

Original Research Paper

Endoscopic Changes of Nasal Mucosa in Patients with Leprosy

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Article history

Received: 09-03-2019

Revised: 22-04-2019

Accepted: 02-05-2019

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Abstract: Leprosy is a chronic granulomatous disease, affecting the skin and Schwann cells of peripheral nerves. In most leprosy cases, the nasal mucosa is affected. We aimed to describe the clinical changes in nasal mucosa using nasal endoscopy, in patients with leprosy attending a dermatology service in an endemic region and compare this changes with those founds in non-leprosy patients nasal mucosa. This cross-sectional study examined and compared 16 leprosy patients and 16 non-leprosy patients. Nasal endoscopy was conducted in both groups to determine differences between the two groups and analysis was applied to evaluate factors related to changes in the nasal mucosa. A larger number of changes in the nasal mucosa was observed in multibacillary patients (75%); infiltration, lepromas and hematic crusts were the changes that were most commonly observed. There was a larger proportion of men (68.8%) diagnosed as having leprosy; they demonstrated a 23-fold increase of nasal mucosa involvement compared to women. There was no positive correlation between nasal symptoms and changes observed in the nasal mucosa. Therefore, it is important to perform an otorhinolaryngological examination and, more importantly, an endoscopic examination of the nasal mucosa, regardless of the presence or absence of symptoms or the clinical presentation of patients with leprosy.

Keywords: Leprosy, Nasal Mucosa, Nasal Endoscopy

Introduction

Leprosy is a chronic infectious disease, caused by *Mycobacterium leprae*, affecting the skin and peripheral nerves, thereby resulting in cutaneous lesions and neuropathy (Oliveira *et al.*, 2013; Queiroz *et al.*, 2015). It is characterized by dermatological and neurological signs and symptoms, which range from hypochromic spots with irregular borders, to hypoesthesia and diffuse and progressive infiltration of the skin. Mucous

membranes may be affected, how eyes, lymph nodes and upper airways (Lastória and Abreu, 2014). The neurological manifestation includes the appearance of lesions occurring mainly in peripheral nerves, which is related to sensorial loss, physical disabilities and deformities (Budel *et al.*, 2011; Lopes *et al.*, 2017). The World Health Organization classifies leprosy as paucibacillary and multibacillary; the latter causes physical disfigurement and disability in severe cases (Gashignard *et al.*, 2016; Lopes *et al.*, 2017). In the early

stages of *M. leprae* infection, the nasal mucosa is primarily affected, with the upper airway being the main form of transmission to untreated patients (Silva *et al.*, 2008). The nasal manifestation of the disease involves tuberculous eruption of the skin invading the nasal mucosa, mouth, throat, larynx and eyes (Martins *et al.*, 2005). At nasal mucosa, there are common complications as hyposmia, nasal obstruction, epistaxis, crusts and rhinorrhea (Sun *et al.*, 2018).

In recently diagnosed cases, the nasal mucosa of leprosy patients is affected (Silva *et al.*, 2008). Despite this, only few studies have investigated the profile of these changes or how these nasal changes manifest clinically. The aim of this study was to describe endoscopic changes in nasal mucosal of patients with leprosy.

Materials and Methods

A cross-sectional study was carried out, involving 16 leprosy patients attending the dermatology outpatient clinic at the State University of Pará (UEPA). These 16 patients were screened for changes to the nasal mucosa and were classified as follows: 8 as paucibacillary and 8 as multibacillary. The control group comprised 16 patients previously diagnosed as having psoriasis, an inflammatory dermatological disease that does not involve the nasal mucosa and was selected as a suitable control sample group for this reason.

The study group comprised of both male and female patients diagnosed as having leprosy and the patients were over 18 years of age. Patients with underlying otolaryngological diseases were excluded. The control group included male and female patients, who were over 18 years of age and presented with a previous clinical and histopathological diagnosis of psoriasis without any symptoms or signs of leprae, clinically or histopathologically. The research was undertaken between May and December 2015.

Inclusion criteria to the study for the leprosy group was as follows: An individual presenting with one or more of the following signs: (1) A lesion and/or skin area with change in sensation; (2) involvement of the peripheral nerve, with or without thickening, associated with sensitivity and/or motor and/or autonomous changes and; (3) positive bacilloscopy, confirmed by obtaining an intradermal swab sample (MSB, 2010). The patients were classified using the Madrid clinical classification (Quagliato, 1999), which takes into consideration both clinical and bacilloscopic aspects of the disease.

Clinical examination consisted of a morphological assessment, including a count of the number and location of the lesions identified. The neurological evaluation consisted of inspection, palpation and percussion tests, in addition to strength and sensation tests. During the examination of the nasal cavity, the presence of secretions, bleeding, ulcers and crusts was observed and noted.

Socio-demographic data (gender, age, ethnicity, education, country of origin), clinical data (clinical form, operational classification, disease duration, presence of reactional state and comorbidities) and specific variables regarding the nasal mucosa (nasal mucosa characteristics, existence and type of secretion, presence or absence of vegetative lesions and ulcers) was collected.

Nasal endoscopy was conducted using optic fiber instrumentation coupled to a micro camera (Olympus). Lidocaine 2% spray was applied to the nasal fossa, to administer local anesthesia. An optic fiber, ranging between 3–4 mm in thickness, was introduced into the nasal region. The images were assessed by two otolaryngologists. In the event of disagreement, a third otolaryngologist made a determining assessment. It is important to emphasize that our aim was to describe macroscopic lesions, so, we have not made biopsy of nasal mucosa in any patient.

The data was subjected to descriptive analysis to obtain the absolute and relative frequencies, measures of central tendency (mean) and variability (standard deviation). An association between each independent and dependent variable was confirmed and obtained by applying the chi-square test, Fisher's exact test, or the G-test. To analyze the factors associated with changes in nasal mucosa, logistic regression analysis was performed. The statistical analyses were processed using Stata 12.0 software (StataCorp). The level of significance of the findings was fixed by the alpha lower than 5%.

The study was approved by the local Research Ethics Committee (Report Number: 945.972).

Results

When considering the socio-demographic profile, a significant difference was observed between the two groups regarding educational qualifications ($p < 0.05$). The control group had attained a more advanced level of education. No such trend was observed in the study group with leprosy (Table 1).

Signs and symptoms of olfactory changes were mostly absent in both groups, despite noting a number of changes to the nasal mucosa in 43.8% of leprosy patients (Table 2). With consideration to the operational classification of leprosy patients, the number of changes in the nasal mucosa was significantly higher in the multibacillary form (Table 3). When assessing neurological responses, we noted that all patients with mucosa alterations also demonstrated leprosy-related neurological responses (Table 4).

When both the leprosy subjects and the control subjects were simultaneously assessed, 90% of individuals presenting with changes to the nasal mucosa were shown to be males (Table 5). Among the otorhinolaryngological symptoms, rhinorrhea is

frequently present and accounts for 30% of individuals with changes to the mucosa (Table 6).

The alterations caused by leprosy were significantly higher in multibacillary patients (Table 7). Endoscopic examination of the nasal mucosa showed

heterogeneous changes to the inferior and middle nasal conchae, as well as to the nasal septum of leprosy patients. The only changes to the control group were seen in the inferior nasal concha and nasal septum (Table 8).

Table 1: Observation groups according to variables of demographic characterization

Variables	Observation groups						p-value
	Psoriasis		Leprosy		Total		
	n	%	N	%	n	%	
Gender							
Female	8	50.0	5	31.2	13	40.6	0.472 [‡]
Male	8	50.0	11	68.8	19	59.4	
Age group (years)							
≤ 30	2	12.5	3	18.8	5	15.6	0.183 [#]
31 to 45	2	12.5	6	37.5	8	25.0	
46 to 60	7	43.8	6	37.5	13	40.6	
> 60	5	31.2	1	6.2	6	18.8	
Procedência							
Metropolitan region	15	93.8	12	75.0	27	84.4	0.333*
Interior of State	1	6.2	4	25.0	5	15.6	
Instruction							
Illiterate	1	6.2	2	12.5	3	9.4	0.007 [#]
Elementary School (incomplete)	3	18.8	7	43.8	10	31.2	
Elementary School (complete)	1	6.2	3	18.8	4	12.5	
Secondary School (incomplete)	-	-	3	18.8	3	9.4	
Secondary School (complete)	5	31.2	-	-	5	15.6	
Graduation (complete or incomplete)	6	37.5	1	6.2	7	21.9	
Total	16	100.0	16	100.0	32	100.0	-----

[‡]Chi-square Test *Fisher's Exact Test. [#]G Test

Table 2: Observation groups according to variables of otorhinolaryngological symptomatology

Variables	Observation groups						p-value
	Psoriasis		Leprosy		Total		
	n	%	n	%	n	%	
Nose pain or irritation							
Yes	4	25	4	25	8	25	1.000*
No	12	75	12	75	24	75	
Epistaxis							
Yes	-	-	2	12.5	2	6.2	0.484*
No	16	100	14	87.5	30	93.8	
Foreign body sensation in the nose							
Yes	-	-	3	18.8	3	9.4	0.226*
Não	16	100	13	81.2	29	90.6	
Olfactory alteration							
yes	-	-	2	12.5	2	6.2	0.484*
Não	16	100	14	87.5	30	93.8	
Rhinorrhea							
Yes	4	25	3	18.8	7	21.9	1.000*
No	12	75	13	81.2	25	78.1	
Another otorhinolaryngological disease							
Yes	-	-	1	6.2	1	3.1	1.000*
No	16	100	15	93.8	31	96.9	
Nasal mucosa							
Normal	13	81.2	9	56.2	22	68.8	0.252*
Altered	3	18.8	7	43.8	10	31.2	
Total	16	100	16	100	32	100	-----

*Fisher's Exact Test

Table 3: Operational classification of leprosy according to variables of otorhinolaryngological symptomatology

Variables	Operational classification						p-value
	Paucibacillary		Multibacillary		Total		
	n	%	n	%	n	%	
Nose pain or irritation							
Yes	1	12.5	3	37.5	4	25	0.569*
No	7	87.5	5	62.5	12	75	
Epistaxis							
Yes	-	-	2	25	2	12.5	0.467*
No	8	100	6	75	14	87.5	
Foreign bod sensation in the nose							
Yes	-	-	3	37.5	3	18.8	0.200*
No	8	100	5	62.5	13	81.2	
Olfactory alteration							
Yes	1	12.5	1	12.5	2	12.5	1.000*
No	7	87.5	7	87.5	14	87.5	
Rhinorrhea							
Yes	1	12.5	2	25	3	18.8	1.000*
No	7	87.5	6	75	13	81.2	
Another Otorhinolaryngological disease							
Yes	-	-	1	12.5	1	6.2	1.000*
No	8	100	7	87.5	15	93.8	
Nasal mucosa							
Normal	7	87.5	2	25	9	56.2	0.0410*
Altered	1	12.5	6	75	7	43.8	
Total	8	100	8	100	16	100	-----

*Fisher's Exact Test

Table 4: Operational classification of leprosy according to variables characterizing leprosy reaction

Variables	Operational classification						p-value
	Paucibacillary		Multibacillary		Total		
	n	%	n	%	n	%	
Leprosy reaction							
Yes	1	12.5	6	75.0	7	43.8	0.041*
No	7	87.5	2	25.0	9	56.2	
Type of leprosy reaction							
Type I	1	12.5	3	37.5	4	25.0	0.102#
Type II	-	0.0	2	25.0	2	12.5	
No information	7	87.5	3	37.5	10	62.5	
Treatment to leprosy reaction							
Yes	1	12.5	5	62.5	6	37.5	0.062#
No	-	0.0	1	12.5	1	6.2	
No information	7	87.5	2	25.0	9	56.3	
Nasal mucosa							
Normal	7	87.5	2	25.0	9	56.2	0.041*
Altered	1	12.5	6	75.0	7	43.8	
Total	8	100.0	8	100.0	16	100.0	----

*Fisher's exact Test. #G Test

Table 5: Alteration of Nasal Mucosa according to variables of demographic characterization

Variables	Nasal mucosa						p-value
	Normal		Altered		Total		
	n	%	n	%	n	%	
Groups							
Psoriasis	13	59.1	3	30	16	50	0.153*
leprosy	9	40.9	7	70	16	50	
Gender							
Female	12	54.5	1	10	13	40.6	0.024*
Male	10	45.5	9	90	19	59.4	
Age Group (years)							
≤ 30	2	9.1	3	30	5	15.6	0.442#
31 to 45	5	22.7	3	30	8	25	
46 to 60	10	45.5	3	30	13	40.6	
> 60	5	22.7	1	10	6	18.8	
Total	22	100.0	10	100.0	32	100.0	-----

*Fisher's Exact Tes. # G Test

Table 6: Alteration of Nasal Mucosa according to variables of otorhinolaryngological symptomatology

Variables	Nasal mucosa						p-value
	Normal		Altered		Total		
	n	%	n	%	n	%	
Nose pain or irritation							
Yes	5	22.7	3	30	8	25	0.681*
No	17	77.3	7	70	24	75	
Epistaxis							
Yes	-	-	2	20	2	6.2	0.091*
No	22	100	8	80	30	93.8	
Foreign body sensation in the nose							
Yes	1	4.5	2	20	3	9.4	0.224*
No	21	95.5	8	80	29	90.6	
Olfactory alteration							
Yes	1	4.5	1	10	2	6.2	1.000*
No	21	95.5	9	90	30	93.8	
Rhinorrhea							
Yes	4	18.2	3	30	7	21.9	0.648*
No	18	81.8	7	70	25	78.1	
Another Otorhinolaryngological disease							
Yes	1	4.5	-	-	1	3.1	1.000*
No	21	95.5	10	100	31	96.9	
Total	22	100.0	10	100.0	32	100.0	-----

* Fisher's Exact Test

Table 7: Operational classification of leprosy according to results of endoscopic examination

Endoscopic examination	Operational classification						p-value
	Paucibacillary		Multibacillary		Total		
	n	%	n	%	n	%	
Nasal mucosa							
Altered by leprosy	1	12.5	4	50.0	5	31.2	0.040#
Altered by another reason	-	-	2	25.0	2	12.5	
No alteration	7	87.5	2	25.0	9	56.3	
Infiltration							
Present	1	12.5	3	37.5	4	25.0	0.569*
Absent	7	87.5	5	62.5	12	75.0	
Leproma							
Present	-	-	2	25.0	2	12.5	0.467#
Absent	8	100.0	6	75.0	14	87.5	
Hematic crust							
Present	-	-	2	25.0	2	12.5	0.467#
Absent	8	100.0	6	75.0	14	87.5	
Total	8	100.0	8	100.0	16	100.0	-----

* Fisher's Exact Test. # G Test

Table 8: Characteristics of the endoscopic examination of the nasal cavity of Fossa and Cavum according to observation groups

Characterization	Observation group						p-value
	Leprosy		Psoriasis		Total		
	n	%	n	%	n	%	
INFERIOR MEATUS							
Unobstructed	13	81.2	16	100	29	90.6	0.3620#
Mucoid secretion	1	6.2	-	-	1	3.1	
Catarrhal secretion	1	6.2	-	-	1	3.1	
INFERIOR TURBINATE							
Increased	8	50.0	4	25	12	37.5	0.2720#
Pale	7	43.8	10	62.5	17	53.1	
High-coloured	2	12.5	-	-	2	6.2	
Hummocky	4	25.0	5	31.2	9	28.1	
Normal	7	43.8	13	81.2	20	62.5	
MIDDLE MEATUS							
Unobstructed	14	87.5	16	100	30	93.8	1.0000#
Mucoid secretion	3	18.8	-	-	3	9.4	
Catarrhal secretion	-	-	-	-	-	-	
MIDDLE TURBINATE							
Increased	8	50.0	5	31.2	13	40.6	0.4909#
Pale	7	43.8	8	50	15	46.9	
High-coloured	1	6.2	-	-	1	3.1	
Hummocky	1	6.2	-	-	1	3.1	
Normal	8	50.0	12	75	20	62.5	
NASAL SEPTUM							
High septal deviation	9	56.2	11	68.8	20	62.5	1.0000#
Anterior septal deviation	3	18.8	2	12.5	5	15.6	
Inferior septal crest	7	43.8	9	56.2	16	50.0	
Tortuous	1	6.2	1	6.2	2	6.2	
Centered	6	37.5	6	37.5	12	37.5	
Perforated	-	-	-	-	-	-	
CAVUM							
Unobstructed	11	68.8	15	93.8	26	81.2	1.0000#
Mucoid secretion	2	12.5	-	-	2	6.2	
Catarrhal secretion	-	-	-	-	-	-	
High-coloured	1	6.2	-	-	1	3.1	

#G Test

Discussion

The present study shows a high prevalence of mucosal symptoms in leprosy subjects. The principal nasal mucosal symptoms in leprosy patients are obstruction and epistaxis (Sun *et al.*, 2018). However, in our research, patients mainly complained of nasal irritation and pain. We considered patient reports complaining of an “obstruction” within the nose as equivalent to reports of the sensation of a foreign body present in the nose. This symptom only occurred in the multibacillary patient group and, in this case, could indicate a more severe presentation of the disease. A higher frequency of nasal symptoms was reported in multibacillary cases. This data supports related research that suggests these symptoms can occur prior to the appearance of skin lesions (Martins *et al.*, 2005).

Leprosy reactions can occur before or, more frequently, during or after treatment. The duration and

number of these mucosal reactions often depends on the clinical presentation. In our analysis, almost half of the leprosy sample had a reaction. This observation does not take in to account reactions produced after treatment, since our investigation only involved patients undergoing polychemotherapy. Multibacillary patients can develop both types of leprosy reactions, either separately or simultaneously. On the other hand, paucibacillary patients do not have Type II reaction and, therefore, are less exposed to systemic complications. Considering that all the leprosy patients presenting changes in nasal mucosa showed some reaction, the clinical surveillance of this specific group was reinforced, in order to avoid further possible otorhinolaryngological complications.

Leprosy compromises the nasal mucosa, producing typical and individualized lesions of leprous rhinitis, including infiltration, lepromas, perforation, ulcerations and crust formation. However, other observations not exclusive to leprous rhinitis, such as discoloration or

paleness of the mucosa, congestion, ectasias, vasculitis, atrophy, dryness and presence of blood, can also present in other nasal disorders (Yang *et al.*, 2014). To establish a positive diagnosis of leprosy, bacterioscopy and, especially, mucosal histopathology is required, using precise perivascular and neural infiltration to confirm the etiology (Oliveira and Diniz, 2016). It was not possible to conduct bacterioscopy and mucosal histopathology in our research. We considered typical leprosy lesions as leprosy-specific, for those identified within our study group. Any other lesions observed were considered as not exclusive to leprosy and were classified as non-specific changes (Martins *et al.*, 2005).

Regarding the endoscopic examination, the only statistical association between the operational classifications of leprosy patients was the alteration in the nasal mucosa. The change caused specifically by leprosy was significantly more frequent in multibacillary patients. Two individuals showed non-specific changes, which could have been attributable to leprosy if they had been subjected to diagnostic confirmation through either bacterioscopy or histopathology. Despite the observed link between each specific alteration in the multibacillary group, there were no significant differences, probably due to the small sample size.

Some authors assert that no lesions occur in the nasal mucosa of patients with the tuberculoid or borderline tuberculoid form of leprosy (Silva *et al.*, 2008) classified as paucibacillary. However, even in our small sample group, there was one patient classified as presenting with tuberculoid leprosy who also presented with a specific leprosy lesion (infiltration) in the mucosa. We also observed that independent of the clinical presentation, mucosal lesions were present despite the absence of symptoms and throughout all stages of the disease.

We worked with three classifications of severity, namely early, intermediate and advanced. In the early classification group, we noted infiltration of the mucosa and abnormal dryness. In the intermediary classification group, the infiltration had increased, causing nasal obstruction, leading to increased nasal secretion and crust formation. Finally, in the advanced classification group, ulcer and secondary infection were observed in addition to a decreased perichondral blood supply. At an advanced stage, perforation of the cartilaginous nasal septum is a potential complication causing changes in sensation and olfactory disruption. Damage to the nasal septum can cause saddle-nose deformity (Silva *et al.*, 2008). In our sample, we noted the presence of early and intermediary changes, but no advanced nasal complications were identified. This finding suggests an improvement in early detection rates in diagnosing patients with leprosy. Early intervention and treatment, in addition to education on simple self-care strategies manageable by patients, may be attributing to a reduction in severe complications and physical changes to the nose.

Other study says that nasal manifestations in leprosy typically develop in 3 stages. The first stage is characterized by a thickening of the mucosa, which appears dry because of the damage of the parasympathetic secretory nerve. The second stage has a characteristic mucosal infiltration. Patients in this stage complain of nasal obstruction, mucopurulent rhinorrhea and epistaxis. The third stage of the disease is a deformity phase (Kim *et al.*, 2015).

The most affected nasal structures are the septum, the nasal conchae and the anterior nasal spine with mucosal coating bilaterally (Silva *et al.*, 2008). In our study, the septum showed the highest number of changes, particularly high septum deviation. No cases of perforation, a particularly stigmatizing characteristic of the disease, were observed.

The higher prevalence of leprosy in men as compared to women may be associated with a wider range of close physical contacts, in association with less attention to self-protective behavior that aims to maintain good physical health (Gashignard *et al.*, 2016; Monteiro *et al.*, 2017). The involvement of this disease throughout the economically active population explains the higher inter-human contact in this population (Barbosa *et al.*, 2014).

The majority of patients lived within the metropolitan region, where there is a higher population density in the capital city areas as compared to other regions, permitting improved access to the dermatology service. Over several decades, awareness has grown of the impact of urbanization on patients with leprosy. Population density and socioeconomic vulnerability serve to increase the risks of identifying and containing leprosy within the urban population (Barbosa *et al.*, 2014).

The levels of education obtained within the leprosy group were consistent with other research carried out in Brazil, which identified limited educational qualifications as a significant characteristic of leprosy patients (Kerr-Pontes *et al.*, 2006). In comparison to the control group, most of the patients had obtained a higher level of education. This characteristic is partially attributable to precarious socioeconomic conditions, resulting in a diminished understanding of this condition and of the intended prescribed treatment pathway. A delay in seeking assistance or abandoning prescribed treatment due to a lack of an appropriate knowledge of the disease has been noted.

All our patients were educated in nasal self-care procedures such as nasal cleansing, lubrication, crust removal, care with hyper-secretion and prevention of traumatizing lesions developing in the mucosa.

Finally, our study suggests that in view of important nasal mucosal changes in leprosy patients compared to controls, it is important to carefully examine this aspect of these patients.

Acknowledgement

To the employees of the Laboratory of Sanitary Dermatology and the University Hospital Bettina Ferro de Souza.

Author's Contributions

Carla Andrea Avelar Pires: Took part in conception, design and revision of the study.

Eline Pinheiro Weba Costa: Responsible for acquisition of data.

Marcus Vinicius Duarte Costa: Responsible for acquisition of data.

Adriana Kamilly Leitão Pitman Machado: Responsible for acquisition of data.

Aline de Lima Dias: Drafted the manuscript.

Gabriela Athayde Amin: Drafted the manuscript.

Manuela Nascimento de Lemos: Revised the manuscript critically.

Alison Ramos da Silva: Drafted the manuscript.

Marcos Antonio Neves Noronha: Revised the manuscript critically.

Marilia Brasil Xavier: Took part in conception, design and revision of the study.

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. CAAP and EPWC took part in conception and design of study. MVDC, AKLPM and ALD were responsible for acquisition of data, while MNL and MANN have done the analysis and interpretation of data. GAA, ARS and MBX have drafted the manuscript together. All authors have revised the manuscript critically and approved the version to be published.

Ethics

This study was developed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by our local ethics committee.

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