Isolated cervical lymphadenopathy: Do not forget atypical leishmaniasis

Adénopathie cervicale isolée, n’oubliez pas la leishmaniose

Introduction
Leishmaniasis is a vector-borne disease caused by *Leishmania* spp. The estimated new cases number is close to 2 million per year. Cases are reported from 98 countries where more than 350 million people live in areas with *Leishmania* transmission [1]. The parasite is transmitted by several genera and species of phlebotomine sandflies [1]. The infection, caused by intracellular amastigotes of the genus *Leishmania*, may affect the skin, mucous membranes or viscera, leading to a wide range of clinical presentations. Three major clinical syndromes are usually recognized: cutaneous (CL), mucocutaneous (MCL) and visceral (VL) leishmaniasis [1]. Isolated lymph node leishmaniasis (LNL) is exceptional.

Case report
We report the case of a 60 year-old female patient, native of Poland and inhabitant of Jendouba (Northwest of Tunisia), with a past history of diabetes mellitus, arterial hypertension and rheumatoid arthritis treated by steroids (prednisone 5 mg/day) and methotrexate (10 mg/week). She presented with a one year gradually increasing left submandibular swelling. Physical examination revealed blood pressure at 140/80 mmHg, regular heartbeat at 86/min, with no fever nor hepatosplenomegaly. Submandibular lymph node was 3 cm large, firm, elastic, mobile and painless, without fistula or abscess. Routine laboratory findings showed elevated gamma-globuline (29 g/l), non-elevated CRP (11 mg/l), a mild anemia (9,6 g/dl) and normal electrolytes. Electrolytes, renal and liver tests were within normal range. Chest X ray was normal as well as thoracic and abdominal CT. ELISA was negative for HIV. The fine needle aspiration (FNA) smears revealed a polymorphic population of cells composed of lymphocytes, histiocytes, epitheloid cells and macrophages infiltrated with *Leishmania* amastigotes. No acid fast bacilli were identified. Real Time Polymerase Chain Reaction (RT-PCR) was performed on lymph node biopsy and identified *Leishmania infantum*. However, it was negative on peripheral blood sample. Serology of leishmaniasis was highly positive by immunofluorescence assay (IFA) at 1/1600. Systemic visceral leishmaniasis was eliminated and localized node leishmaniasis was the retained diagnosis. The patient was treated with amphotericin B deoxycholate at a dose of 1 mg/kg/day. The duration identified at starting was 21 days because of the immunosuppressive treatment. At day 10, she developed renal insufficiency and despite giving amphotericin B 1 day/2, she altered her renal function at day 18 (creatinine 28 mg/l) and treatment was stopped. The clinical course was favorable. Creatinine has normalized. The lymph node size decreased quickly. She was found asymptomatic for 1 year of follow-up with a disappearance of lymphadenopathy.

Discussion
A rare case of LNL is reported. At our knowledge, it is the second Tunisian case after the one reported by Aoun et al. [2]. Such clinical presentation could be the first grade of visceral leishmaniasis or an aborted VL. Unusual manifestations of leishmaniasis occur mainly in patients with immunosuppression leading to delay in diagnosis and treatment [3]. Common causes for lymphadenopathy include viral illnesses, tuberculosis and malignancies [4,5]. Rarely, lymphadenopathy may be associated with parasitic diseases like toxoplasmosis but exceptionally leishmaniasis [5]. This protozoan infection is classified by geographic area, specific causative *Leishmania* species, arthropod vector and clinical presentation. Immunosuppression such as HIV infection or long term corticotherapy is a well-established risk factor for this disease [3]. Our patient lived in the north of Tunisia in an historical endemic area for leishmaniasis. Actually, the geographical distribution of cases in Tunisia revealed the spreading of the disease to the Center and recently to the South [6]. She had also rheumatoid arthritis since 2009 undergoing steroids and methotrexate. Clinical presentation can be atypical in immunocompromised individuals, leading to misdiagnosis, clinical complications and enhanced morbidity and mortality. Asymptomatic phases and relapses suggest that parasite can persist in tissues for a long time before and/or after clinical onset of the disease [7]. Dereure et al. described two cases of VL occurring in a patient with lymphoma and in a pregnant woman; in both cases, parasites were identified by culture and staining in lymph nodes after clinical cure [7]. Lymph node leishmaniasis is not the only known atypical presentation. Other cases reported from *Leishmania* endemic regions were described such as intestinal mucosa and liver locations [8]. The etiological investigation of isolated lymph nodes is based on the fine needle aspiration (FNA) and/or biopsy. In leishmaniasis,
the diagnosis confirmation requires the demonstration of the parasite amastigote in smears or its DNA by PCR [9]. Smears may show macrophages and granulomas without any necrosis. *Leishmania* parasites are 2–4 μm sized and well-stained with Romanowsky stains [10]. Tuberculosis is also a necrotizing disease frequent in Tunisia and more associated to lymph nodes. So, it is important to use a highly sensitive and specific method to correctly diagnose leishmaniasis cases with few parasites in the sample. PCR is more sensitive (92.1%) compared to graded microscopy (37% to 49% using only the correctly stained samples) [9].

Culture on appropriate medium should be made whenever it is possible. In addition to confirming the diagnosis, it allows complete epidemiological data and evaluation of the sensitivity to treatment. Contrarily to our patient, serology is often negative in the unusual locations and contributes rarely to the diagnosis.

Therapeutic guidelines are only recognized for VL and CL. Atypical presentations are not included in therapeutic guidelines leading to more difficulties in treatment choices and management. Decisions are to be made case by case according to the patient's immune status.

Liposomal amphotericin B is actually the drug of choice for VL. Amphotericin B deoxycholate use is limited by renal toxicity [8]. Antimoniate are less used because of renal toxicity and resistance. Our case was not a VL but a lymph node involvement in an immunocompromised patient. We prescribed amphotericin B deoxycholate (the unique formulation of amphotericin B in Tunisia) and the course was favorable.

**Conclusion**

Only a few cases of isolated cervical lymphadenopathy due to leishmaniasis had been reported. This case highlights the need of detailed examination and evaluation mainly in endemic areas of some infectious diseases such as leishmaniasis. The combination of parasitological, serological and molecular methods is the best approach for diagnosis confirmation.

**Disclosure of interest:** the authors declare that they have no competing interest.

**References**


