Mucosal Leishmaniasis and Abnormalities on Computed Tomographic Scans of Paranasal Sinuses

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INTRODUCTION

The global incidence of tegumentary leishmaniasis is increasing. Nevertheless, leishmaniasis is a neglected disease. Financial donors, public-health authorities, and medical professionals have shown little interest in implementing activities to investigate, prevent, or control the disease.† Mucosal leishmaniasis (ML) is the most severe form of this disease because of its progressive lesions that can destroy cartilage and osseous structures of the face, pharynx, and larynx.2,3

The natural history of this disease and its complications were well described by Phillip Marsden in 1986.4 However, there have been no studies that evaluated the structural alterations of the face and paranasal sinuses by using radiologic methods. Moreover, the incidence of sinusitis is not described, although the most common symptoms of patients are related to nasal discharge, epistaxis, posterior drainage, and rhinorrhea.5 The absence of studies that evaluated radiologic aspects, local complications, and structural alterations of the paranasal sinus led us to perform a study to determine the radiologic alterations of the paranasal sinuses in patients with ML by using computed tomography (CT).

MATERIALS AND METHODS

Patients. In this prospective study, we evaluated 26 patients with ML who were admitted to the Leishmaniasis Ambulatory at the Hospital das Clínicas (University of São Paulo) in São Paulo from December 2008 through June 2009. The diagnostic approach for ML included clinical examination, the Montenegro skin test and a mucosal biopsy. The Montenegro skin test was performed with an intradermal injection of Leishmania amazonensis OMS MHOM/BR/73/M2269; Centro de Produção e Pesquisa de Imunobiologia, Piracuru, Paraná, Brazil, and the size of the skin response was measured after 48 hours. The diameter of induration was measured in millimeters (> 5 mm was considered a positive result).

The epidemiologic and clinical findings of all patients were evaluated according to age, sex, race, region of origin, scar from previous cutaneous leishmaniasis, comorbidities, symptoms, and lesion location.

Laboratory tests. All patients were subjected to a Montenegro skin test and a mucosal biopsy. The Montenegro skin test was performed with an intraderal injection of Leishmania amazonensis OMS MHOM/BR/73/M2269; Centro de Produção e Pesquisa de Imunobiologia, Piracuru, Paraná, Brazil, and the size of the skin response was measured after 48 hours. The diameter of induration was measured in millimeters (> 5 mm was considered a positive result).

Immunohistochemical analysis for detection of Leishmania antigens was performed as described by using antibodies from L. chagasi (provided by Heitor Andrade Jr., Instituto de Medicina Tropical, São Paulo, Brazil).7

Radiologic aspects. Computed tomography scans of the paranasal sinuses were obtained for all patients. The examinations were performed by using a 16-channel multidetector scanner (IDT16; Philips Medical Systems, Best, The Netherlands) without contrast media with the following parameters: 120 kV, 100 mA, a rotation time of 0.75 seconds in the axial

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515
plane, a slice thickness of 1 mm, and an increment of 0.5 mm with bone and standard algorithms of reconstruction. Extra-
sinusual abnormalities were observed in nine patients; for these patients, another CT scan was obtained by using intravenous contrast media (ioibitridol, Henetix 300; Guerbet, Rio de Janeiro, Brazil) at a dose of 1.5 mL/kg.

The volumetric data was transferred to a workstation,
and multiplanar reconstructions (axial, coronal, and sagittal planes) were obtained. All CT scans were analyzed by a radiologist who was unaware of the clinical condition of the patient (treated or untreated). The radiologist evaluated the grade of opacification of the paranasal sinuses (sinusopathy) and ostio-meatal complexes, and the presence of any abnormality that could be related to leishmaniasis such as foci of erosion of the nasal septum; deformity of the nasal pyramid; or cutaneous, subcutaneous, or mucosal lesions.

Sinusopathy was graded according to the Lund-McKay system, which establishes a value for the grade of opacification for each sinusual system and for the ostio-meatal complexes (Table 1).6

**Statistical analysis.** This study was essentially descriptive. Continuous data are expressed as means or medians with SD values or ranges. Frequencies are expressed as percentages. A cross-table analysis using chi-square and Fisher tests was performed to compare patients with recurrent disease and those who were cured. All tests were performed using Epi-Info software (Centers for Disease Control and Prevention, Atlanta, GA). A *P* value < 0.05 was considered statistically significant.

**RESULTS**

**General data.** The mean age of the 26 patients was 57.8 years (range = 25–80 years). Of the 26 patients, 12 were men and 14 were women. Twelve patients were Caucasian and 14 patients were of African descendent. Twelve (46.2%) patients were from northeastern Brazil. Fourteen (53.8%) patients had scars from previous cutaneous lesions (Table 2).

The most common symptoms were nasal obstruction (88.5%), epistaxis (65.4%), and rhinorrhea (50%) (Table 3). The nasal septum was the most common site of mucosal lesions (88.5%), epistaxis (65.4%), and rhinorrhea (50%) (Table 3).

**Radiologic findings.** Thickening of the paranasal sinus was observed in 25 patients (96%). Nasal perforation was described in 17 patients (65%), and the CT scan showed collapse of the nasal pyramid in 3 patients (11.5%). Other findings included alterations of the nasal conchae (n = 8, 30%), retention cyst/polyp of the maxillary sinus (n = 4, 15%), and bilateral mastoidopathy (n = 2, 8%). Less frequent alterations included erosion of the nasolacrimal duct, erosion of the nasal bone, osteitis of the paranasal sinuses, and thickening of the soft palate and the nasal wings (each alteration corresponding to n = 1, 4%). More details are shown in Table 4. Examples of radiologic findings are shown in Figure 1 and Figure 2.

Lund-Mackay scoring differed for patients given re-treatment compared with those without previous treatment: scores of 6.0 (95% confidence interval = 5.29–6.70) and 4.3 (95% confidence interval = 3.58–5.12), respectively (*P* < 0.05).

**DISCUSSION**

We evaluated radiologic findings for patients with ML in São Paulo, Brazil by using CT. In our study, CT scans showed mucosal thickening of at least one of the paranasal sinuses in all but one patient. This finding suggests that the disease in patients with ML is not limited to the nasal mucosa but extends to the paranasal sinuses. Mucosal thickening, opacified air cells, bony remodeling, and bony thickening caused by inflammatory osteitis of the sinus cavity walls are CT findings suggestive of chronic sinusitis. Bony erosion can also occur in severe cases.3
The pathophysiology of paranasal involvement remains unclear. Mucosal thickening may be caused by direct infection of the sinus mucosa by the Leishmania protozoan, which can live in the mucosa despite scar cicatrization. A third hypothesis is chronic inflammation with continuous expression of tumor necrosis-α in situ after cicatrization of the mucosal lesion, as described. A third hypothesis is chronic sinusitis secondary to obstruction of the natural drainage pathways of the paranasal sinuses. Direct infection of the sinus mucosa by the parasite, which would require surgical procedures to obtain sinus mucosal biopsy specimens, was not investigated in the present study. Most of our patients did not satisfy the formal indication for sinus surgery. We believe that these three hypotheses are simultaneously present and contribute to paranasal thickening.

Obstruction of the sinus ostium or drainage pathways may occur in some patients with mucosal leishmaniasis who have inflammatory or cicatricial lesions that extend to the lateral nasal wall in the region of the middle meatus or the ethmoidal recess. Obstruction of these key drainage regions may lead to stasis of secretions inside the sinuses, resulting in chronic sinusitis. In some patients in our study, massive destruction of the nasal structures led to the formation of a large nasal cavity, scarring and thickening nasal mucosa including the lateral nasal wall, and opacification of the paranasal sinuses.

It is important to comment on the relevance of mucosal thickening in the interpretation of sinus disease. Mucosal thickening may occur after a virus infection in an upper airway, even in asymptomatic patients. It may also be secondary to surgical intervention in the paranasal sinuses. In our study, none of the patients had a virus infection in an upper airway, acute worsening of nasal symptoms by the time the CT scan was obtained, or a history of previous sinus surgery.

The mucosal thickening described is a CT finding that suggests chronic rhinosinusitis. This entity occurs in 16% of the American population, and is the second most common chronic disease in this population.

We did not include a control group to determine if ML is a risk factor for chronic rhinosinusitis. However, mucosal thickening in the patients (96%) was superior to results of any epidemiologic studies.

Although we cannot exclude the possibility that the paranasal sinus changes found in our patients were caused by other factors or were even incidental, the high prevalence of these findings in our study suggests the need to further investigate the pathogenesis of sinus involvement in such patients.

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Table 4: Radiologic findings of patients with mucocutaneous leishmaniasis in São Paulo, Brazil

<table>
<thead>
<tr>
<th>Finding</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paranasal thickness from paranasal sinus</td>
<td>25</td>
<td>96</td>
</tr>
<tr>
<td>Nasal perforation</td>
<td>17</td>
<td>65</td>
</tr>
<tr>
<td>Alterations of the nasal conchae</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>Retention cyst/polyp of the maxillary sinus</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Collapse of the nasal pyramid</td>
<td>3</td>
<td>11.5</td>
</tr>
<tr>
<td>Erosion of the lacrimal duct</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Erosion of the nasal bone</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Bilateral mastoidopathy</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Osteitis of paranasal sinuses</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Thickening of the soft palate</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Thickening of the nasal wings</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

REFERENCES


