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Mucocutaneous leishmaniasis of the nose: a case report

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Abstract. *Mucocutaneous leishmaniasis of the nose: a case report*. Leishmaniasis is a parasitic infection that is rarely seen in Belgium. The majority of new diagnoses are seen in patients living in or visiting endemic regions, which are mostly developing countries. Here we describe the case of a 60-year-old male patient who was referred to an ENT specialist because of an erythematous swelling of the left side of the nose tip, which had persisted for 3 months. Biopsies showed the presence of leishmaniasis. This case report alerts ENT physicians that leishmaniasis is part of the differential diagnosis in patients who present with an uncommon persistent lesion in the head and neck region and who have travelled to endemic regions or are immunodeficient.

Introduction

Leishmaniasis refers to a group of disorders caused by protozoan parasites of the genus *Leishmania* that are transmitted by phlebotomine mosquitoes (sand flies). Leishmaniasis can be cutaneous (CL), mucosal (ML), or visceral (also called kala-azar). Leishmaniasis of the CL or ML types may be limited to one or a few lesions, but the visceral form can be life threatening due to (multi-) organ damage.[1,2]

Here we present the case of a 60-year-old patient with a persistent nasal lesion who was diagnosed with leishmaniasis. He developed this lesion after visiting the south of Spain. This case report discusses the epidemiology, pathogenesis, clinical presentation, diagnosis, and treatment of leishmaniasis, particularly that caused by *Leishmania infantum*.

Case report

A 60-year-old man was referred to an ENT physician because of an erythematous swelling of the left side of the nose tip that had appeared three months earlier. He had no other complaints. His medical history notably included curative surgery and radiochemotherapy for colon cancer, liver function disorders, toxic hepatitis, Barret's oesophagus, atrial fibrillation, and a history of alcoholism.

Clinical investigation of the patient's head and neck region revealed a red swollen nose tip, columella, and philtrum on the left side of the face, which was slightly painful with palpation (Figure 1). Anterior rhinoscopy showed scabs and an ulcer-like lesion in the left nasal vestibule. The red swelling had been present for about three months and was slowly progressive. His general practitioner had treated him three times with amoxicillin, but the lesion did not respond.

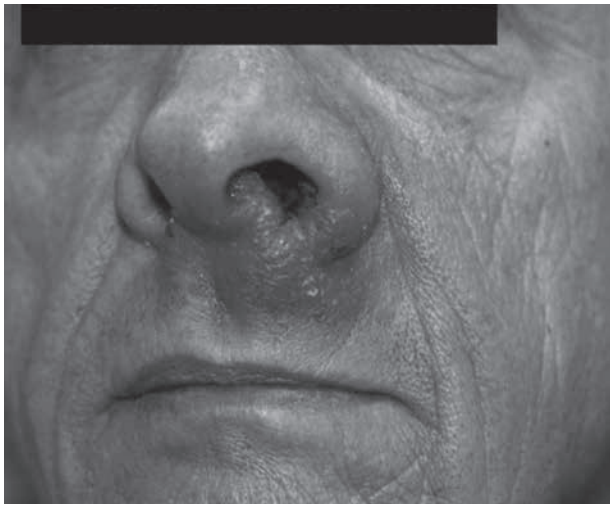

Figure 1
Red swollen nose tip, columella, and philtrum on the left side of the face with a few scabs present in the left nostril.

Treatment with a topical antibiotic ointment was initiated. Because of the uncommon and persistent nature of the lesion, a mucosal biopsy was taken. Histological investigation of this nasal biopsy led to the diagnosis of a parasitic infection, specifically leishmaniasis. Following this diagnosis, a specific anamnesis was performed to determine where the infection was acquired. The patient had travelled to Marbella in the south of Spain twice during the last six months. Beyond that, he had travelled twice to the African continent about 15 years ago and he had never been to Asia or South America.

Due to this uncommon diagnosis, the patient was referred to a reference centre, the Institute of Tropical Medicine in Antwerp. Clinical investigation further revealed a cutaneous lesion on that patient's left arm. He also began to experience nose bleedings due to the ulcer-like lesion in his nose. The nasal biopsies were reviewed at the tropical institute and a polymerase chain reaction (PCR) was performed, which confirmed the presence of leishmaniasis. Skin biopsy revealed a dermal diffuse inflammatory infiltrate comprising lymphocytes and histiocytes. *Leishmania* amastigotes were identified in the cytoplasm of the dermal macrophages. PCR results revealed *Leishmania infantum* as the causative parasite of the mucocutaneous leishmaniasis. Visceral leishmaniasis was ruled out.

Intralesional injection of Glucantime® (meglumine antimoniate) was not possible because the lesion was too hard. Therefore, a 12-week course of daily treatment with fluconazole 400 mg per os was started, but was unsuccessful. Next, therapy was initiated with intravenous meglumine antimoniate for 3 weeks, which led to prompt amelioration of the extra- and intranasal lesions over several weeks.

Discussion

In 2007, the World Health Organization (WHO) reported that around 12 million people were infected with leishmaniasis worldwide.[3] Each year, there are about 2 million new diagnoses and the actual incidence is probably even higher.[3,4] The majority of new diagnoses are seen in developing countries, with rare diagnoses also made in developed countries. In Europe, leishmaniasis is endemic around the Mediterranean sea.[2,5] However, it has been proposed that the endemic region is extended to the north, due to the recent diagnoses of leishmaniasis in a child and in a horse that never left Germany.[6]

Leishmaniasis is transmitted by the bite of a female sand fly. The *Leishmania* parasite multiplies in the gut of the sand fly, which becomes contagious 8 to 20 days after biting an infected animal or human. Twenty *Leishmania* species are pathogenic for humans, and more than 30 described sand fly species can function as a vector.[4] In Europe, the *Leishmania infantum* subgenus is responsible for almost all leishmaniasis cases,[2,7] and the cutaneous and visceral forms are most common. Sporadic *L. infantum* can also cause mucosal lesions. Good environmental circumstances (e.g. hygiene and nutrition) combined with a normal immune system may result in an asymptomatic leishmaniasis infection.[8] Important risk factors for symptomatic infections include malnutrition, poor housing, poor water facilities, urbanization, and travel to endemic areas.[9] Another important risk factor is a deficient immunological defence system. Leishmaniasis, specifically the visceral form, is an important opportunistic infection in human immunodeficiency virus (HIV)-positive patients.[1,3,9]

Cutaneous leishmaniasis is seen worldwide and presents as a skin papule on exposed body parts, such as the face or limbs. These lesions can evolve to ulcers ranging from 0.5 to 3 cm in diameter.[1,5] Particularly in immunocompetent patients, single lesions may heal spontaneously over a period of months, leaving a characteristic scar with a depigmented centre. [1]

Mucosal leishmaniasis is mainly diagnosed in South America, in areas where *Leishmania braziliensis* is transmitted.[1,10] Infected mucosa looks hyperaemic, with a rough, crusty, and ulcerative appearance.[11] The preferential site of this disease is the cartilaginous nasal septum, but the lesions can also involve the upper airway and digestive tract.[2,10] Nasal septal lesions may evolve to a perforation and necrosis of the nose cartilage. Patients may complain of bloody rhinorrhea, discharge of bloody clots, and nasal obstruction. Severe cases can involve total destruction of the nasal architecture with distinct aesthetic deformities.[10,11,12] Mucosal leishmaniasis never heals spontaneously and the lesions are prone to secondary bacterial infections.[1] In comparison, mucosal leishmaniasis contracted near the Mediterranean sea is most often seen in the buccal, pharyngeal, or laryngeal mucosa, while the nasal mucosa is affected in only about 15% of

cases.[2,13] The Mediterranean form seems to be less invasive and has a better prognosis.[7,13] About 50% of the patients with mucosal leishmaniasis in Europe have problems with their immune system.[13]

Diagnosis of cutaneous and mucosal leishmaniasis requires the detection of the parasite in a biopsy. A tissue sample is subjected to histological investigation, culture, or PCR.[4,5,6] PCR testing can identify the involved species with the highest sensitivity and specificity, which is important to guide treatment.[1,6,13,14] Serodiagnosis is also possible but the sensitivity is variable.[2,4]

Treatment is recommended for patients with more than 3-5 cutaneous lesions, lesions that are larger than 3-5 cm, lesions that persist for more than 6 months, or lesions located in the face or a joint. Treatment is also initiated in many cases that do not meet these criteria to promote healing and reduce scarring.[13,15] Pentavalent antimonial drugs — namely sodium stibogluconate and meglumine antimoniate — are the most commonly used therapy for cutaneous leishmaniasis.[1,15] These drugs are administered intralesionally if the lesion is less than three months old and less than 3 cm in diameter. In more extensive cases, intravenous or intramuscular administration of the pentavalent antimony is advised.[4,15] Resistance and therapy failure sometimes occur due to underdosing or to poor response of the *Leishmania* species.[1,13,15] Second-line agents for cutaneous leishmaniasis include parenteral pentamidine,oralmiltefosine(hexadecylphosphocholine), parenteral or topical paromomycin (aminoglycoside), and intravenous liposomal amphotericin B.[13,15] Other described therapies for cutaneous leishmaniasis — which can be used alone or in combination with pentavalent antimony — include cryotherapy, imiquimod, photodynamic therapy, local heat therapy, allopurinol, and azoles, which are associated with variable results.[13,15]

Mucosal or mucocutaneous leishmaniasis should always be treated.[1,13,15] The first-line therapy is pentavalent antimony and the second-line therapy is amphotericin B.[2,15] Beneficial effects have also been described with pentamidine.[15] A panel of experts recently provided recommendations for treating imported CL and ML in Europe, advising the administration of systemic treatment with miltefosine, pentavalent antimony, or liposomal amphotericin B for all cases of mucocutaneous or mucosal leishmaniasis. However, no comparative studies are available and most recommendations are based on successful treatment regimens in case reports.[13] After treatment, it is important to organize a systematic follow-up (at least after 3 and 12 months) to detect relapse.[13]

Figure 2
Evolution of the nose lesions following intravenous treatment with meglumine antimoniate and after the liver transplantation.

The patient in our present case most likely developed mucocutaneous leishmaniasis due to a disturbance of his immune system after chemotherapy with high doses of corticosteroids for his colon carcinoma. He was treated with intravenous meglumine antimoniate (pentavalent antimony) 20 mg/kg for three weeks, in accordance with the European recommendations.[13] Full-body investigations after the diagnosis of leishmaniasis revealed a hepatocellular carcinoma, which necessitated liver transplantation. At that time, the *Leishmania* lesions were under control (Figure 2). Because of the patient's immune compromised condition before and, even more so, after the transplantation, he will receive life-long monthly prophylactic intravenous Ambisome® (liposomal amphotericin B).

To the best of our knowledge, this is the first reported case of a patient requiring life-long suppressive therapy for a mucocutaneous leishmaniasis due to immune suppressive medication after transplantation.

Conclusion

Persistent inflammatory mucocutaneous lesions that do not respond to standard treatments in patients who have travelled to endemic regions should be considered to potentially be leishmaniasis. This parasitic disease should be part of the differential diagnosis for inflammatory and reactive lesions in the head and neck region, especially if the patient is immunocompromised. The present case report highlights the importance of taking biopsies when confronted with an uncommon lesion. Leishmaniasis necessitates a thorough specialized treatment and follow-up to avoid relapse.

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