Am. J. Trop. Med. Hyg., 81(3), 2009, pp. 384–386

Short Report: The Value of the Otorhinolaryngologic Exam in Correct Mucocutaneous Leishmaniasis Diagnosis

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Abstract. An increase in mucocutaneous leishmaniasis (ML) cases in northern (Brazil) motivated this study. In 44 ML patients with clinical diagnosis, only 13 parasitologically confirmed cases exhibited mucosal lesion suggestive of ML. Other conditions involving nasal manifestations are frequently confounded with ML. Therefore, otorhinolaryngologic examination is important in the clinical management of ML.

Tegumentary leishmaniasis (TL) remains a serious public health problem in several areas of the World, including Brazil. Mucosal leishmaniasis (ML) appears in about 3% of cutaneous leishmaniasis (CL) patients in the Americas, and leads to destructive lesions in the nose, mouth, and larynx.[1,2] Mucosal leishmaniasis diagnosis remains difficult because clinical findings are nonpathognomonic and parasites are rarely found in mucosal lesions.[3,4] The intradermal delayed-type hypersensitivity (DTH) skin test is highly sensitive and is usually required to confirm clinical suspicion.[3,5] In parallel, histopathologic analysis or anti-*Leishmania* serology are used for diagnosis of ML. Considering that ML patients do not undergo spontaneous cure and present fatal outcome if left untreated and that ML treatment requires a longer drug regiment than CL,[6–8] a proper diagnosis of this particular clinical manifestation is of utmost importance.

In this report, we took advantage of an unexpected rise in the number of reported ML cases that occurred in Acre State (northern Brazil) from 2000 to 2002, to address the role of otorhynolaryngologic assessment in the diagnosis of ML. In this period, the incidence of TL (ML + CL) scaled from 141.9 to 223.7 cases/100,000 habitant. The ML cases represented 25% (197) of total TL (594) cases in 2000 and reached 28% (363) of total TL (1313) cases in 2002 (Secretaria de Saúde do Estado do Acre, Brazil, personal communication), both values above the previously documented 4% of total TL cases.[1–3] Such an increase in ML frequency could be attributable to differences in virulence of the circulating *Leishmania* strain,[9] or to incorrect or incomplete treatment of CL[10] or to, for example, inadequate physical exam that could over diagnose ML.

To study the high proportion of mucosal involvement within TL cases in Acre, we performed a complete otorhinolaryngologic examination and, in parallel, we performed parasitologic and immunologic tests applied at the diagnosis of leishmaniasis in 44 patients with previous diagnosis of ML.

THE STUDY

Patients originated from three areas in Acre (Rio Branco, Sena Madureira, and Antimari) where the rate of ML was estimated as being 24.9% of TL cases (Secretaria de Saúde do Estado do Acre, Brazil, personal communication). Forty-four patients (68% men, 30 ± 17 years) with an ML diagnosis the previous year were submitted to a new evaluation incorporating an othorhinolaryngologic exam in 2002. Initial ML diagnosis was performed by a clinical physician in rural or urban health centers based on a nasal clinical complaint combined with one of the following: positive intradermal skin test; positive anti-*Leishmania* serology, or diagnosis of CL in the past (Table 1). Routine examination of mucosal surface by an otorhinolaryngologist had not been performed previously. For the present report, ML diagnosis was based on presence of lesions compatible with ML, a positive anti-*Leishmania* DTH skin test, positive anti-*Leishmania* serology, and the presence of *Leishmania* in biopsy samples detected by immunohistochemistry or by polymerase chain reaction (PCR).[2,11,12] Complete otorhinolaryngologic examination (anterior rhinoscopy, oropharynx exam, and a fiberoptic exam) was performed in all 44 patients. Complementary exams were performed if a characteristic ML lesion with edema, erosion, septal perforation and/or granulomatous aspect was detected. Patients were informed of procedures and consented to participate in the study.

After otorhinolaryngologic evaluation, only 13 patients (29%) presented mucosal lesion compatible with ML. Three patients within this group had been previously treated for ML and, accordingly, presented mucosal scars in the nasal septum. The remaining 10 patients presented active ML with ulceration, hyperemia, and granulomatous aspect, usually at the inferior turbinate and nasal septum perforation. Extensive lesions with pharynx and/or larynx involvement were detected in three patients. Mucosal complaints initiated from 2 months to 16 years of age before ear-nose-throat (ENT) exam. *Leishmania* infection was confirmed by PCR in all of the eight patients who consented to a biopsy procedure (Table 1). The remaining two patients with active mucosal lesion presented a positive DTH skin test in addition to a characteristic ML lesion. All 10 patients were treated with antimoniate-n-methylglucamine (20 mg/sb/kg/d) for 47 ± 16 days with clinical cure after 6 years follow-up time.

Nonetheless, ML diagnosis was not confirmed in 70% patients (31/44) present in the initial group. Otorhinolaryngologic examination did not detect scars, active ML, or other lesions of granulomatous aspect. Instead, clinical evaluation suggested other pathologies such as atrophic or allergic rhinitis, septum deviation, chronic sinusitis, and nasal polyps and biopsy procedures were not performed. Diagnoses were later confirmed by additional exams, such as skin prick test to allergens and face computed tomography (CT).[13,14]

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TABLE 1
Clinical and laboratory data of ML and other mucosal disease patients*

	Confirmed ML	Other disease
	$N = 8$	$N = 6$†
	Positive (%)	
Clinical complaints	100	100
Previous CL	75	83
Serology	75	66
DTH	87	100
Histopathology	75	NP
PCR	100	NP

*ML = mucosal leishmaniasis; CL = cutaneous leishmaniasis; DTH = delayed-hypersensitivity; PCR = polymerase chain reaction.
† Biopsy not performed.

Although ML lesions were not detected in 31 patients, these presented clinical data suggestive of ML diagnosis. Thirteen patients (42%) with erroneous ML diagnosis presented evidence of previous CL, as suggested by clinical history, the presence of scar, positive intradermal skin test and/or parasitologic confirmation. Unspecific nasal symptoms, such as epistaxis, itch, sneeze, nasal crust, secretion and/or obstruction, were detected in all 31 patients. Ten out of 31 (32%) patients were submitted to DTH skin test and all of them presented a strong positive reaction to *Leishmania* antigen (Table 1). Based on initial ML diagnosis, 14/31 patients (45%) initiated antimoniate-n-methyl-glucamine therapy and treatment was interrupted when ML diagnosis was not confirmed.

CONCLUSIONS

Our study presents strong evidence that ML diagnosis based only in clinical nasal symptoms and positivity in anti-*Leishmania* immunologic tests, such as DTH or serology, leads to overestimation in the number of ML cases. Immunologic tests such as the Montenegro skin test remain positive for a long period of time and may lead to false diagnosis.[1–3] Conversely, parasitologic diagnosis, albeit reliable, may face resistance from patients due to need of performing a biopsy. In the present series, all 44 patients that were initially diagnosed as ML cases were not, at the time of their first clinical examination, evaluated by an otorhinolaryngologist. A proper otorhinolaryngologic examination confirmed ML in only 13 of the 44 initially diagnosed patients. If mucosal examination were to be included in the initial diagnostic procedure, complementary exams would have eliminated 31 patients, because of the lack of mucosal lesion compatible with ML.

A positive immunologic exam associated to clinical complaints confounded the diagnostic procedure. Positive intradermal DTH skin test and serology are frequently detected among healthy endemic area residents.[1] In this case, 83% of those individuals had CL previously, which explains their positive immunologic tests, and all of them presented symptoms that are not specific to ML, such as epistaxis, sneeze, and nasal obstruction.

Complementary tests were not necessary to exclude ML suspicion in those patients. However, they are important to confirm ML diagnosis if a characteristic mucosal lesion is detected. Certain granulomatous diseases such as paracoccidioidomycosis, leprosy, and syphilis present similar clinical aspects.[3] In these cases, histopathologic analysis may rule out incorrect initial suspicion, but PCR is of utmost importance for definitive diagnosis.[11,12] Furthermore, a positive DTH skin test may suggest this etiology but cannot be used to predict active disease in mucosal leishmaniasis because most individuals in endemic areas have been exposed to infected sand fly bites and may, therefore, present a positive reaction. Nonetheless, a negative result strongly suggests another diagnosis.[2] We propose an algorithm for ML diagnosis: otorhinolaryngologic examination may be first performed if ML is suspected. Complementary exams such as intradermal DTH skin test, serology, and histopathology should be executed if a characteristic ML lesion is detected.

In the present context, incorrect ML diagnosis determined antimonial therapy for as long as 3 months. Indication to start antimonial therapy without ENT examination was inappropriate and, consequently, treated patients were submitted to unnecessary adverse side effects, penalizing the health system as well. Otorhinolaryngologic examination, as the first step in evaluation of suspect ML cases, may avoid incorrect ML diagnosis, which reached 70% in this study, preventing inappropriate treatment. The increased number of reported ML cases in Acre state was attributed to an incomplete clinical exam and overestimation of the value of complementary exams. Otorhinolaryngologic evaluation should be performed in all ML suspected cases before other diagnostic methods to avoid incorrect diagnosis and treatment.

Received December 15, 2008. Accepted for publication May 7, 2009.

Acknowledgments: We thank the clinical personnel at the Barral y Barral health post for assistance with patient recruitment and Ana Nilce Maia-Elkhoury from Fundação Nacional de Saúde (FUNASA).

Financial support: This study was funded by the Brazilian Ministry of Health. V. Boaventura and F. O. Novais were supported by a CAPES fellowship. J. M. Costa, C. I. de Oliveira, M. Barral-Netto, and A. Barral are senior investigators from CNPq.

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