ISOLATED LARYNGEAL LEISHMANIASIS IN A 55-YEAR-OLD MAN WITH DYSPHONIA AND RHEUMATOID ARTHRITIS: CASE REPORT AND LITERATURE REVIEW

ALESSIO STRAZZULLA, SALVATORE COCUZZA, MARILIA RITA PINZONE, MARTINES FRANCESCO, AGOSTINO SERRA, STEFANO COSENTINO, BRUNO CACOPARDO, GIUSEPPE NUNNARI
1Department of Clinical and Molecular Biomedicine, Division of Infectious Diseases, University of Catania - 2Department of Medical-Surgical Specialties, ENT Clinic, University of Catania - 3Section of Otorhinolaryngology, Department of Clinic Neuroscience, University of Palermo, Italy

ABSTRACT

We describe a case of isolated laryngeal leishmaniasis in an 55-year-old smoker, treated with steroids for rheumatoid arthritis, in the absence of concomitant visceral or cutaneous localizations. Clinical presentation was dominated by dysphonia. Laryngeal biopsy revealed the presence of Leishmania amastigotes, which were characterized by species-specific polymerase chain reaction as L. donovani parasites. In endemic areas, Leishmania infection may present with atypical localizations and it has to be considered as a possible cause of laryngeal symptoms, especially in subjects with known immunosuppressive diseases or under treatment with immunosuppressive drugs.

Key words: Laryngeal lesion, Leishmania, Leishmaniasis, Rheumathoid arthritis.

Received July 05, 2013; Accepted August 28, 2013

Introduction

Leishmania spp. are sandfly-transmitted protozoa causing a spectrum of diseases in humans(1,2). Three main clinical syndromes are described: visceral, cutaneous and mucosal leishmaniasis(1). Mostly in Latin America, Leishmania (L.) braziliensis may be responsible for a severe mucous membrane involvement extended from the nose and oral cavity towards pharynx and larynx(2). In the Mediterranean Basin, L. donovani and L. infantum have been shown to cause occasionally localized mucosal disease in the absence of any concomitant visceral or cutaneous involvement(3,4).

Atypical mucosal localizations of Leishmania with variable clinical presentations are rare among immunocompetent individuals(5), whereas they have been reported in immunodeficient patients, such as those infected with human immunodeficiency virus type 1 (HIV-1), as well as organ transplant recipients and individuals on immunosuppressive thera-
pies(4,17). Mucosal leishmaniasis may result from lymphatic or haematogenous spread of the parasites. In the respiratory tract, descending invasion from oral or nasal mucosa may occur, leading to a destructive disease.

Here, we describe a case of laryngeal leishmaniasis in a 55-year-old smoker, with a recent diagnosis of rheumatoid arthritis (RA) treated with steroids, who presented with dysphonia. Moreover, we review other published cases of isolated laryngeal leishmaniasis in immunocompromised subjects.

Methods

We report a case of isolated laryngeal leishmaniasis in an immunocompromised patient who presented to the Division of Infectious Diseases of the Garibaldi-Nesima Hospital of Catania. Furthermore, we review 13 case reports from 10 articles(4,9-17) (Table 1).
Other articles were discarded because they did not meet the following criteria: 1) full description of the case; 2) absence of any other mucosal lesion; 3) access to English full text. Patients were considered immunocompromised in presence of known immune compromising factors, such as HIV infection, corticosteroid therapy and malignancies.

Case report

In September 2010, a 55-year-old man presented with a two-month history of progressive dysphonia and globus sensation. He denied dyspnea, dysphagia, cough or sputum production. The patient was taking lansoprazole for gastroesophageal reflux disease (GERD) and he was receiving prolonged courses of high-dose steroids, hydroxychloroquine and diclofenac since January 2009 for the treatment of RA. He had been smoking 20 cigarettes a day for 20 years and drinking about 30 milliliters of alcohol daily. At the age of 45, he had developed visceral leishmaniasis (VL), which had been treated with amphotericin B. When he was 47, he had undergone microsurgical surgery because of bilateral Reinke’s edema.

Neither lymphadenopathies nor other abnormal findings were detected on head and neck examination. The liver was slightly enlarged. Laboratory investigations, including complete blood cell count, serum biochemical studies and urinalysis, were all within the normal range, with the exception of augmented erythrocyte sedimentation rate (ESR) (33 mm/h), C reactive protein (58.8 mg/l) and lactate dehydrogenase (482 UI/l). HIV test was negative, as well as Mantoux intradermal reaction. Cardiological evaluation and chest radiograph were

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Nation</th>
<th>Comorbidities</th>
<th>Lesion site</th>
<th>Lesion description</th>
<th>Signs and symptoms</th>
<th>Diagnosis</th>
<th>Leishmania spp.</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>M</td>
<td>Spain</td>
<td>Asthma (treated with corticosteroids), gastroesophageal reflux disease (GERD), diabetes and hypertension</td>
<td>Larynx</td>
<td>...</td>
<td>Weight loss, cough, subcutaneous edema, dysphonia Sleep and restlessness with exacerbations covered by grey eschara</td>
<td>Eosinophils, epithelial hyperplasia Larynx</td>
<td>Laryngoscopy, dysphagia</td>
<td>Histologic</td>
<td>Liposomal amphotericin B 0.5 mg/kg/day for 14 days</td>
</tr>
<tr>
<td>50</td>
<td>M</td>
<td>France</td>
<td>Sarcoidosis (treated with corticosteroids)</td>
<td>Larynx</td>
<td>...</td>
<td>Dysphonia</td>
<td>Histologic</td>
<td>...</td>
<td>Liposomal amphotericin B 0.5 mg/kg/day for 14 days</td>
<td>Clinical recovery</td>
</tr>
<tr>
<td>52</td>
<td>F</td>
<td>India</td>
<td>Diabetes, hypertension, anemia (treated with corticosteroids), stroke</td>
<td>Larynx</td>
<td>...</td>
<td>Dysphagia, dysphonia and dysphonia</td>
<td>Histologic</td>
<td>...</td>
<td>Liposomal amphotericin B 0.5 mg/kg/day for 14 days</td>
<td>Clinical recovery</td>
</tr>
<tr>
<td>55</td>
<td>M</td>
<td>Italy</td>
<td>GERD (treated with corticosteroids and diclofenac)</td>
<td>Larynx</td>
<td>...</td>
<td>Dysphagia, respiratory distress, dysphonia</td>
<td>Histologic</td>
<td>...</td>
<td>Liposomal amphotericin B 0.5 mg/kg/day for 14 days</td>
<td>Clinical recovery</td>
</tr>
</tbody>
</table>

Table 1: Features of 14 cases of isolated laryngeal leishmaniasis in immunocompromised subjects.
unremarkable. Flexible laryngoscopy showed a swollen vocal cord on the right side with an irregular surface and a white patch on its middle third. On the left side, some areas of mild leukoplakia were described between the middle and anterior third of the vocal cord (Fig.1). Histological examination of laryngeal specimens showed the presence of non-necrotizing granulomatous inflammation in the subepithelium, with lymphocytes, granulocytes and many histiocytes. Giemsa staining showed cytoplasmic inclusions within histiocytes, which were suggestive of Leishmania amastigotes. Serological test for Leishmania was positive with a titer of 1/640. L. donovani was detected by polymerase chain reaction (PCR). Bone marrow biopsy was negative for Leishmania parasites. The patient was treated with liposomal amphotericin B at a dose of 3 mg/kg/per day for seven days and, subsequently, 3 mg/kg once a week for 5 weeks, obtaining a complete clinical and endoscopic recovery.

Fig. 1: Flexible laryngoscopy showed a swollen vocal cord on the right side with an irregular surface and a white patch on its middle third. On the left side, some areas of mild leukoplakia between the middle and anterior third of the true vocal cord.

Review of published works and discussion

In our review of the literature, we considered fourteen cases (4,9-17) (Table 1): median patient age was 52 years (Interquartile range 42-64), ten (72%) were men. Five patients (37%) came from the United Kingdom, three (21%) each from France and Spain, one (7%) each from Malta, Portugal and Italy. Four patients (29%) had travelled to countries where leishmaniasis is endemic, mainly in the Mediterranean basin. Immunodeficiency was related to HIV infection in five cases (37%). Nine patients (63%) were taking steroids, in the majority of cases for the treatment of asthma. Six patients (43%) complained of dysphonia, eight subjects (57%) had hoarseness. Less common symptoms were dysphagia, odynophagia and globus sensation. Histological examination was essential to diagnose leishmaniasis, as parasites were visualized in the biopsy specimens in all cases, usually with Giemsa stain. Anti-leishmania antibodies were positive in six cases (43%). Identification of Leishmania spp. was possible in 50% of patients: L. donovani was isolated in four cases (29%), L. infantum in three cases (21%).

Seven patients (50%) received meglumine antimoniate, generally at a dose of 20 mg/kg/day; in two cases (14%) sodium stibogluconate was administered, whereas in four cases (29%) patients were treated with liposomal amphotericin B. Twelve patients (86%) achieved cure; two patients (14%) developed visceral leishmaniasis, respectively nine and twenty-four months after treatment for laryngeal leishmaniasis.

The presence of dysphonia in a smoker with GERD, taking steroids for RA, certainly needs a thorough investigation. In differential diagnosis, cancer and infections have to be ruled out; laryngoscopy, with histological evaluation of laryngeal biopsies, represents the best approach to reach the correct diagnosis. In our case, laryngeal biopsy revealed the presence of inclusions within the cytoplasm of histiocytes. The detection of L. donovani by PCR, along with a positive serology test, led to the diagnosis of laryngeal leishmaniasis.

In recent years an increase in visceral and mucosal leishmaniasis has been observed in patients with immunodeficiency, such as patients undergoing organ transplantation or immunosuppressive therapy, patients with malignancies or HIV infection (4-17). In our case, the patient was receiving steroids, hydroxychloroquine and diclofenac for the treatment of RA. The immunosuppressive role of these agents is well known and could have led to Leishmania reactivation with laryngeal localization. Analogously, reactivation of latent diseases, such as tuberculosis, hepatitis B virus and herpes viruses, is a critical issue in patients treated with new biological drugs, i.e. tumor necrosis factor-alpha inhibitors, so that pre-treatment screening and monitoring are essential (18-20). Considering the widespread use of biological drugs for the treatment of several immune-mediated diseases (i.e. psoriasis, RA) and the capability of Leishmania to reactivate, it is critical for physicians to keep into account the possibility of mucosal or even visceral leishmaniasis to occur when using these drugs.

The pathogenesis of isolated laryngeal leish-
miasis is still unclear: Aliaga et al. suggested that
the lower temperature of the upper airways may
favor the survival of some Leishmania strains
\(^{(10)}\). In asthmatic patients, long-term use of inhaled
steroids may cause local immunosuppression. For
homosexual individuals, veneral transmission of
Leishmania has also been hypothesized
\(^{(12)}\).

Unfortunately, no standardized protocols are
available for the treatment of laryngeal leishmaniasis,
because of the limited number of cases observed
so far. Both pentavalent antimonials and liposomal amphotericin B seem to be effective but
available evidence does not allow to recommend
any specific protocol in terms of both dosage and
duration of treatment. Follow up is important in
the management of laryngeal leishmaniasis since local
or visceral relapses may occur
\(^{(13)}\).

In conclusion, although rare, leishmaniasis has
to be suspected in all patients presenting with laryngeal symptoms, especially if they are immunocompromised or they have lived or travelled to endemic areas. Healthcare providers should be aware of this clinical entity in order to avoid misdiagnose or delayed diagnose.

References


