Laryngeal leishmaniasis as initial opportunistic disease in HIV infection

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Abstract
A case of laryngeal leishmaniasis, with symptoms of hoarseness and odinophagia which had developed over the past year, is presented. Clinical features and histological findings are discussed. Visceral leishmaniasis is increasingly associated with HIV infection and some authors have suggested the possibility of including it as a diagnostic criterium for AIDS in HIV-positive patients.

When any case of leishmaniasis presents atypical clinical features, localization or treatment response in endemic areas, HIV infection should be ruled out.

Key words: Leishmaniasis; laryngeal disease; acquired immunodeficiency syndrome

Introduction
Leishmaniasis is a disease caused by protozoans of the genus Leishmania. It can be divided into three clinical syndromes: visceral (Kala-azar), cutaneous and mucosal. The disease occurs in numerous areas scattered throughout the world including the Mediterranean basin which is considered an endemic area. In Spain, dogs and small rodents are the reservoirs of the disease, although other reservoirs have been described in other areas. It is transmitted to the human host through the bite of the female sandfly (Phlebotomus spp.). They ingest leishmania amastigotes when feeding on infected mammals; amastigotes convert into promastigotes in the gut of the sandfly and then they are inoculated into the mammalian host. Once in the mammalian host, promastigotes are phagocytosed by mononuclear cells and then convert back into aflagellated and intracellular amastigotes. Multiplication is by binary fission. Classically, the four species producing disease in man are L. donovani, L. tropica, L. mexicana and L. braziliensis. Whereas the first is fundamentally viscerotrophic, the others produce cutaneous and mucosal disease.

Of the different clinical presentations, visceral leishmaniasis (Kala-azar) and cutaneous leishmaniasis (bouton d’orient) are endemic within the Mediterranean basin, particularly in southern Spain. The incidence of visceral leishmaniasis in Spain is rather low but recently there have been many reports associating it with HIV infection and other immunosuppressive conditions (Fernández-Guerrero et al., 1987; Montalbán et al., 1987; Berenguer et al., 1989; Altés et al., 1987).

We present a case of laryngeal leishmaniasis the onset of which presented as long-term dysphonia. This opportunistic infection led to the diagnosis of HIV infection in a patient not known to be HIV positive.

Case Report
A 29-year-old male came to the ENT clinic complaining of progressive hoarseness, dysphagia and odinophagia over the past year with dyspnoea. He had lost weight (about 6 kg) over the last three months. He smoked 40 cigarettes per day and drank 80 g/day of alcohol. He denied intravenous drug use but reported homosexual behaviour with risky sexual contacts. By the age of 17 years, he had been treated for a primary luetic infection with penicillin. He had an apparently healthy dog and lived in an urban area.

The ENT exploration was normal, except for the indirect laryngoscopy which showed large epiglottic and hypopharyngeal swellings and reddening with several ulcerations covered by
Mucosal corion infiltration by lymphohistiocytes. The arrow marks an histiocyte with vacuolated cytoplasm and corpuscles inside. (H&E; x100).

A dirty grey exudate. Suspecting a neoplasm or laryngeal tuberculosis it was decided to perform a direct laryngoscopy.

The pre-operative chest X-rays and ECG were normal and the results of the haematological study were: white blood count 5.0 \(10^3\text{ mm}^{-3}\) with 45 per cent lymphocytes (2.3 \(10^3\text{ mm}^{-3}\), 41.3 per cent neutrophils (2.0), 13.7 per cent monocytes, eosinophils and basophils; red blood count 4.21 (10\(^6\) \text{ mm}^{-3}\), haemoglobin 13.4 (g/dl), haematocrit 39.8 per cent. The erythrocyte sedimentation rate (1st hour) was 76 mm per hour. Liver and kidney function tests were normal.

An hypopharyngeal and laryngeal diffuse swelling and reddening were confirmed by direct laryngoscopy (Figure 1). The mucosa was granular in appearance, covered with a dirty grey exudate that fell off easily, leaving a bleeding ulcer. At the base of the tongue a verrucous mass was detected. Vocal folds were swollen, granular and covered with the same exudate, but no ulcers were apparent (Figure 1). Epiglottic and tongue base mass biopsies were taken.

The histological study showed a mucosa covered with a squamous epithelium which presented pseudoepitheliomatous hyperplasia with moderate dysplasia. A dense inflammatory infiltration with histiocytes containing leishmania amastigotes were found in the corion using giemsa (Figure 2) and haematoxylin and eosin (Figure 2) stains. Because of these results, a serological test for HIV was carried out (Western-Blot) with a positive result.

The patient, male, white, and weighing 47 kg was admitted. He had a septic mouth, but no oropharyngeal candidiasis, was present. His temperature was of 38°C. There were no enlarged cervical or axilar lymph nodes and no skin lesions suggesting cutaneous leishmaniasis. His chest examination was normal and abdominal palpation showed no liver enlargement but a small spleen enlargement. His haemoglobin was 11.7 g/dl, the white blood count 4.1 mm\(^3\) (1,800 lymphocytes), and the erythrocyte sedimentation rate 83 mm/hour (1st hour). The liver and renal function tests were within normal limits. A polyclonal hypergammaglobulinaemia was detected with a serum albumin of 3.5 g/dl and beta-2-microglobulin 4.380 \(\mu\)g/l. The urinalysis showed 10–15 red blood cells and 1–3 leucocytes per field. No proteinuria was found. The abdominal ultrasonography showed a slightly enlarged liver and spleen, with no structural abnormalities.

The patient was treated with meglumine antimoniate (Glucantine\textsuperscript{®}, 20 mg/kg/day of antimony). Fever and chills continued for five days from the onset of the treatment, and then disappeared.

The results of the serological study were: HB, Ag-negative, anti-HB\(_\text{s}\), positive. anti-HB\(_\text{s}\)-positive, HCV (ELISA) negative, CMV IgG positive (583.5 IU/ml), toxoplasma (EIA) IgG positive (02.4 IU/ml), lues (RPR) positive (1/4), leishmania (ELISA) positive (1/1280), HIV positive (ELISA). HIV Ag (p 24) positive.

The lymphocyte subpopulations were: CD4 21 per cent (normal 44±14 per cent) with an absolute number of 235 cells/mm\(^3\); CD8 70 per cent (normal 28±13 per cent) with an absolute number of 784±1 cells/mm\(^3\). The CD4/CD8 ratio was 0.3 (inverted). No amastigotes were observed in the bone marrow with giemsa and haematoxylin–eosin stains. Cultures were negative and thus characterization of the leishmanias was not possible.

The patient experienced a significant improvement in his dysphagia and hoarseness by the 13th day of treatment, but still presented moderate dyspnoea. The patient was discharged by the
15th day of treatment. The treatment was continued for a further three weeks, with continuous improvement in the symptoms.

Discussion

HIV infection causes a progressive depletion of the CD4 lymphocytes, leading to an immunosuppressive state, with the risk of opportunistic infections. These infections greatly depend on the endemic microorganisms in each area. In Spain, the increasing incidence of HIV infection and AIDS produces a significant increase in reports of tuberculosis (Aguado-García and Castillo-García, 1985) and visceral leishmaniasis (Montalbán et al., 1987; Berenguer et al., 1989), among other opportunistic infections. The incidence of visceral leishmaniasis during the course of AIDS among patients with AIDS in the Balearic Islands is at least six per cent (Altes et al., 1993).

Laryngeal leishmaniasis is extremely rare in the Western World, with a few cases described in patients coming back from tropical areas (Zinneman et al., 1961). Several cases of laryngeal involvement in a leishmania infection have been described in the Mediterranean basin (Ranque et al., 1962; D’Anna and Jemma, 1964; PotschIGIN, 1965; MeynæF et al., 1974; RAVISSE et al., 1984; FERLITO et al., 1986), and none of them were related to HIV infection. Laryngeal involvement is more frequent in other species of Leishmania such as L. braziliensis or L. mexicana, but they are limited to Central and South America (Jaffé, 1960).

In this case, the patient reported a short one-week vacation in Chile, 16 years previously. This presents the possibility of infection by a New World Leishmania sp. which orientates towards the mucosa, causing oral, hypopharyngeal and laryngeal lesions more often than other strains, with the possibility of secondary mucosal lesions after a very long period of time (as long as 24 years) (Walton et al., 1973). On the other hand, venereal transmission of leishmaniasis has been suggested in homosexuals (Rosenthal et al., 1988), related to a rectal swelling (mass) in which Leishmania spp. were identified and venereal inoculation was thought to be the cause. This possibility has to be considered as a possible way of infection in our case. Finally, another option to be considered as the cause, is infection by autochthon Mediterranean strains of Leishmania (mainly L. donovani), although they have no special mucosal orientation, because recently a case of nasal septum mucosal involvement in which L. infantum was isolated has been described.

The characterization of the Leishmania strains was not possible because different cultures of the bone marrow specimens and the laryngeal biopsy using Novy-MacNeal-Nicolle (NNN) medium were always negative. However, we believe the cause of infection was a local strain of Leishmania (possibly L. donovani) because the haematological results (with polycyonal hyperglobulinaemia and relative leucopenia), moderate spleen enlargement and the malaise pointed to a disseminated infection of the reticuloendothelial system, although the clinical features were basically the symptoms of an upper aerodigestive tract infection, and the possibility of mucosal involvement during autochthon Leishmania infection has been documented (Alvar et al., 1990).

At the time of the diagnosis of leishmaniasis, the patient did not know he was HIV positive and had not presented with any other infection related to the AIDS complex, so this opportunistic infection led to the diagnosis of HIV infection. This has never been described before. The association between HIV infection and leishmaniasis has been reported increasingly and expected.

Conclusions

In the case reported, leishmaniasis of the larynx, presenting as intense hoarseness, dysphagia and odinophagia, led to the diagnosis of HIV infection in a patient not known to be HIV positive. This, as far as we know, has never been described before.

When leishmaniasis presents atypical localization, clinical features or anomalous evolution, HIV infection should be ruled out, even more so if the response to treatment is not as good as expected.

References


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