Braz J Otorhinolaryngol.
2010;76(5):579-87.

BJORL.org

Nasal mucosa study of leprosy contacts with positive serology for the phenolic glycolipid 1 antigen

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Keywords:
endoscopy,
glycolipids,
nasal mucosa,
mycobacterium leprae,
polymerase chain reaction.

Abstract

Leprosy is a chronic infectious disease caused by Mycobacterium leprae. The disease more frequently affects the nasal mucosa and can occur independently of its clinical form or even before lesions on the skin or on other parts of the body. It is necessary to employ epidemiological surveillance of household contacts with new leprosy cases for early disease diagnosis.

Aim: identify specific and early leprosy lesions through endoscopic, baciloscopy, histopathology exams, and real time polymerase chain reaction of the nasal cavity mucosa on household and peridomiciliary contacts with positive serology for the phenolic glycolipid 1 antigen.

Methodology: Between 2003 at 2006 there was a prospective cross-sectional clinical study with 31 contacts with patients with leprosy with positive serology against PGL-1, 05 negative controls and 01 positive control.

Results: Between seropositive contacts, real-time PCR was positive for M. leprae DNA in 06 (19.35%) of them and the higher number of genome copies were found in contacts who became sick.

Conclusion: Nasal mucosa tests alone did not enable the early diagnosis of Leprosy. However, through the combination of various methods, tests on the contacts can help identify subclinical infection and monitor the contacts that could be responsible for spreading the disease.

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Paper submitted to the BJORL-SGP (Publishing Management System – Brazilian Journal of Otorhinolaryngology) on October 26, 2009;
and accepted on March 15, 2010. cod. 6739

INTRODUCTION

Rabello classified leprosy as a polar disease with two forms (tuberculoid leprosy or TT, and lepromatous leprosy or LL) based on the bodily response to this infection starting with an initial indeterminate form (indeterminate leprosy or IL). New clinical forms - borderline forms - were added to this classification in the VI International Leprosy Conference of 1953 in Madrid. These new dimorphic forms were attributed to patients that progressed from IL to uncharacteristic clinical presentations of polar TT (paucibacillary with high cellular immune response) and LL (multibacillary and low cellular immune response).

After the introduction of polychemotherapy (PCT/WHO) in the 1980s, new diagnostic tools for an early diagnosis of leprosy have been sought. The ability to identify groups at an increased risk in highly endemic areas in and out of households, together with BCG vaccination of contacts, are measures developed in Brazil to help decrease the multibacillary forms of this disease. The efficacy of these measures, however, has been compromised by several operating issues that have resulted in high detection coefficients in the majority of Brazilian states.

Disease transmission has been debated for year; the upper airways, in particular the nose, appear to be the main entry and transmission route for Mycobacterium leprae. It is thought that 95% of LL patients will have an early involvement of the nose. There are specific histopathological changes in the mucosa even without visible lesions.[1] There are many mucus-producing cells, edema, and increased vascularization of the plasmocyte and lymphocyte-infiltrated submucosa in the bacillary invasion phase of LL patients. This significant amount of mucus explains the typical nasal block and rhinorrhea in this initial stage. A proliferation phase ensues, in which these findings are exacerbated, resulting in a granulous aspect of the mucosa; at this point, macrophages predominate in the inflammatory infiltrate. In the next stage the mucosa becomes ulcerated and damaged; inflammation consists of macrophages and numerous bacilli, lymphocytes and plasmacytes. In the final phase - resolution and fibrosis - bacilli are rare and fibrosis is intense.[2]

The nasal epithelium is ciliated cylindrical pseudostratified with goblet cells, and rarely remains normal because of multiple insults. Such insulting factors include: extreme temperatures, infection, pollution, and trauma. This continuous aggression decreases the number of cilia on which air interacts, and increases the number of goblet and inflammatory cells. The progression of squamous metaplasia in this context starts in childhood; it is a normal phenomenon, a protective response to external factors. It is often seen in allergic rhinopathy.[3]

Histopathology is extremely valuable for diagnosing and classifying the clinical forms of leprosy, especially in indeterminate cases; this approach may show early on to which polar type (tuberculoid or lepromatous) the disease will progress. Biopsies should be preserved in 10% formaldehyde or Millonig (buffered formaldehyde) and hematoxylin-eosin, Ziehl-Wade-Klingmuller or Fite Faraco stained.

Among the new support tools for an early diagnosis and prediction of these groups there is the serology test that detects antibodies against the specific phenolic glycolipid antigen 1 (PGL-1) of M. leprae. The PGL-1 is specific to this bacillus and comprises about 2% of the total bacterial mass; it is found in tissues, circulating blood and urine of multibacillary patients. This test has been used for diagnosis worldwide,[4,5,6] and positivity is proportional with the bacillary load; increased exposure to bacilli relates with a higher test positivity, ranging from 1+ (low bacillary load) to 4+ (high bacillary load). The DNA-amplification method using the polymerase chain reaction (PCR) technique appears to be more specific and sensitive for detecting bacilli in the nasal mucosa.[7-18] Several cohort studies,[9,10,14-17] based on serum positivity (anti-PGL-1) and PCR investigation of bacilli in the nasal mucosa, have shown persistent subclinical infection, especially in highly endemic areas.

These numbers guided an endoscopic study of the nasal cavity mucosa for investigating subclinical infection in serum positive contacts in an urban area of metropolitan Rio de Janeiro, the Duque de Caxias municipality. At the beginning of the study in 2003, the incidence and the prevalence of leprosy were respectively 5.04 and 7.29 per 10 thousand inhabitants in the 2nd district - the study micro area. A high endemic rate is evidenced by the fact that 11% of new cases were subjects aged below 15 years, which reflects active and recent transmission of this disease, as shown in several studies.[19-22] In 2003 there was a high rate of new cases with deformity, especially in the 1st - and most populated - district (10.7%), 75.7% of the cases that were evaluated.

METHOD

A cross-sectional study was carried out from 2003 to 2006 of 31 contacts of leprosy patients that were positive for PGL-1 (out of 1886 contacts that comprised the total sample in the serological investigation),[23] and 6 controls, of which one was positive and 5 were negative. Contacts and controls underwent nasal endoscopy, nasal mucosa smears, and lower right turbinate biopsy for acid-fast bacilli (AFB) testing, histopathology and real-time polymerase chain reaction (RT-PCR). A new data base was