

CLINICO-PATHOLOGICAL PATTERN OF NASOPHARYNGEAL CARCINOMA IN ILORIN, NIGERIA

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ABSTRACT

Background: Nasopharyngeal carcinoma is an uncommon tumour in Nigeria but the burden of the disease in terms of morbidity and mortality is very high.

Aim: The aim of the study was to document the clinic-pathological characteristics of nasopharyngeal carcinoma in Ilorin, North central Nigeria.

Materials and Methods: This was a retrospective review of all patients seen in ENT department, University of Ilorin Teaching Hospital with the diagnosis of nasopharyngeal carcinoma between January 1st 1999 and December 31st, 2008. The patient's biodata, clinical presentation and histopathological findings are presented. The histopathological diagnosis was in accordance with the 1991 WHO classification.

Results: A total of 30 patients with histologically confirmed nasopharyngeal carcinoma seen during the study period accounted for 2% of the total cancers recorded in Ilorin cancer registry. There were 20 males and 10 females with a mean age of 48.7 ± 15.9 years. The commonest presenting complaint was cervical lymphadenopathy in 96.7% of patients followed by epistaxis (66.7%) and hearing loss (66.7%). Identifiable risk factors included regular intake of ungutted salted smoked fish (76.7%) and tobacco use (23.3%) with some having both risk factors. Histologically, undifferentiated carcinoma was the commonest (70%) followed by well-differentiated keratinizing squamous cell carcinoma (20%) and differentiated nonkeratinizing squamous cell carcinoma (10%).

Conclusion: Undifferentiated carcinoma was the commonest type of nasopharyngeal carcinoma reported from this study especially among males in the 4th and 5th decades of life. Identifiable risk factors included consumption of ungutted salted smoked fish with tobacco usage.

Early diagnosis with effective referral system and easy access to radiotherapy would improve the survival outcome in patients with the disease.

Key Words: Nasopharynx, Undifferentiated carcinoma, cervical lymphadenopathy, smoked fish.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is an uncommon tumour worldwide with high prevalence rates in South-East Asia and some parts of Middle East and North Africa.¹ NPC shows both racial and geographic variations with the highest incidence rate of 20-50/100,000 person-years in Southern China that decreases towards Northern China.² The world incidence rate has been put at $<1/100,000$ person-years. In the year 2002, NPC was reported as the 23rd most common cancer worldwide with estimated incident rates of 80,000 new cases and over 50,000 estimated deaths during that year.³ In Nigeria, most reports suggest that it was the commonest form of head and neck cancer except in Ilorin where it was the third most common.^{4,6} Although the incidence tend to increase with increasing age, bimodal pattern of distribution has been observed with peak incidence in

late adolescent and another peak in the 5th or 6th decade of life.⁷

Clinical presentation is usually that of epistaxis, nasal obstruction, nasal discharge with occasional bloody drainage and serious otitis media may be among the earliest symptoms.⁸ Other symptoms include difficulty breathing, cervical lymphadenopathy, and cranial nerve involvement.⁹ Presentations by NPC patients are usually advanced and by virtue of the anatomical location of this tumour, curative surgical resection may not be achievable. However, NPC is highly radiosensitive and external beam radiotherapy has been the mainstay of primary treatment even in cases with nodal metastasis.¹⁰ Notable among prognostic factors that dictates treatment outcome is the histological type. According to WHO, nasopharyngeal carcinoma can be classified into three types: keratinizing squamous cell carcinoma (type I) and nonkeratinizing carcinoma

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characterized as differentiated (type II) and undifferentiated (type III).¹¹ In endemic regions of the world, nonkeratinizing carcinoma particularly the undifferentiated type is the commonest type and has also been found to be the most radiosensitive.¹⁰ The purpose of this study is to review the clinico-pathologic characteristics that define NPC presentation among our patients in Ilorin, North central Nigeria.

MATERIALS AND METHODS

This was a retrospective review of all patients seen in the Ear, Nose and Throat (ENT) department, University of Ilorin Teaching Hospital with the diagnosis of nasopharyngeal carcinoma over ten year period 1999-2008 when the department became fully functional. The patient's biodata as well as clinical presentation were retracted from the case notes. The histopathological request cards and the slides were retrieved and reviewed. The histopathological diagnosis consisted of keratinizing squamous cell carcinoma and nonkeratinizing carcinoma and this was classified into three according to the WHO classification.¹¹ The WHO classification consisted of type I (keratinizing squamous cell carcinoma), type II (differentiated nonkeratinizing carcinoma) and type III (undifferentiated nonkeratinizing carcinoma). Cases without histopathological biopsy confirmation were excluded. The data entry was done using SPSS 14 and results were presented in simple frequencies and percentages.

RESULTS

A total of 34 clinically diagnosed cases of nasopharyngeal carcinoma were seen during the study period, however only 30 patients with histopathological diagnosis and complete data formed the basis of our discussion. Over the same period, total cancer recorded in our cancer registry was 1510, thus making NPC to account for approximately 2% of all cases. There were 20 males and 10 females with M:F ratio of 2:1. The age ranged from 23 - 80 with a mean of 48.7 ± 15.9 years. The peak incidence of occurrence was in the 41-50 years age group (29.7%) closely followed by 31-40 years (23.2%).

The duration of symptoms before presentation were found to range from 2 months to 96 months with a mean duration of 14.2 months. However in majority of the patients, presentation was within 2-6 months of onset of symptoms with 6.6% presenting after 24 months. Twenty-three patients (76.7%) admitted regular intake of smoked fish while 7 patients (23.3%) used tobacco in different forms. The commonest symptom was cervical lymphadenopathy in 96.7% while the least common

was seizure observed in 10% of the patients as shown in table 1.0. Based on the WHO classification, type III (undifferentiated carcinoma) was the commonest histological type observed in the study in 70% of the patients. This comprised of the so called "Schmincke's type 3 cases, Regaud's type - 5 cases" and the remaining 13 cases that have overlapping features of these two described entities. Type I (keratinizing SCC) was 20% while the least common was type II (differentiated, nonkeratinizing SCC) seen in 10%. Table 2.

Table 1: Common Clinical Presentation by Patients.

Presentations	Freq (%)	Presentations	Freq (%)
Cervical			
lymph node	29 (96.7)	Otalgia	14 (46.7)
Epistaxis	20 (66.7)	Diplopia	12 (40)
Hearing loss	20 (66.7)	Cranial nerve Palsy	6 (20)
Nasal			
Blockage	19 (63.3)	Seizure	3 (10)

Table 2: WHO Histological Classification of Nasopharyngeal Carcinoma Cases in Ilorin.

WHO Classification types	Histological diagnoses	Frequency	Total (%)
I	Well Differentiated keratinized SCC	7	7 (23.3)
II	Differentiated non-keratinized SCC	2	2 (6.7)
III	Undifferentiated carcinoma	13	21 (70.0)
	Schmincke's Undifferentiated carcinoma	3	
	Regaud's undifferentiated carcinoma	5	
	Total	30	

DISCUSSION

Throughout the world, NPC forms an important component of the head and neck tumours although it is an uncommon cancer worldwide except for the areas of endemicity earlier mentioned.¹ It accounts for approximately 2% of the total reported cancer from Ilorin cancer registry during the study period which is not too different from 1.7% earlier reported in Plateau that fall within the same north-central Nigeria.¹² Notwithstanding this low figure, presentation by most patients (29.7%) at the height of their productivity between 41-50 years has far

reaching implications in terms of their socioeconomic output. The mean age of 48.7 years at presentation is slightly higher compared to figures from earlier reports from different parts of Nigeria where the mean age ranges from 41.1 to 44.4 years.¹²

¹⁴ The peak age incidence among Nigerian patients is about a decade lower when compared to patients from endemic region such as South East Asia.³ The disease tends to affect more males than females in a ratio of 2:1 which is in consonance with what has been reported in the rest of the world.²

Delayed presentation by most patients is worsened by obscured tumour location and lack of access to specialist care. In addition to these, ineffective referral system coupled with cheaper alternative medical care in Nigeria may be critical at determining the mean duration of symptomatology before presentation at specialist clinics which was 14.2 months in our patients. In the vast majority of our patients, cervical adenopathy (96.7%) closely followed by epistaxis (66.7%), hearing loss (66.7%) and nasal blockage (63.3%) were the most common clinical presentations. These are not too different from observations reported in patients from both endemic and non-endemic areas.⁷ Other important but less common symptomatology includes neuro-ophthalmic manifestations - diplopia, cranial nerve palsy and seizures which sometimes may be the sole presentation and as such misleading with resultant delay in treatment.¹⁵ The presentation of neck mass by the patients often times in the form of unilateral cervical lymphadenopathy reinforces the suspicion of metastatic carcinoma through the instrument of cytological diagnosis and or histological biopsy.

Epstein-Barr virus (EBV) has been shown to be an important aetiological factor in the carcinogenesis of NPC.¹⁶ EBV infection is known to infect over 90% of the world population with most infection being latent and subclinical.³ However, in virtually all cases of NPC from endemic region of the world, elevated antibody titres against EBV viral capsid antigen IgA and early antigen, latent viral nuclear antigens 1 and 2 (EBNA-1, EBNA-2) and neutralizing antibodies to EBV-specific DNase have been documented.³ These elevated antibody titres tend to precede tumour development by several years and correlates well with tumour burden, remission and recurrence. Despite the important role played by EBV in the pathogenesis of NPC, only a small percentage of those infected develop the cancer which tend to suggest that other environmental/genetic factors are critical to eventual development of NPC.¹ The other risk factors/modulators identified include salt-preserved food, tobacco and other smokes, occupational exposures, genetic and racial factors.^{1,16} Epidemiological studies have shown that salt preserved foods are a dietary staple in all NPC-

endemic region of the world and this may partly explain the international distribution.^{1,3} The inefficiency of this salt preservation results in putrefaction, accumulation of nitrosamines, bacterial mutagens and EBV-reacting substances all of which could contribute to the observed association. In Nigeria, salt-preservation of food is widely practiced in the absence of regular electricity supplies and this could possibly contribute to the pathogenesis of some of the cases of NPC seen in the country. In addition, 76.7% of our patients relied on smoked fish as source of animal proteins while 23.3% uses tobacco in various ways including smoking. Cigarette smoking was found to be strongly associated with keratinizing squamous cell carcinoma variant of NPC and the recent decline in prevalence of this variant has been attributed to the decline in smoking habit.¹⁷

Apart from the large number of environmental risk factors, genetic susceptibility studies have shown quite a lot of interesting lead that could be further explored. Human leukocyte antigen gene (HLA) studies in both low-incidence and high-incidence populations have identified some high-risk HLA types.^{18,19} Meta-analysis studies in southern Chinese populations identified some alleles such as HLA-A2, B14 and B46 having positive association with NPC while others such as HLA-A11, B13 and B22 showed inverse association.²⁰ Several other genetic studies are still on going but the results are yet to be conclusive.

Although Nigeria is not a high-incidence region, undifferentiated variant of NPC was the most common type reported in this study as well as in other centres across the country.^{12,13} Undifferentiated nonkeratinizing variant (type III) accounted for 21 cases (70%) and it includes Schminke's type - 3 cases, Regaud's type 5 cases and 13 cases with overlapping features of these two entities. Notwithstanding the fact that this variant is the predominant histological type found in children and adolescent, and has the strongest association with EBV infection, none of our patient is adolescent. Other histological variants from the study include well-differentiated keratinizing SCC (type I) seen in 7 cases (23.3%) and differentiated nonkeratinizing SCC (type II) in 2 cases (6.7%). It is significant to note that majority of those who admitted to smoking had well-differentiated keratinizing SCC which agrees with high risk of developing NPC in chronic smokers.¹ Undifferentiated variant tend to respond well to radiotherapy and are less aggressive in behaviour when compared to well-differentiate keratinized SCC that responds poorly and behave in an aggressive manner.²¹

All the studied patients were referred for radiotherapy in another teaching hospital following

diagnosis due to lack of radiotherapy facility in our hospital. Logistics delay in enlisting patients for radiotherapy often times adversely affect the prognosis although most patients came in advanced disease. NPC is common in individuals in their 4th to 5th decades of life with identifiable risk factors of smoked fish and tobacco usage.

Prompt referral to otolaryngologists coupled with high index of suspicion and provision of more radiotherapy units would reduce the morbidity and mortality associated with NPC in these patients.

REFERENCES

1. **Vaughan TL, Shapiro JA, Burt RD, Swanson GM, Berwick M, Lynch CF, Lyon JL.** Nasopharyngeal cancer in a low-risk population: defining risk factors by histological type. *Cancer Epidemiol Biomarkers Prev.* 1996;5:587-93.
2. **Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB, editors.** Cancer incidence in five continents, vol. VIII. IARC scientific publications No. 155. Lyon: IARC; 2002.
3. **Chang ET, Adami HO.** The enigmatic epidemiology of nasopharyngeal carcinoma. *Cancer Epidemiol Biomarkers Prev.* 2006; 15:1765-77.
4. **Ketiku KK, Igbino F, Okeowo PA.** Nasopharyngeal cancer in Nigeria a revisit. *Nig Postgrad Med J.* 1998;5:7-12.
5. **Nwawolo CC, Ajekigbe AT, Oyenehin JO, Nwankwo KC, Okeowo PA.** Pattern of head and neck cancers among Nigerians in Lagos. *West Afr J Med* 2001;20:111-16.
6. **Ologe FE, Adeniji KA, Segun-Busari S.** Clinicopathological study of head and neck cancer in Ilorin, Nigeria. *Tropical Doctor* 2005;35:2-4.
7. **Wei WI, Sham JS.** Nasopharyngeal carcinoma. *Lancet*, 2005; 365:2041-54.
8. **Voke EE, Liebowitz DN, Weichelsbaum RR.** Nasopharyngeal carcinoma. *Lancet* 1997; 350:1087-1103.
9. **Williams S, Williams C.** *Cancer: A guide for patients and their families.* 1986. Hobokon, NJ: John Wiley and Sons.
10. **Khademi B, Mahmoodi J, Omidvari S, Mohammadianpanah M.** Treatment results of Nasopharyngeal carcinoma: A 15-year single institutional experience. *J Egypt Natl Canc Inst.* 2006; 18:147-155.
11. **Shanmugaratnam K, Sobin LH.** eds Histological typing of tumours of the upper respiratory tract and ear. 2nd edn. Berlin: Springer-Verlag:Berlin; 1991:32-33.
12. **Obafunwa JO, Bhatia PL.** Nasopharyngeal carcinoma in Plateau State, Nigeria: a pathological study. *Eur J Surg Oncol.* 1991;17:335-7.
13. **Nwaorgu OG, Ogunbiyi JO.** Nasopharyngeal cancer at the University College Hospital Ibadan Cancer registry: an update. *West Afr J Med.* 2004;23:135-8.
14. **da Lilly-Tariah OB, Somefun AO.** Malignant tumours of the nasopharynx at Jos University Teaching Hospital, Nigeria. *Niger Postgrad Med J.* 2003;10:99-102.
15. **Ogunleye AO, Nwaorgu OG, Adaramola SF.** Ophthalmo-neurologic manifestation of nasopharyngeal carcinoma. *West Afr J Med.* 1999; 18:106-9.
16. **Pathmanathan R, Prasad U, Chandrika G, Sadler R, Flynn K, Raab-Traub N.** Undifferentiated, nonkeratinizing, and squamous cell carcinoma of the nasopharynx. Variants of Epstein-Barr virus-infected neoplasia. *Am J Pathol.* 1996;146:1355-1367.
17. **Tse LA, Yu IT-S, Mang OW-K, Wong S-L.** Incidence rate trends of histological subtypes of nasopharyngeal carcinoma in Hong Kong. *BJC.* 2006;95:1269-1273.
18. **Lu SJ, Day NE, Degos L, Lepage V, Wang PC, Chan SH, Simons M, McKnight B, Easton D, Zeng Y, de-The G.** Linkage of a nasopharyngeal carcinoma susceptibility locus to the ELLA region. *Nature (Lond.)* 1990;346:470-471.
19. **Burt RD, Vaughan TL, Nisperos B, Swanson GM, Berwick M.** A protective association between the HLA-A2 antigen and nasopharyngeal carcinoma in the US Caucasians. *Int J Cancer.* 1994;56:465-467.
20. **Goldsmith DB, West TM, Morton R.** HLA associations with nasopharyngeal carcinoma in Southern Chinese: a meta-analysis. *Clin Otolaryngol.* 2002;27:61-7.
21. **Rivera S, Keryer C, Busson P, Maingon P.** [Nasopharyngeal carcinomas: From biology to clinic] *Cancer Radiother.* 2005;9:55-68.