Nasopharyngeal Tuberculosis in a Philippine Tertiary General Hospital

Mark Anthony T. Gomez, MD, MPM-HSD[1]
Romeo L. Villarta, Jr., MD, MPH[1,2]
Ruzanne M. Caro, MD[3]
Criston Van C. Manasan, MD[4]
Jose M. Carnate, Jr., MD[5]

[1]*Department of Otorhinolaryngology*
Philippine General Hospital
University of the Philippines Manila

[2]*Department of Epidemiology and Biostatistics*
College of Public Health
University of the Philippines Manila

[3]*Department of Otorhinolaryngology*
College of Medicine – Philippine General Hospital
University of the Philippines Manila

[4]*Department of Laboratories*
Philippine General Hospital
University of the Philippines Manila

[5]*Department of Pathology*
College of Medicine
University of the Philippines Manila

Correspondence: Dr. Jose M. Carnate, Jr.
Department of Pathology
Philippine General Hospital
Taft Avenue, Ermita, Manila 1000
Philippines
Phone: (632) 8554 8400 local 3200
Email: jmcjpath@yahoo.com

The authors declared that this represents original material that is not being considered for publication or has not been published or accepted for publication elsewhere in full or in part, in print or electronic media; that the manuscript has been read and approved by all the authors, that the requirements for authorship have been met by each authors, and that each author believes that the manuscript represents honest work.

Disclosures: The authors signed disclosures that there are no financial or other (including personal) relationships, intellectual passion, political or religious beliefs, and institutional affiliations that might lead to a conflict of interest.

Presented at the Philippine Society of Otolaryngology Head and Neck Surgery Annual Convention Free Paper Forum, December 2, 2017, The Manila Hotel.

ABSTRACT

Objective: This study aimed to determine the prevalence of nasopharyngeal tuberculosis among patients who were initially assessed to have a nasopharyngeal mass and subsequently underwent biopsy in a Philippine Tertiary General Hospital from Year 2013 to 2015.

Methods:

Design: Case Series

Setting: Tertiary National University Hospital

Participants: All patients with nasopharyngeal mass identified from January 2013 to December 2015 from a hospital wide census who underwent biopsy were investigated using chart and histopathology review. The prevalence of tuberculosis, malignancies and other findings were determined.

Results: Among 285 nasopharyngeal biopsies done between 2013 and 2015, 33 (11.6%) were histologically compatible with nasopharyngeal tuberculosis, 177 (62.1%) were different types of nasopharyngeal carcinoma, 59 (20.7%) were chronic inflammation, 4 (1.4%) were lymphoma, 5 (1.8%) were normal, and 7 (2.5 %) had diagnoses other than those above..

Conclusion: This study suggests a relatively high prevalence rate (11.6%) of nasopharyngeal tuberculosis in patients who have a nasopharyngeal mass. This indicates that nasopharyngeal tuberculosis should always be a differential when confronted with a mass in the nasopharynx especially in tuberculosis endemic areas.

Keywords: *nasopharyngeal tuberculosis; prevalence; censuses; tertiary care centers; Philippines; carcinoma; nasopharynx; biopsy; tuberculosis; lymphoma*

While the majority of tuberculosis infection is found in the lungs, tuberculosis can manifest in the head and neck region including cervical lymph nodes, parotid, the larynx, middle ear and tonsils.[1-4] Nasopharyngeal tuberculosis (NPTB) is rarer and to the best of our knowledge, has been characterized in only a few case reports and series worldwide. There has only been one published case report in the Philippines.[5]

Philipp J Otolaryngol Head Neck Surg 2019; 34 (2): 7-10

Based on available literature, NPTB usually presents with nasopharyngeal mass associated with cervical lymphadenopathy as well as nasal, ocular and otologic symptoms.[6-10] These findings overlap with the clinical presentation of nasopharyngeal malignancies, posing important diagnostic and therapeutic issues.[6,11-15]

The study aimed to determine the prevalence of nasopharyngeal tuberculosis among patients who underwent nasopharyngeal biopsy in the Philippine National University Hospital from January 2013 to December 2015.

METHODS

With Institutional Ethical and Technical Review Board approval (UPMREB ORL - 2016-387-01), this descriptive case series sought to review records of patients of any age who were previously assessed to have a nasopharyngeal mass on endoscopy and who eventually underwent nasopharyngeal mass biopsy at the Philippine General Hospital from January 1, 2013 to December 31, 2015.

Patients who underwent nasopharyngeal mass biopsies were initially identified from the Department of Otorhinolaryngology census and logbooks of the in-patient and out-patient operating rooms.

Records were retrieved by the first author and basic demographic (age and sex) and histopathologic data were collated and recorded using Microsoft Office Professional Plus 2010 for Windows (Microsoft Corporation, Redmond, WA USA).

Excluded were patients whose biopsies were deferred due to other health reasons, who underwent intranasal (instead of nasopharyngeal) mass biopsies and those with incomplete entries. Patients who had previous recurrences of the condition and appeared twice in the registry were considered as one patient.

The final histopathological diagnoses were retrieved from the database of histopathology results at the Department of Laboratories. Full hospital chart reviews were attempted on all patients with NPTB.

Descriptive statistics were used to define demographics and summarize and describe the data. The prevalences of each of the diagnosis were computed based on the data. The different prevalences were then described.

RESULTS

Among the 285 nasopharyngeal biopsies we identified between 2013 and 2015, 33 (11.6%) were histologically compatible with nasopharyngeal tuberculosis (NPTB), 177 (62.1%) were different types of nasopharyngeal carcinoma (NPCA), 59 (20.7%) were interpreted as chronic inflammation, four (1.4%) were lymphoma, five (1.8%) were normal, and seven (2.5 %) were diagnosis other than those mentioned.

The mean age of all patients with nasopharyngeal mass was 43.47 years old. The mean age of patients with nasopharyngeal carcinoma was 47.84 years old while the mean age of patients with nasopharyngeal tuberculosis was younger at 29.15 years old. The mean age of patients with chronic inflammation and lymphoma were 38.82 and 40.5 years old, respectively. The youngest patients with NPCA, chronic inflammation, NPTB and lymphoma were 15, 15, 14 and 17 years old, respectively. The oldest patients with NPCA, chronic inflammation, NPTB and lymphoma were 78, 70, 60 and 66 years old, respectively.

The patients had variable distributions among different age groups. The distribution of disease according to age group is shown in *Table 1*. In terms of sex, the ratio of nasopharyngeal carcinoma and chronic inflammation were almost the same at 3:1. On the other hand, the sex ratio for nasopharyngeal tuberculosis and lymphoma were the same and equal at 1:1. The distribution of patients is shown in *Table 2*.

Of the 33 patients with NPTB, only seven complete patient charts were retrieved. Most of the records of other patients had been transferred to their local Tuberculosis Treatment Center or were missing. Among the seven patients whose complete charts were reviewed, two had a previous history of pulmonary tuberculosis and had been treated with anti-tuberculosis chemotherapy and one had a history of unrecalled chronic lung illness which could also be pulmonary tuberculosis. All the seven patients had presence of cervical lymphadenopathy which prompted the initial medical consult. There was no mention of history of Human Immunodeficiency Virus infection, multidrug resistant tuberculosis infection or diabetes mellitus in the charts of the seven NPTB patients.

Table 1. Distribution of Disease according to Age Group

Age Group (years)	Nasopharyngeal Carcinoma (%) N=177	Nasopharyngeal Tuberculosis (%) N=33	Chronic Inflammation (%) N=59	Lymphoma (%) N=4
14-20	5 (2.8%)	10 (30.3%)	9 (15.3%)	1 (25%)
21-55	127 (71.8%)	20 (60.6%)	38 (64.4%)	2 (50%)
56-70+	45 (25.4%)	3 (9%)	12 (20.3%)	1 (25%)

Table 2. Distribution of Disease according to Sex

Diagnosis	Sex	
	Male (%)	Female (%)
NPCA (N=177)	132 (74.6%)	45 (25.4%)
NPTB (N=33)	17 (51.5%)	16 (48.5)
Chronic Inflammation (N=59)	45 (76.3%)	14 (23.7%)
Lymphoma N=4	2 (50%)	2 (50%)

DISCUSSION

Nasopharyngeal Tuberculosis (NPTB) has been described prior to the advent of the anti-tuberculosis antibiotics in 1936 by Graff who identified a high presence (82%) of nasopharyngeal tuberculosis by histology in 118 pulmonary tuberculosis cases.[16] After the emergence of anti-tuberculosis medications, there was a dramatic decrease in cases of nasopharyngeal tuberculosis. A 1976 survey of 843 cases of pulmonary tuberculosis by Rohwedder found 16 patients with tuberculosis of the upper respiratory tract and only one of these had nasopharyngeal tuberculosis.[17] The recent worldwide upsurge in the incidence of nasopharyngeal tuberculosis in the literature could be due to increased awareness of disease, improvement of knowledge regarding the entity, improved diagnostic techniques and of course, increase in incidence of the disease itself.[6]

Most of the literature on the topic is only in the form of case reports and series that were gathered over many years and are not enough to give a clear picture of the prevalence of the illness. As of this writing, we could find no other studies detailing its prevalence. Based on our study, the prevalence of NPTB can reach as high as 1.1 for every 10 nasopharyngeal biopsies. This prevalence of nasopharyngeal tuberculosis is second only to nasopharyngeal carcinoma and even higher than lymphoma.

There are several important implications of the results of our study. First, clinicians usually have two main differential diagnoses when faced with a nasopharyngeal mass –nasopharyngeal carcinoma or lymphoma. The results of our study would add nasopharyngeal tuberculosis to the differentials especially in areas where tuberculosis is endemic. These three diagnoses each entail totally different managements and accurate diagnosis is necessary to provide proper treatment. The additional differential should guide other medical specialists. Pathologists must thoroughly analyse histopathologic slides especially those with chronic inflammatory patterns because hidden in the sea of inflammatory cells might be islands of tuberculosis or granulomatous lesions that may be overlooked. Pathologists should also be careful in making diagnosis because concomitant TB infection of the nasopharynges of patients with nasopharyngeal carcinoma may be present.[18] Radiologists should consider the possibility of nasopharyngeal tuberculosis in interpreting CT Scans of patients with a nasopharyngeal mass. The possibility of nasopharyngeal tuberculosis should also be mentioned in patient education, and patient anxiety may be decreased by the knowledge that not all nasopharyngeal masses are cancer.

There are also important implications related to the safety of clinicians. Although it is the usual practice for otorhinolaryngologists to wear standard personal protective equipment in performing nasopharyngeal biopsies, the high prevalence of tuberculosis in patients with nasopharyngeal mass will require additional precautions such as wearing N95 masks instead of regular masks and ultraviolet disinfection after surgery. As patients with nasopharyngeal tuberculosis may have other co-morbidities such as HIV infection, these additional precautionary measures mentioned are well-justified.

Diagnosis of NPTB in previous reports were done initially by nasal endoscopy, biopsy and culture of tuberculous bacilli from secretions and nasopharyngeal tissue. Histopathology of the biopsied nasopharyngeal may also be helpful since results of TB culture may cause delays in diagnosis up to 6 weeks.[6] Additional radiologic examinations may also be helpful such as CT scan and MRI.[6] A study in China reported that a presence of necrosis and striped pattern in nasopharyngeal lesions and lack of invasion of regional structures as seen in CT and MRI of 36 NPTB patients may suggest the diagnosis of NPTB instead of malignancy.[19] In terms of management, previous reports differed in the duration of anti-tuberculosis treatment. Some had the minimal six-month course of triple combination therapy that included isoniazid, rifampicin and ethambutol. Others were treated with nine months of quadruple therapy (adding an initial short course of pyrazinamide). There is even a study in China which used an oral anti tuberculosis regimen of 3HRZS(E)/9HR(E) for one year combined with nasal spray combination medication of isoniazid, rifampicin and streptomycin injection solution for 3 months.[20] However, to the best of our knowledge, there have been no published recommendations on the proper diagnosis, treatment and monitoring of response to treatment specifically for nasopharyngeal tuberculosis. While this may reflect the global rarity of the disease, further studies must be performed in tuberculosis endemic countries like the Philippines to evaluate the means of diagnosis and treatment response of nasopharyngeal tuberculosis so that management can be optimised to prevent development of multiple drug resistance.

There were at least two patients in our study with a past history of previously treated pulmonary tuberculosis. Although it is not known whether the nasopharyngeal tuberculosis appeared before or after pulmonary tuberculosis treatment, this finding could mean that the nasopharyngeal tuberculosis in these patients may not have been affected by the initial treatment given or may have developed despite treatment. Although there have been no studies that state the clear association between disseminated tuberculosis and development of multi-drug resistant tuberculosis, having multiple sites in a patient might trigger the development of resistance especially if the other sites are not known or undiagnosed. For example, a known pulmonary tuberculosis patient with a hidden or undiagnosed nasopharyngeal component will only be given six months of initial pulmonary tuberculosis treatment. Because an extrapulmonary site is involved, nasopharyngeal tuberculosis might need a longer anti-

tuberculosis treatment regimen or additional medications on top of the usual medications for pulmonary tuberculosis. The treatment for such a hypothetical patient may only be enough for the pulmonary involvement but insufficient for the nasopharyngeal disease which may lead to development of drug resistance. Moreover, should nasal endoscopy be recommended to search for nasopharyngeal masses in patients with pulmonary tuberculosis prior to treatment? Further studies are needed in this regard.

There are several limitations of our study. The purely observational and descriptive study design makes it only a preliminary study to generate epidemiological knowledge and local information among Filipinos. The study only involved a database review and it is possible that not all data were available. The study only sought to establish a local picture of nasopharyngeal tuberculosis using the limited data gathered within a tertiary general hospital. Even if it is the National University Hospital, many other regions of the country were not represented by the study population and our findings may not be generalizable to them.

In conclusion, this study suggests a relatively high prevalence rate of nasopharyngeal tuberculosis (11.6%) in patients who have a nasopharyngeal mass. Although nasopharyngeal carcinoma (62.1%) remains to be the most common diagnosis, nasopharyngeal tuberculosis should always be a differential aside from lymphoma (1.8%) when confronted with a mass in the nasopharynx in areas with high tuberculosis endemicity.

ACKNOWLEDGEMENTS

We would like to thank Dr. Cristina C. Arcinue - Gomez for assistance with data collection and initial editing of the manuscript. We would also like to express our gratitude to Dr. Jose Florencio F. Lapeña Jr. for helping us rewrite the manuscript. Lastly, we are also immensely grateful to the nurses of the TB-DOTS office and personnel of the Records Section at the Philippine General Hospital for their time and effort in helping us retrieve the patient records within their respective offices.

REFERENCES

1. Menon K, Bem C, Gouldesbrough D, Strachan DR. A clinical review of 128 cases of head and neck tuberculosis presenting over a 10-year period in Bradford, UK. *J Laryngol Otol*. 2007 Apr;121(4):362-8. DOI: 10.1017/S0022215106002507. PMID: 16923320.
2. Choudhury N, Bruch G, Kothari P, Rao G, Simo R. 4 years' experience of head and neck tuberculosis in a south London hospital. *J R Soc Med*. 2005 June; 98(6): 267–269. DOI: 10.1258/jrsm.98.6.267 PMID: 15928377 PMCID: PMC1142231.
3. Das S, Das D, Bhuyan UT, Saikia N. Head and neck tuberculosis: scenario in a tertiary care hospital of north eastern India. *J Clin Diagn Res* 2016 Jan;10(1): MC04-7. DOI:10.7860/JCDR/2016/17171.7076 PMID: 26894099 PMCID: PMC4740627.
4. Vayisoglu Y, Unal M, Ozcan C, Görür K, Horasan ES, Sevük L. [Lesions of tuberculosis in the head and neck region: a retrospective analysis of 48 cases]. *Kulak Burun Bogaz Ihtis Derg* 2010 Mar-Apr;20(2):57-63. [Turkish] PMID: 20214547.
5. Nieves CS, Onofre RD, Aberin-Roldan FCA, Gutierrez RLC. Nasopharyngeal Tuberculosis in a patient presenting with upper airway obstruction. *Philipp J Otolaryngol Head Neck Surg*. 2010 Jan-Jun;25(1):20-22. DOI: 10.32412/pjohns.v25i1.653.
6. Srivanitchapoom C, Sittitrai P. Nasopharyngeal Tuberculosis: Epidemiology, Mechanism of Infection, Clinical Manifestations, and Management. *Int J Otolaryngol*. 2016; 2016:4817429 DOI: 10.1155/2016/4817429 PMID: 27034677 PMCID: PMC4789561.
7. Kim KS. Primary nasopharyngeal tuberculosis mimicking carcinoma: a potentially false-positive PET/CT finding. *Clin Nucl Med*. 2010 May;35(5):346-8. DOI: 10.1097/RLU.0b013e3181d624ff PMID:20395711.
8. Basal Y, Ermişler B, Eryilmaz A, Ertuğrul B. Two rare cases of head and neck tuberculosis. *BMJ Case Rep*. 2015 Oct 23;2015. DOI: 10.1136/bcr-2015-211897 PMID: 26498669 PMCID: PMC4620213.
9. Richardus RA, Jansen JC, Steens SC, Arend SM. Two immigrants with tuberculosis of the ear, nose, and throat region with skull base and cranial nerve involvement. *Case Rep Med*. 2011; 2011:675807. DOI: 10.1155/2011/675807 PMID: 21541186. PMCID: PMC3085480.
10. Zhang Y, Chen Y, Huang Z, Cai L, Wu J. Nasopharyngeal tuberculosis mimicking nasopharyngeal carcinoma on (18)F-FDG PET/CT in a young patient. *J.Clin Nucl Med*. 2015 Jun;40(6):518-20. DOI: 10.1097/RLU.0000000000000656. PMID: 25546210.
11. Takagi A, Nagayasu F, Sugama Y, Shiraishi S. Primary nasopharyngeal tuberculosis. *Kekkaku*. 2013 May;88(5):485-9. PMID: 23882729.
12. Sithinamsuwan P, Sakulsaengprapha A, Chinvarun Y. Nasopharyngeal tuberculosis: a case report presenting with diplopia. *J Med Assoc Thai*. 2005 Oct;88(10):1442-6. PMID: 16519394.
13. Taş A, Yağiz R, Koçyiğit M, Karasalihoğlu AR. Primary nasopharyngeal tuberculosis. *Kulak Burun Bogaz Ihtis Derg*. 2009 Mar-Apr;19(2):109-11. PMID: 19796011.
14. Kuran G, Sagit M, Saka C, Saka D, Oktay M, Hucumenoglu S, et al. Nasopharyngeal tuberculosis: an unusual cause of nasal obstruction and snoring. *B-ENT*. 2008;4(4):249-51. PMID: 19227032.
15. Prstačić R, Jurlina M, Žižić-Mitrečić M, Janjanin S. Primary nasopharyngeal tuberculosis mimicking exacerbation of chronic rhinosinusitis. *J Laryngol Otol*. 2011 Jul;125(7):747-9. DOI: 10.1017/S0022215110002835 PMID: 21481293.
16. Graff S. [Die bedeutung des epipharynx for die menachlidie pathologie]. *Klin Wochenschr*. 1936; 15:953-7. 11. [German] DOI: 10.1007/BF01777670.
17. Rohwedder JJ. Upper respiratory tract tuberculosis. Sixteen cases in a general hospital. *Ann Intern Med* 1974; 80:708-13. DOI:10.7326/0003-4819-80-6-708. PMID: 4832158.
18. Zalesska-Krecicka M, Krecicki T, Morawska-Kochman M, Mosiniak-Trajnowicz K, Kuliczkowski. [Nasopharyngeal carcinoma coexistent with lymph node tuberculosis, diagnostic difficulties--case report]. *K.Otolaryngol Pol*. 2005;59(4):607-9. [Polish] PMID: 16273871.
19. Cai PQ, Li YZ, Zeng RF, Xu JH, Xie CM, Wu YP, et al. Nasopharyngeal tuberculosis: CT and MRI findings in thirty-six patients. *Eur J Radiol*. 2013 Sep;82(9):e448-54. DOI: 10.1016/j.ejrad.2013.04.015 PMID: 23689055.
20. Jian Y, Liu B, Guo L, Kong S, Su X, Lu C. Pathogeny and treatment of 50 nasopharyngeal tuberculosis cases. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*. 2012 Dec;26(24):1138-40. PMID: 23477122.