Contribution of nasal biopsy to leprosy diagnosis

Marcell Melo Naves, M.D.,* Lucas Gomes Patrocínio, M.D.,* José Antonio Patrocínio, M.D., Ph.D.,‡ Flávia Marques Naves Mota, M.D.,*‡ Antônio Diniz de Souza, M.D.,*‡ Raul Negrão Fleury, M.D., Ph.D.¶ and Isabela Maria Bernardes Goulart, M.D., Ph.D.§

ABSTRACT

Background: The nasal mucosa plays the main role as the entry and the exit of leprosy bacilli and the nasal involvement may precede the skin lesions by several years. Nasal biopsy has been used in research but its clinical application has not been described. We evaluated the contribution of the nasal biopsy for the diagnosis of leprosy and its correlation to skin biopsy and skin smear in untreated patients.

Methods: We evaluated changes in nasal biopsy in 227 leprosy patients. Patients were clinically classified and skin and nasal biopsies and skin smear were performed.

Results: Nasal biopsy showed positivity in 100% of the lepromatous spectrum, decreasing toward the tuberculoid (TT) pole. Patients with TT or intermediate forms did not present any nasal alterations, showing that they are the true paucibacillary forms. Also, the nasal biopsy of two patients were the only exams to show positivity. The bacillary index of the nasal biopsy was strongly correlated to skin biopsy and skin smear. Additionally, the agreement among the exams was good, revealing the reliability of the nasal biopsy in leprosy diagnosis.

Conclusion: The present study showed a rate of 48% of positivity in nasal biopsy of untreated patients, correlating well with skin biopsy and skin smear. Thus, the method in leprosy diagnosis and clinical form classification has shown great reliability.


Key words: Biopsy, early diagnosis, histopathology, leprosy, Mycobacterium leprae, nasal mucosa, nose diseases, otolaryngology

Despite being one of the most ancient diseases affecting mankind, leprosy still displays a high worldwide incidence of >407,000 new cases per year. In Brazil, reported 47,612 new cases in 2006, ranking the country in second place in number of new cases detected. Hence, leprosy is considered a priority on the political agenda and the World Health Organization (WHO) and the Pan-American Health Organization are working in a coordinated way toward its eradication.

In 1995, the WHO standardized leprosy classification based on clinical criteria to facilitate its diagnosis. Skin smear and skin biopsy are methods that can be used to aid in the diagnosis and currently are considered “gold standard” tests for the classification of leprosy. Clinical and immunologic signs from these tests can uncover a multitude of leprosy forms, from paucibacillary (PB) to multibacillary (MB) patients. PB patients have one or few skin lesions, low or absent bacillary index (BI), show specific cell-mediated immunity against Mycobacterium leprae with low or absent titers of M. leprae–specific antibodies and granulomatous dermatopathology. In marked contrast, MB patients display multiple symmetric skin lesions, a high BI, high titers of anti-M. leprae antibodies with absent specific cell-mediated immunity, and a dermatopathology largely devoid of functional lymphocytes. The involvement of the ear, nose, and throat in leprosy is well established. The nasal mucosa is the main route of contamination and transmission of the bacilli; and the nasal involvement generally precedes skin lesions for several years, depending on the immunologic condition of the patient. A nasal biopsy has been used in research, but a clinical application of the assay still has not been described. In this study, we evaluate the contribution of the nasal biopsy for the diagnosis of leprosy and its correlation to skin biopsy and skin smear in untreated patients.

PATIENTS AND METHODS

Two hundred twenty-seven leprosy patients from the Leprosy Ambulatory, at the National Reference Center for Sanitary Dermatology, Federal University of Uberlandia, MG, Brazil, were enrolled in this study. This study had the approval of the Federal University of Uberlandia Ethics Committee, protocol number 09/2006.

Address correspondence and reprint requests to Isabela Maria Bernardes Goulart, M.D., Ph.D., A. Arpoador Mgrs. 77-Santuário, Uberlandia, MG 38410-000, Brasil. E-mail: isabelam@ufu.br; eliaertm@lagnostoanet.com.br

Figure 1. Typical bacilluscoppy of nasal biopsy specimen of lepromatous leprosy patients showing an acid-fast bacilli inside a mucous gland (200x; Ziehl-Nielson stain).
Table 1  Correlation of positive results between nasal biopsy, skin biopsy, and skin smear, according to clinical forms of leprosy

<table>
<thead>
<tr>
<th>Clinical Forms</th>
<th>Nasal Biopsy</th>
<th>Skin Biopsy</th>
<th>Skin Smear</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>0/2</td>
<td>0</td>
</tr>
<tr>
<td>TT</td>
<td>0</td>
<td>0/2</td>
<td>0</td>
</tr>
<tr>
<td>BT</td>
<td>6.8</td>
<td>05/73</td>
<td>46.6</td>
</tr>
<tr>
<td>BB</td>
<td>62.2</td>
<td>28/45</td>
<td>95.6</td>
</tr>
<tr>
<td>BL</td>
<td>93.1</td>
<td>27/29</td>
<td>100</td>
</tr>
<tr>
<td>LL</td>
<td>100</td>
<td>49/49</td>
<td>100</td>
</tr>
</tbody>
</table>

f = indeterminate; TT = tuberculoid; BT = borderline-tuberculoid; BB = borderline—borderline; BL = borderline lepromatous; LL = lepromatous.

r (Pearson’s): SB/NB, 0.9272 (p < 0.001); SB/SS, 0.9576 (p < 0.001); NB/SS, 0.9668 (p < 0.001)

RESULTS

The mean age of the patients used in this study was 46.14 ± 16.96 years (age range: 8-87 years; n = 227). The BI was positive in nasal mucosa biopsy specimens of 109 patients (48%), in skin smear of 129 patients (56.8%), and in skin biopsy specimens of 158 patients (69.8%); Table 1. The nasal biopsy specimens showed a BI of 0 in 1 patients, 0 in BB patients, 0.14 in BT patients, 2.02 in BB patients, 4.4 in BL patients, and 5.11 in LL patients. The skin smear revealed a BI of 0 in 1 patients, 0.1 in TT patients, 0.32 in BT patients, 1.88 in BB patients, 4.32 in BL patients, and 5.01 in LL patients. The skin biopsy specimens showed a BI of 0 in 1 patients, 0.0 in BB patients, 0.61 in BT patients, 3.28 in BB patients, 5.25 in BL patients, and 5.54 in LL patients. The correlation between the BI of nasal and skin biopsy specimens was equal to 0.983 and 1.00 between the BI of nasal biopsy specimens and skin smear (p < 0.001; Pearson’s linear correlation coefficient, Fig. 2).

One hundred six (46.7%) of 227 cases showed classic histopathological features of leprosy in both skin and nasal biopsy specimens, and 68 patients (30.0%) were negative in both samples, which resulted in a concordance index of 0.5399. Nasal biopsy specimens and skin smear from 201 patients (88.6%) displayed similar histopathological findings: 106
Table 2  Concordance between the results of nasal biopsy, skin smear, and skin biopsy of leprosy patients

<table>
<thead>
<tr>
<th>Nasal Biopsy</th>
<th>Skin Biopsy No. (%)</th>
<th>Skin Smear No. (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Negative</td>
<td>68 (30.0)</td>
<td>50 (22.0)</td>
<td>95 (41.9)</td>
</tr>
<tr>
<td>Positive</td>
<td>3 (1.3)</td>
<td>106 (46.7)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Total</td>
<td>71 (31.3)</td>
<td>156 (68.7)</td>
<td>98 (43.2)</td>
</tr>
</tbody>
</table>

Nasal and skin biopsy: χ² = 0.5399 (p < 0.0001).
Nasal biopsy and skin smear: χ² = 0.7722 (p < 0.0001).

(46.7%) cases were positive and 95 (41.9%) were negative in both samples (χ² = 0.7722; Table 2).

DISCUSSION

An early and accurate diagnosis of leprosy is extremely important in all aspects of leprosy epidemiology, case management, and prevention of disability. Current diagnostic methods based on clinical criteria with additional skin smear and skin biopsy are relatively adequate in MB patients. However, the diagnosis of leprosy in patients with no apparent skin lesion is still problematic. In some PB patients (especially clinical forms I, II, and BT), the physician has to rely only on clinical signs and symptoms for the diagnosis of leprosy. The nasal mucosa presents several alterations that precede the skin lesions by several years. Studies of the mucosa could, therefore, serve as an accurate method for early detection of M. leprae. Patients enrolled in this study had a mean age of 46 years (range, 9-87 years). The age used here is in agreement with the literature, because leprosy occurs in all ages, but in endemic areas, the occurrence is higher among adults and more prevalent in the borderline spectrum (64.7%).

The interest in nasal biopsy in leprosy research has been reviewed after almost 30 years without much publication. To our knowledge, this study is the first to show the potential usage of nasal biopsy for the early (and differential for distinct disease forms) diagnosis of leprosy. We have also shown that findings in nasal biopsy can be correlated to changes in skin smear and skin biopsy (p < 0.001). Our results show the striking involvement of the nasal mucosa in the disease (100% in LL patients), decreasing to the TT pole. Furthermore, in two (0.8%) patients the nasal biopsy was the only positive finding. Thus, nasal evaluation is a powerful tool for early diagnosis, which, in turn, minimizes the impairment caused by advanced stages of the disease and reduces its incidence. Additionally, nasal biopsy associated with other diagnostic tests can increase considerably the diagnosis sensitivity.

Previous studies have shown that BL and BB can also show nasal involvement, whereas BT and TT leprosy patients do not exhibit intranasal involvement. However, we have found the M. leprae in nasal biopsy specimens of BT leprosy in 6.2% of cases. Hence, all patients with positive results on nasal biopsy specimens may have nasal bacillary discharge and they are a potent source of infection to the population. Therefore, these BT patients have to be managed as MB and should be given 1 year of multidrug therapy, instead of 6 months (which is the recommended treatment to PB patients). This may explain the failure of the drug treatment and the recurrence that can occur in these patients.

Finally, nasal biopsy is an important exam that enhances considerably leprosy diagnosis. However, it should not be used as a replacement of traditional and well-establish skin smear. Nasal biopsy has the advantages of early diagnosis and better differential for distinct clinical forms (especially in those with no skin lesions). However, the necessity of an otolaryngologist to perform the biopsy limits its universal use. Additional studies are needed to assess the application of nasal biopsy in the evaluation of leprosy drug therapy and for early diagnosis of the disease in endemic areas, where the reduction of the incidence of new cases is a priority.

CONCLUSION

The present study showed a 48% rate of positivity in nasal biopsy specimens of untreated leprosy patients, reaching 100% in LL patients. The results observed in the nasal biopsy were highly correlated with changes in skin biopsy and skin smear. Our results indicate that nasal biopsy can be an important tool for early leprosy diagnosis.

ACKNOWLEDGMENTS

The authors are grateful to all the staff of the National Reference Center of Leprosy of the Federal University of Uberlandia for fundamental support.

REFERENCES