned from Spain and Latin America. She had no other signs or symptoms of disease. *Leishmania infantum/chagasi* was identified as the causative agent. With extended travel activities localized lymph node enlargement due to leishmanial infection should be included in the differential diagnosis of lymphadenopathy of unknown origin.

## **Key Words**

Leishmaniasis · Localized lymphadenopathy · *Leishmania* infantum/chagasi

### Introduction

The leishmaniases have been considered classical tropical infections. However, due to the increasing international travel activities and the inclusion of visceral leishmaniasis as a complication of AIDS, they have become a topic of general medical concern in the developed world.

Commonly, visceral leishmaniasis is a chronic infectious disease of the monocyte-macrophage system characterized by fever, pancytopenia, hepatosplenomegaly and weight loss. Cutaneous leishmaniasis presents as single or multiple papular, nodular or ulcerous skin lesions. We describe a case of an isolated cervical lymph node enlargement due to leishmanial infection without any cutaneous or systemic manifestations.

## **Case Report**

A 25-year-old German student presented to the otorhinolaryngology outpatient department with an indolent left supraclavicular lymph node enlargement of 1-month duration. She did not complain about any symptoms. She had been on a 2-week hiking tour in the Pyrenees of northern Spain 4 months before, to Guatemala and Mexico 16 months before and to Ecuador and Peru 40 months before the onset of the lymph node swelling. She

recalled occasional insect bites during these travels but no skin lesions

Apart from the isolated lymphadenopathy, the physical examination and an abdominal ultrasonography were unremarkable. No skin abnormalities indicative of current or healed cutaneous lesions were detected. Laboratory tests including hematological (RBC, WBC, differential and platelet count, erythrocyte sedimentation rate) and biochemical parameters (aspartate and alanine aminotransferase, IgG, IgM) were all normal. Since symptomatic and antibiotic treatment showed no improvement, the lymph node was excised. Histological examination revealed Leishmania amastigotes within macrophages. Antibodies to Leishmania donovani were detected in low concentration (1:160) by immunofluorescence (IFT). A culture from biopsy material grew Leishmania which were identified as Leishmania infantum/chagasi by DNAfingerprinting. The search for Leishmania in peripheral blood by PCR was negative. Due to the lack of any signs or symptoms indicative of systemic disease, further invasive investigations such as a bone marrow aspirate were not done. The patient was not infected by HIV or otherwise immunocompromised.

The patient was treated with liposomal amphotericin B (Am-Bisome®, 3mg/kg/d on days 1–5 and on day 10). Titers of antibodies to *L. donovani* had decreased to marginal concentrations (IFT 1:20) 2 and 6 months after treatment. Ultrasonography of the neck performed 2 and 6 months after treatment did not reveal any further lymph node enlargement.

## Discussion

Due to the preference of *Leishmania* parasites for the monocyte-macrophage system, generalized lymphadenopathy can occur with classical visceral leishmaniasis [1]. Lymph node enlargement associated with cutaneous le-

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sions caused by *Leishmania tropica* or by *Leishmania major* has been reported [2]. In the New World, lymphadenopathy may accompany or even precede skin lesion due to the *Leishmania braziliensis* complex, indicating that spread from the skin to lymph nodes occurs early in the course of infection [3–5]. However, localized lymphadenopathy without cutaneous or systemic manifestations is unusual and has been rarely reported [4–15]. Most cases were diagnosed by surgical biopsy because of a suspected lymphoma. Interestingly, in most of these patients the lymph node enlargement affected the left neck without further specification. In our case, the affected lymph node was located on the left neck at the junction of the ductus thoracicus which drains the lymph system of the viscera. It may be speculated that this particular location hints at a visceral involvement.

Although certain *Leishmania* spp. are more commonly associated with certain clinical syndromes than with others, there is a spectrum of clinical manifestations that can be seen with infections caused by the same species. This is particularly true for *L. infantum* which may cause the whole spectrum of disease, namely visceral, cutaneous and mucosal manifestations. The mechanisms underlying tissue tropism are poorly understood. However, the extent of the organ involvement in infections with *Leishmania* spp. mainly depends on the ability of the host to generate an effective cellular response [16]. Accordingly, dissemination of the parasites increases with decreasing immunocompetence. In fact, in patients with advanced HIV disease, parasites will eventually invade all organs including the skin and can appear in considerable numbers in the peripheral blood.

The absence of organ and laboratory abnormalities and the confinement to one lymph node indicate that our patient was able to control the infection over a period of several months. However, a change in immunocompetence, such as that occurring during pregnancy, might initiate generalization of the infection.

We assume that the infection was most likely contracted in northern Spain; all cases reported in this region so far were caused by *L. infantum* and the patient's visit to Spain was the most recent one. Due to the genetic similarities between *L. infantum* and *L. chagasi*, a differentiation of the two species is hardly possible.

The patient was treated with liposomal amphotericin B (AmBisome®), a drug which concentrates in macrophages, the target cells of *Leishmania*. It is currently the most effective and least toxic drug and, due to its short application schedule, the most practical treatment for leishmaniasis [17–19].

We conclude, that localized lymph node enlargement due to infection with *Leishmania* needs to be included in the spectrum of unusual presentations of leishmanial infections and should be considered in the differential diagnosis of lymphadenopathy of unknown origin.

#### References

- World Health Organization: Manual on visceral leishmaniasis control. WHO, Division of Control of Tropical Diseases, Geneva 1996.
- 2. Gafaar A, Ismail A, El Kadaro A, Hashim E, Khalil EAG, El Hassan AM: Necrotizing and suppurative lymphadenitis in *Leishmania major* infections. Trop Med Int Health 1996; 1: 243–250.
- Barral A, Barral-Neto M, Almeida R, de Jesus AR, Grimaldi Jr G, Netto EM, Santos I, Bacellar O, Carvalho EM: Lymphadenopathy associated with *Leishmania braziliensis* cutaneous infection. Am J Trop Med Hyg 1992; 47: 587–592.
- Barral A, Guerreiro J, Bomfim G, Correia D, Barral-Netto M, Carvalho EM: Lymphadenopathy as the first sign of human cutaneous infection by L. braziliensis. Am J Trop Med Hyg 1995; 53: 256–259.
- Sousa A de Q, Parise ME, Pompeu MML, Filho JMC, Vasconcelos IAB, Lima JWO, Oliveira EG, Vasconcelos AW, David JR, Maguire J: Bubonic leishmaniasis: a common manifestation of *Leishmamia* (*Viannia*) braziliensis infection in Ceara, Brazil. Am J Trop Med Hyg 1995; 53: 380–385.
- 6. Chung HL: Localized leishmaniasis of the lymph gland. Chin Med J (Engl) 1942; 62: 284–292.
- Angevine DH, Hamilton TR, Wallace FG, Hazard JB: Lymph nodes in leishmaniasis: report of two cases. Am J Med Sciences 1945; 2190: 33-38.
- Bell DW, Carmichael JAG, Williams RS, Holman RL, Stewart PD: Localized leishmaniasis of lymph nodes. BMJ 1958; 1: 740–743.
- Daneshbod K. Localized adenitis due to *Leishmania* simulating toxoplasmosis: Am J Clin Path 1978; 69: 46–47.
- Azadeh B: Localized *Leishmania* lymphadenitis: a light and electron microscope study. Am J Trop Med Hyg 1985; 43: 447–455.
- 11. Kumar PV, Hambarsoomina B, Vaezzadeh K: Fine needle cytology of localized *Leishmania* lymphadenitis. Acta Cytol 1986; 31: 14–16.
- Morsy TA, Mangoud AM, Aly MA, Farrag AM: Lymphatic leishmaniasis: An adult case without visceral involvement from Sharkia Governorate. J Egypt Soc Parasitol 1992; 22: 533–537.
- 13. Tallada N, Raventos A, Martinez S, Compano C, Almirante B: Leishmania lymphadenitis diagnosed by fine-needle aspiration biopsy. Diag Cytopathol 1993; 9: 673–676.
- Peachey AM, Irvine GH, White H: Visceral leishmaniasis: an unusual cervical presentation. Br J Oral Maxillofac Surg 1994; 32: 325–327.
- Vera-Alvarez J, Marigil-Gomez M, Abascal-Aborreta M, Lacasa-Laliena M: Diagnosis of localized *Leishmania* lymphadenitis by fine needle aspiration cytology. Acta Cytol 1999; 43: 529–553.
- Zwingenberger K, Harms G, Pedrosa C, Omena S, Neifer S: Determinants of the immune response in visceral leishmaniasis: evidence for predominance of endogenous interleukin 4 over interferon-γ production. Clin Immunol Immunopathol 1990; 57: 242–249.
- Gradoni L, Bryceson ADM, Desjeux P: Treatment of Mediterranean visceral leishmaniasis. Bull WHO 1995; 73: 191–197.
- 18. Sundar S, Murray HW: Cure of antimony-unresponsive Indian visceral leishmaniasis with amphotericin B lipid complex.

  J Infect Dis 1996; 173: 762–765.
- Meyerhoff A: US food and drug administration approval of Am-Bisome (liposomal amphotericin B) for treatment of visceral leishmaniasis. Clin Infect Dis 1999; 28: 42–48.