Nasal mucocutaneous leishmaniasis – An unusual form of presentation

Clinical Case

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Abstract

Leishmaniasis is caused by the protozoan parasite Leishmania which is transmitted through bites of infected female phlebotomine sandflies. There are 3 main forms – visceral, cutaneous and mucocutaneous, with mucosal affection being the rarest manifestation of the disease. The incidence in Portugal is considered hypoendemic.

We present a case of a 48 years old female, with complaints of nasal obstruction, epistaxis and irregular erythematous scaly plaques surrounding the nostrils. Histology of the nasal septum and skin revealed the presence of Leishmania-Donovan bodies. She was treated with amphotericin-B and itraconazole with clinical improvement and disappearance of lesions.

Mucocutaneous leishmaniasis preferably affects the nasal mucosa and if not diagnosed and treated in time can lead to cartilage destruction and dissemination of mucosal lesions to the nasopharynx, larynx, compromising the airway and even leading to disfigurement.

Keywords: leishmaniasis; mucocutaneous leishmaniasis; nasal leishmaniasis

Introduction

Leishmaniasis is an infectious disease caused by protozoan parasites belonging to the Leishmania genus, which is transmitted through the bite of a female phlebotomine sandfly belonging to the genera Phlebotomus and Lutzomyia . Phlebotomus pernicious and Phlebotomus ariasi are the most important species in Western Europe.[1,2,3]

The number of new cases of leishmaniasis occurring annually worldwide is estimated to be approximately 0.7 to 1 million, with approximately 350 million people at risk. It is endemic to underdeveloped regions such as Latin America and the Middle East, but rarer in European countries. Human leishmaniasis is considered hypoendemic in Portugal.[4,5]

When leishmaniasis is symptomatic, there are three main forms of clinical manifestation:

cutaneous, mucocutaneous, and visceral. Mucocutaneous leishmaniasis is the rarest form and is mainly caused by the species Leishmania Braziliensis. It may occur as a primary manifestation of the disease or secondary to the cutaneous presentation.[1,3,6]

The case presented herein is that of a woman with a previous history of cutaneous leishmaniasis treated five years ago who was referred to the otorhinolaryngology (ORL) clinic due to de novo nasal complaints.

Case description

The patient was a 48-year-old woman who lived in a rural area and was referred to the ORL clinic for nasal congestion and self-limited episodes of epistaxis. She had a relevant history of type II diabetes mellitus and cutaneous leishmaniasis (Leishmania tropica) diagnosed in 2015, which was treated with oral itraconazole (600 mg once/day for 28 days), with lesion resolution. She did not have a history of nasal trauma or chronic rhinosinusitis. She denied having recently travelled abroad or before the diagnosis of cutaneous leishmaniasis.

Objective examination showed erythematous lesions, infiltrating the sides of the nose, columella, and nasal vestibule (Figure 1). Nasal endoscopy also showed thick, erythematous plaque lesions with scabs in the anterior region of the septum. Concomitantly, an anterior septal perforation of approximately 0.50.5 cm was observed in the Cottle areas 2 and 3 (Figure 2).[7] Neck palpation was normal, as was the remaining objective ORL examination. There were no erythematous lesions at other sites of the body.

Figure 1
Before treatment. Well demarcated erythema in the middle third of the face, homogeneous at the level of the sides of the nose, nasal columella, and nasal philtrum

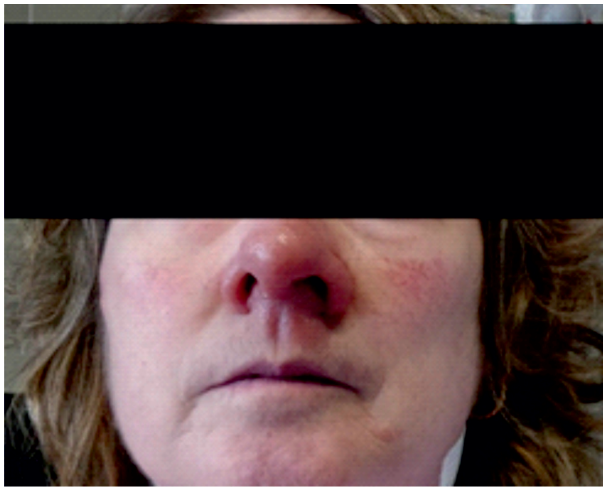
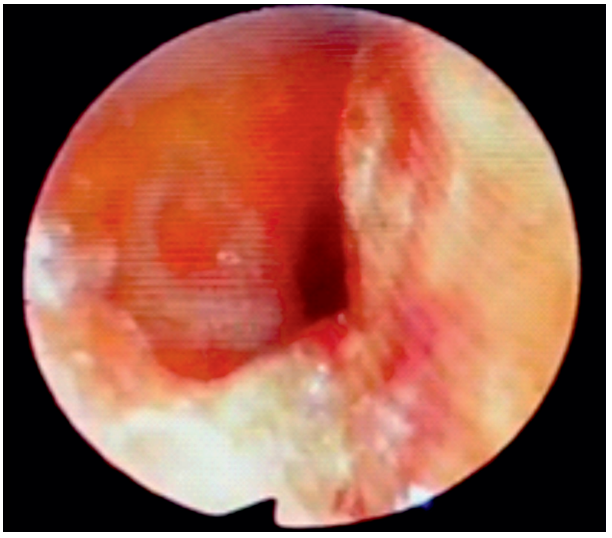


Figure 2
Nasal endoscopy of the right nasal cavity. Multiple small lesions, with erythematous borders can be seen



Blood tests showed mild lymphopenia (0.7910^9/L), glycated hemoglobin of 6.9%, and sedimentation rate of 7 mm/h. The results of tests for autoimmunity, vasculitis, VDRL, and HIV serology were negative.

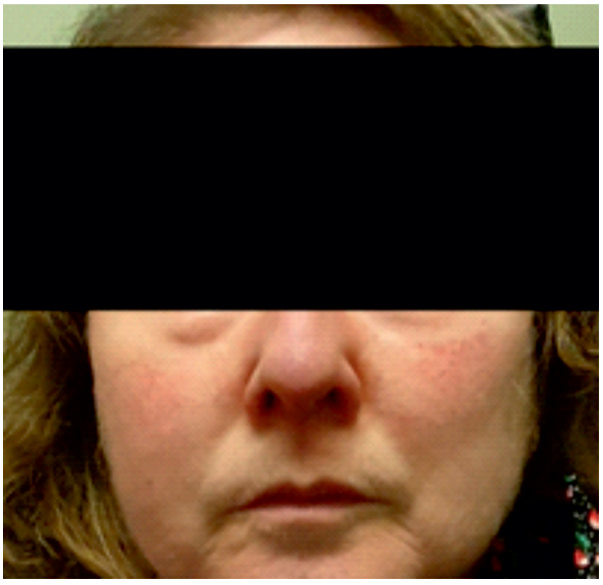
Computed tomography (CT) of the paranasal sinuses showed discontinuity of the cartilaginous portion of the anterior region of the nasal septum and thickening of the soft tissues of the septal mucosa. Abdominal CT did not show any relevant changes. Skin and endonasal biopsies were performed and the histological examination showed a dense inflammatory infiltrate with numerous histiocytes containing intracytoplasmic structures compatible with Leishman-Donovan bodies. The result of the polymerase chain reaction assay was compatible with a diagnosis of leishmaniasis.

The patient was hospitalized for treatment with amphotericin B (4 mg/kg, IV). Three weeks after the treatment, there was no

clinical improvement and the patient developed nephrotoxicity and muscle pain; therefore, amphotericin B was replaced by itraconazole (600 mg once/day), which was given for three months. Subsequently, clinical resolution was achieved with improvement in the erythema, nasal congestion, epistaxis, and nasal discomfort; in addition, the post-treatment biopsies showed no Leishman-Donovan bodies.

The patient is being followed up in the dermatology and ORL clinics and, so far, has exhibited no further manifestations of the disease.

Figure 3
After treatment



Discussion

Leishmaniasis is a primarily zoonotic infection, caused by protozoan parasites of the genus Leishmania spp. All species of Leishmania are transmitted through the bite of female sand flies of the genera Lutzomyia and Phlebotomus. Transmission occurs by inoculation of the promastigote forms into the skin of the vertebrate host.[1,3,8]

This disease is mostly endemic to the tropical rural areas of Central and South America (New World), Africa, India, and the Middle East (Old World), as well as Mediterranean regions of Europe. In Portugal, the most recently collected data show that the prevalence of the infection among dogs (the main reservoir of human leishmaniasis) and cats is a cause for concern regarding the risk of increased number of cases and dissemination of this parasitosis.[5,6]

The severity of the clinical manifestations of leishmaniasis depends on factors such as the parasite, the natural host's resistance, and the magnitude of the immune response. Visceral leishmaniasis is usually more severe and is often fatal if not treated. HIV increases the host's susceptibility to active disease, which usually manifests as a more aggressive and atypical form. In Portugal, there has been an increase in the number of cases of visceral leishmaniasis in adults with HIV co-infection, a trend that has been decreasing since the introduction of anti-retroviral therapy.[2,9]

Leishmaniasis may be cutaneous, mucocutaneous, or visceral. Cutaneous and mucocutaneous leishmaniasis is not a notifiable disease; therefore, it is believed to be underdiagnosed given the usually benign course of the lesions. Visceral leishmaniasis has been a notifiable disease since the 1950s.[2]

Cutaneous leishmaniasis is the most common presentation of the disease and is characterized by single or multiple pinkish macular lesions that progress to nodules and subsequently to painless well-defined ulcers with raised borders that can affect any area of the body. It is usually accompanied by painless enlarged lymph nodes located near the site of parasite inoculation.[1,3,8]

Mucocutaneous leishmaniasis is the rarest manifestation of the disease and is mainly caused by L. Braziliensis. It is almost always secondary to the cutaneous presentation. It may appear when the cutaneous lesion is still active, but it usually appears months or years after its resolution. It primarily affects the nasal mucosa; however, as the disease becomes more aggressive, it can affect the mucosa of the oral cavity, pharynx, and larynx. The anterior region of the nasal septum is a favorable environment for the development of amastigotes. Low temperatures in this part decrease the ability of macrophages to carry

out phagocytosis and consequently favor the parasite's growth.[1,6,8,10]

The symptoms and signs include nasal congestion, epistaxis, rhinorrhea, nasal granuloma, ulcers, and scabs. As the disease progresses, the skin of the nose thickens with an increase in the volume of the nasal pyramid (leishmaniasis facies) and may progress to destruction of the septal cartilage.[1,6,8,11]

The differential diagnoses of mucocutaneous leishmaniasis include tumors, rhinophyma, septal perforation from trauma or substance abuse, vasculitis, syphilis, and other granulomatous diseases such as paracoccidioidomycosis, tuberculosis, and leprosy.[3,6,8]

Visceral leishmaniasis is the most severe form of the disease and presents with systemic manifestations such as fever, hepatosplenomegaly, anorexia, weight loss, and anemia.[1,8]

A biopsy of the lesion should be performed when there is a suspicion of this diagnosis. Leishman-Donovan bodies can be visualized in appropriate culture media and the polymerase chain reaction technique allows the molecular detection of the protozoan's DNA. Testing for anti-Leishmania spp. antibodies is only recommended when visceral leishmaniasis is suspected because their specificity to distinguish between past exposure and present infection is low. [10,12,13]

The risk of morbidity (cosmetic disfigurement) and mortality associated with mucocutaneous leishmaniasis is higher than that with cutaneous leishmaniasis; therefore, these cases should be given systemic treatment. The choice of anti-leishmaniasis medication, dose, and treatment duration should be individualized. Its administration can be oral or parenteral. In the former case, the drugs used are azoles (itraconazole 600 mg once/day or ketoconazole 600 mg once/day for four weeks or fluconazole 200 mg once/day for six weeks) and miltefosine (2.5 mg/kg maximum, 150 mg/day for four weeks); for parenteral administration, the drugs used are pentavalent antimony compounds (20 mg/kg idI IV [intravenous] or IM [intramuscular] for four weeks) or liposomal amphotericin B (3-7 mg/kg with a total cumulative dose between 20 and 60 mg/kg). The aim of the treatment is clinical cure and not parasitological clearance.[12,13]

The criteria for cure include the disappearance of the lesions and symptoms in the three months following treatment. Monthly follow-up is recommended until the criteria for cure are met, followed by annual follow-up because there is a high probability of relapse.[8,9,10]

The diagnosis and guidance of patients with leishmaniasis should involve a multidisciplinary team that includes the specialties of dermatology, infectious diseases, internal medicine, otorhinolaryngology, and anatomical pathology.

Leishmaniasis is a disease with significant morbidity. However, it has an excellent prognosis when diagnosed at an early stage. Although it rarely occurs in Portugal, it is important that otorhinolaryngologists include it as a differential diagnosis when presented with similar cases.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

Bibliographic references

1.Neto FX, Rodrigues AC, Silva LL, Palheta AC, Silva FA. Manifestações otorrinolaringológicas relacionadas à leishmanisoe tegumentar americana: revisão de literatura. Arq. Int. Otorrinolaringol. [Internet] 2008; 12(4): 531-537. Disponível em: http://www.arquivosdeorl.org.br/conteudo/pdfForl/568.pdf.

2.Campino L, Maia C. Epidemiologia das leishmanioses em Portugal. Acta Med Port 2010; 23(5): 859-864.

3.Handler MZ, Patel PA, Kapila R, Al-Qubati Y, Schwartz RA. Cutaneous and mucocutaneous leishmaniasis: Clinical perspectives. J Am Acad Dermatol. 2015 Dec;73(6):897-908; quiz 909-10. doi: 10.1016/j.jaad.2014.08.051.

4.World Health Organization. Leishmaniasis key facts. [Internet] [Accessed 2022 May 3] Geneva: WHO; 2022. Disponível em: https://www.who.int/news-room/fact-sheets/detail/leishmaniasis.

5.Maia C, Campino L. Leishmaniose em Portugal no início do século XXI. Anais IHMT, Saúde Global e Doenças Tropicais. 2014; 3: 25-29. doi: 10.25761/anaisihmt.167.

6.Marra F, Chiappetta MC, Vincenti V. Ear, nose and throat manifestations of mucocutaneous Leishmaniasis: a literature review. Acta Biomed. 2014 May 9;85(1):3-7.

7.Hsu DW, Suh JD. Anatomy and physiology of nasal obstruction. Otolaryngol Clin North Am. 2018 Oct;51(5):853-865. doi: 10.1016/j.otc.2018.05.001.

8.Lessa MM, Lessa HA, Castro TW, Oliveira A, Scherifer A, Machado P. et al. Leishmaniose mucosa: aspectos clínicos e epidemiológicos. Rev. Bras. Otorrinolaringol. 2007: 73(6): 843-847. doi: 10.1590/S0034-72992007000600016.

9.Cipriano P, Miranda AC, Antunes I, Mansinho K. Leishmaniose visceral em doentes com infeção VIH: o desafio da recaída e falência terapêutica. Acta Med Port. 2017 Jun 30;30(6):443-448. doi: 10.20344/amp.8291.

10.Diniz JL, Costa MO, Gonçalves DU. Mucocutaneous leishmaniasis: clinical markers in presumptive diagnosis. Braz J Otorhinolaryngol. 2011 Jun;77(3):380-4. doi: 10.1590/s1808-86942011000300018.

11.Casalle N, de Barros Pinto Grifoni L, Bosco Mendes AC, Delort S, Massucato EMS. Mucocutaneous leishmaniasis with rare manifestation in the nasal mucosa and cartilage bone septal. Case Rep Infect Dis. 2020 Sep 22;2020:8876020. doi: 10.1155/2020/8876020

12.Manual de Controle da Leishmaniose Tegumentar Americana. 5th rev. ed. [Internet] Brasilia: Ministério da Saúde. Fundação Nacional de Saúde; 2000; 62 p. Disponível em:https://bvsms.saude.gov.br/bvs/publicacoes/funasa/manu_leishman.pdf.

13.Aronson N, Herwaldt BL, Libman M, Pearson R, Lopez-Velez R, Weina P. et al. Diagnosis and treatment of Leishmaniasis: clinical practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH). Clin Infect Dis. 2016 Dec 15;63(12):1539-1557. doi: 10.1093/cid/ciw742.

14.Rojas-Jaimes J, Frischtak HL, Arenas J, Lescano AG. Case report: mucosal leishmaniasis presenting with nasal septum perforation after almost thirty years. Am J Trop Med Hyg. 2018 Aug;99(2):327-330. doi: 10.4269/ajtmh.17-0831.