Maxillary Osteonecrosis in Visceral Leishmaniasis: a Case Report

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Summary: Visceral Leishmaniasis is a vector-borne systemic parasitic infection found in many areas of the world. Typically, Leishmaniasis manifests with fever, hepatosplenomegaly, and pancytopenia. Oral lesions are uncommon. Definitive diagnosis still relies on the demonstration of the Leishmania parasite in tissues, although molecular methods appear promising as a non-invasive diagnostic tool. Pentavalent antimonial compounds remain the mainstay of treatment worldwide, but lipid formulations of amphotericin B, and more recently miltefosine, an oral active agent, have been introduced as antileishmanial treatment. We report a patient with visceral Leishmaniasis, who presented with the rare complication of maxillary osteonecrosis.

Key words: oral, Leishmaniasis, bone, tropical infection

Oral Biosci Med 2004; 1: 145-148 *Submitted for publication 30 September 2003; accepted for publication 16 March 2004.*

INTRODUCTION

Leishmaniasis is a vector-borne systemic parasitic infection, a predominantly rural zooantroponose, spread by the bite of some types of sand flies – cryptozoite dipterous insects (Diptera) belonging to the *Psychodidae family* (*Phlebotomus* or *Lutzomya longipalpis*). The most frequent animal hosts are the canids (e.g, dog, fox: *Lycalopex vetulus*) but smaller animals may also be infected. Sand flies become infected by biting an infected animal (for example, a rodent or dog), or person, and are most active in twilight, evening, and night-time hours (from dusk to dawn). Rarely, Leishmaniasis is spread by blood transfusions or contaminated needles, or from a pregnant mother to her baby.

Over 20 species and subspecies of the genus *Leishmania* (named after W.B. Leishman, who developed one of the earliest stains for Leishmania in 1901) infect humans. Each parasite causes a different spectrum of disease, ranging from simple, self-healing skin ulcers (e.g. due to infection with *L. major*), to severe, life-threatening disease (e.g. visceral Leishmaniasis caused by *L. donovani s.l*).

Cutaneous Leishmaniasis is characterized by one or more skin sores (either open or closed) that develop weeks to months after a person is bitten by infected sand flies. Cutaneous Leishmaniasis may cause lip (Sangueza et al, 1993) or facial swelling (Castling et al, 1994), and the mouth may be involved by direct extension (oriental sore or chiclero ulcer) (Goto et al, 1990; Meyruey et al, 1974). However, oral lesions are most frequent in mucocutaneous Leishmaniasis and appear especially in patients who have defective macrophage function or cytokine production (Sangueza et al, 1993). The hard palate is typically involved (espundia) but lesions can spread to the soft palate, uvula and pharynx or, less commonly to involve the gingivae and upper lip. A mid-facial granulomatous destructive lesion may result. Oral lesions seen in Sudan are typically caused by *L. donovani* (el Hassan et al, 1995; Meyruey et al, 1974), and present with fungating oral lesions.

Oral involvement in visceral Leishmaniasis is rare, but pain, loss of teeth, swollen and bleeding gingivae have been described in a patient with visceral Leishmaniasis (Abbas et al, 1992). Most patients with Leishmaniasis affecting the oral cavity complain of pain or of a sensation of a foreign body in the mouth, gingival bleeding, or loosening of teeth (Abbas et al, 1992; el Hassan et al, 1995).

Although Leishmaniasis is seen in otherwise healthy individuals, it is particularly prevalent in immunocom-

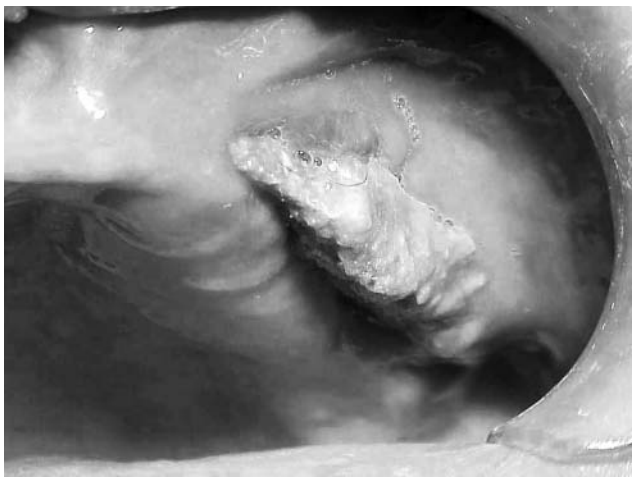

Fig. 1 Mucosal ulceration with evidence of bone sequestration.

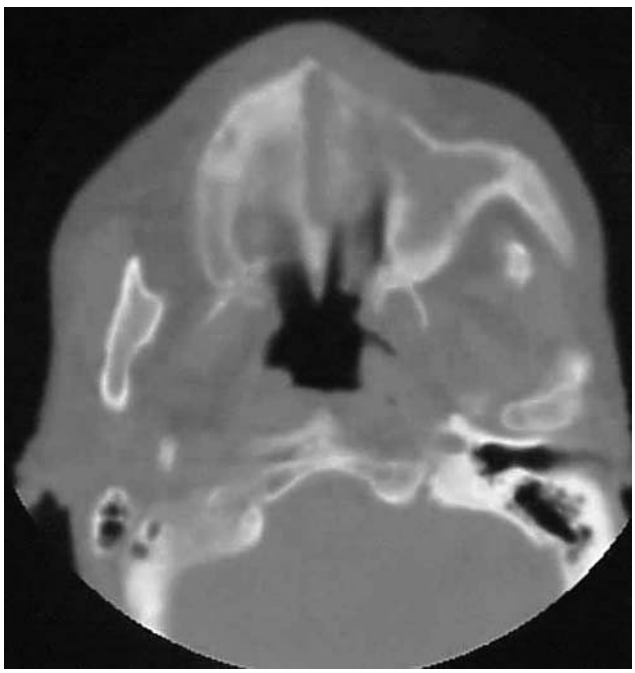

Fig. 2 CT scan. The alveolar process and anterior wall of maxillary sinus substituted by low density area, with poor defined margins, limited by hyperostosis of contralateral hemimaxillary medial margin.

promised persons and, for example, it is reported to be the third commonest opportunistic infection amongst the HIV-positive population in Spain; and it has therefore been suggested that it should be added to the list of AIDS-defining conditions (Albrecht, 1997). Oral lesions have been recorded in such HIV-infected patients (Milian et al, 2003).

The number of new cases of visceral Leishmaniasis annually is thought to be about 500,000 and epidemics cause thousands of deaths. Visceral Leishmaniasis affects particularly the spleen, liver, and bone marrow, but the manifestations, such as fever, hepatosplenomegaly, and anaemia, typically develop months, or even years, after infection.

We report a patient with visceral Leishmaniasis, who presented with a rare complication of maxillary osteonecrosis.

CASE REPORT

A 70-year-old Italian female with no history of travel to the tropics, had virtually continuous fever for six months and, in August of 2000, was admitted to the infectious disease unit where she was found to have hepatosplenomegaly, increased ESR, with pancytopenia, hyperglycaemia, and anti-Leishmania antibodies (at a titre of 1 in 80), with amastigotes on bone marrow aspiration. She had no evidence of HIV infection. She was thus diagnosed as visceral Leishmaniasis and treated with methylglucamine, amphotericin B and calcium gluconate.

However, she then developed pain and a swelling in her maxilla and was seen in November 2000, while still on treatment with amphotericin B, when examination revealed an exophytic lesion on the left maxillary alveolar ridge with evidence of underlying bone sequestration (Fig. 1). This lesion was probably due to local infection (similar to the lesions in mucocutaneous Leishmaniasis). CT scan showed the alveolar process

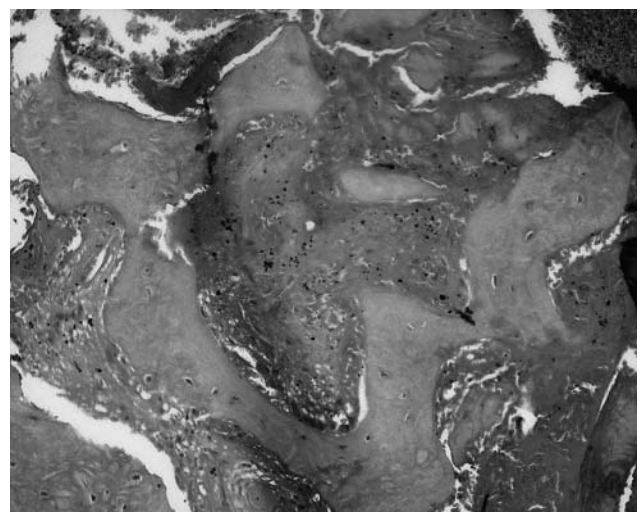

Fig. 3 Histopathology of surgical specimen H & E ×250, showing necrotic bone.

and anterior wall of the maxillary sinus replaced by a low density area, with poor defined margins, limited by hyperostosis of the contralateral hemi-maxillary medial margin (Fig. 2).

She was admitted for management of diabetes and excision of the lesion which, on histopathology and histochemistry, showed only inflammatory and necrotic bone (Fig. 3).

DISCUSSION

Leishmaniasis is the main tropical parasitic disease in which oral lesions may be found. Most of the affected patients have mucocutaneous or cutaneous Leishmaniasis, and are from countries in the tropics and subtropics, but the settings in which Leishmaniasis is found range from rain forests in Central and South America to deserts in West Asia. Widespread in 22 countries in the New World and in 66 nations in the Old World, human Leishmaniasis is also found in 16 countries in Europe, including France, Italy, Greece, Malta, Spain and Portugal. Indeed, our patient had not travelled outside Europe. However, Leishmaniasis is not found in South-east Asia, Australia or Oceania.

The Leishmaniases can be classified into 4 main forms:

1. Cutaneous Leishmaniasis (CL) – the most common form, causes simple skin lesions which self-heal within a few months but leave unsightly scars (e.g. Baghdad ulcer, Delhi boil or Bouton d'Orient, due to infection with *L. major* in Africa and Asia). Chemotherapy is indicated.
2. Mucocutaneous Leishmaniasis (MCL), due to *L. braziliensis* infection – begins with skin ulcers which spread, causing massive tissue destruction, especially of the nose and mouth. Mucocutaneous leishmaniasis may heal spontaneously but, since there can be extensive destruction of tissue, chemotherapy is still indicated.
3. Diffuse cutaneous Leishmaniasis (DCL) – produces disseminated and chronic skin lesions resembling those of lepromatous leprosy. Chemotherapy is indicated, but the condition is difficult to treat.
4. Visceral Leishmaniasis (VL) – is fatal if untreated (e.g. Kala azar due to *L. donovani s.l.*). The ancient Indian scriptures mention 'kala-azar' or 'black fever', which discolours the skin black (referring to post-kala-azar dermal leishmanoid – PKADL).

VL is the most dangerous form of the disease, and affects particularly the spleen, liver, and bone marrow, though the manifestations such as hepatosplenomegaly, anaemia and fever typically develop months, or even years, after infection.

Since the first VL epidemic reported in 1870, several epidemics have swept the Ganga-Brahamputra plains of northern India, causing widespread disease and taking a huge toll of lives. Currently, more than 90% of the world's cases of VL occur in Bangladesh, India, Nepal, Brazil, and Sudan.

Diagnosis is from clinical features: haematological changes (low blood counts, including a low red blood cell count (anaemia); low white blood cell count, and low platelet count), and serologic (enzyme linked immunosorbent assay or indirect fluorescent antibody) tests along with the demonstration of parasites (Leishman-Donovan bodies) in biopsies or smears (el Hassan et al, 1995); or in VL from the direct search for *L. donovani* (amastigote forms) in bone marrow material and through myeloculture in NNN (Mc Neal, Novy and Nicole) culture medium.

Management is by chemotherapy. Pentavalent antimony (Pentostam), N-methyl glutamine (meglumine) antimonate (Glucantime), or sodium stibogluconate (e.g. Pentostam), ketoconazole, amphotericin, or pentamidine isethionate are the available therapies. Conventional therapy for VL typically consists of parenteral pentavalent antimony (sodium stibogluconate and meglumine antimoniate), given for 28 days (20 mg/kg/day). Severe adverse reactions can result. Pancreatitis and cardiac toxicity have limited the use of conventional therapy, and relapse is common. Recently, resistance to these drugs has been reported, requiring the use of more toxic drugs, such as amphotericin B. Resistance to antimony is about 50%. Miltefosine is the first effective oral drug for Leishmaniasis, giving cure rates of about 98%, with negligible side effects, and it has been used successfully to treat cases resistant to conventional antimony therapy. Development of other drugs (paromomycin and sitamaquine) is slow, and there is a place for a vaccine, not least since HIV co-infection is changing the epidemiology and presenting management problems.

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