

A COMPREHENSIVE STUDY ON THE INCIDENCE AND DIAGNOSIS OF NASOPHARYNGEAL CARCINOMA

B Swapna Kumari¹, Y Kavitha², Sanam Divya Goud³, Induri Sreelakshmi⁴, Maloth Devojee⁵, Kavitha Devi Bhukya⁶

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Corresponding Author:

Dr. Kavitha Devi Bhukya

Email: drkavithasam@gmail.com

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^{1,2,3}Assistant Professor, Department of Pathology, Gandhi Medical College, Hyderabad, Telangana, India

^{4,5}Professor, Department of Pathology, Gandhi Medical College, Hyderabad, Telangana, India.

⁶Associate Professor, Department of Pathology, Gandhi Medical College, Hyderabad, Telangana, India.

Abstract

Background: Nasopharyngeal carcinoma (NPC) is an uncommon malignancy arising from the epithelial cells that cover the surface and lines the nasopharynx. The current study aims to examine clinical, histopathological, and Pancytokeratin expression in nasopharyngeal carcinoma. Present study was a retrospective study conducted on surgical biopsies of cases diagnosed as nasopharyngeal carcinoma from January 2013 to December 2019 in a tertiary care center at Gandhi Medical College/Hospital, Hyderabad, Telangana. Demographic and clinical parameters were retrieved from medical records. After being preserved in 10% buffered formalin, specimens underwent tissue processing. The tissue sections were examined under a microscope after routine paraffin embedding and staining in five-micron sections with hematoxylin and eosin. Due to its proximity to the skull base and infiltrating ability, Nasopharyngeal carcinoma presents as an asymptomatic neck mass (metastasis), a disease which poses difficulties in diagnosis and management. NPC is common in males with a higher incidence in 10-30 & 50-70 yrs. Pancytokeratin expression helps to differentiate nasopharyngeal carcinoma from other poorly differentiated nasopharyngeal tumors. **Materials and Methods:** Surgical biopsies of cases diagnosed as Nasopharyngeal carcinomas were included in the study from a period of 2013 to 2018 in a tertiary care center & Clinical parameters were retrieved. Pancytokeratin expression was done on all histologically diagnosed cases of nasopharyngeal carcinoma. **Result:** Maximum number of cases were Non keratinizing undifferentiated carcinomas. All cases showed pancytokeratin positive. **Conclusion:** commonest presentation of NPC is cervical lymphadenopathy. Most of the cases were non keratinizing undifferentiated carcinomas. pancytokeratin expression is used to differentiate Nasopharyngeal carcinomas from other undifferentiated nasopharyngeal tumors.

INTRODUCTION

Nasopharyngeal carcinoma (NPC), which accounts 85% of all nasopharyngeal malignant tumors, is an epithelial cell malignancy that develops on the surface and lining of the nasopharynx. NPC has a distinct worldwide distribution,^[1,2] and is regarded as endemic in southern China, where the incidence is nearly 1550/1,00,000 population, as well as in Indonesia, Malaysia, and South East Asia.^[3] Nasopharyngeal carcinoma manifests as an asymptomatic cervical neck mass, nasal obstruction, epistaxis, otitis media, and other symptoms. Clinical signs and symptoms are nonspecific, which delays diagnosis. The location and the degree of tumor

dissemination are related to the symptoms that nasopharyngeal carcinoma patients present with. Until the disease grows to a serious stage, the early clinical presentation is usually confusing. The post-nasal region is difficult to examine, hence it is challenging to correctly diagnose nasopharyngeal carcinoma for the presence of normal lymphoid epithelium. These factors contribute to a delay in diagnosis.^[4]

Nasopharynx is located just beneath the skull's base and the tumor's potential to infiltrate involves cranial nerve due to its close proximity to the base of the skull.^[5] Nasopharyngeal carcinomas come in three different histological forms: The WHO Classification of Head and Neck Tumors 2017

(4th edition), classified nasopharyngeal carcinoma into keratinized squamous cell carcinomas, non-keratinized, and basaloid squamous cell carcinoma. Additional classifications for the second category include differentiated and undifferentiated carcinomas.^[6] In locations where NPC is endemic, the undifferentiated variety is the most common histological type (> 90%).^[7] Majority of head and neck carcinomas are squamous cell carcinomas, which can be easily diagnosed. Nasopharyngeal carcinoma is one exception to this pattern, with a high proportion of tumors being undifferentiated tumors that can be difficult to separate from other malignancies.

A relevant immunohistochemistry (IHC) panel can frequently corroborate the differential considerations.^[8] Nasopharyngeal samples are often small and significantly distorted by crushed artefacts, resulting in only partially representing the tumor makes identification challenging.^[9] The routine histological examination with immunohistochemistry using monoclonal antibodies can now reliably resolve the diagnostic dilemma of whether a nasopharyngeal carcinoma or a lymphoma, mucosal malignant melanoma, embryonal rhabdomyosarcoma, and its subsequent effect on the patient's treatment and prognosis.^[8,10,11] The current study aims to examine clinical, histopathological, and Pancytokeratin expression in diagnosing nasopharyngeal carcinoma.

MATERIALS AND METHODS

The current research was a retrospective study on surgical biopsies of cases diagnosed as nasopharyngeal carcinoma from January 2013 to December 2019 in a tertiary care center at Gandhi Medical College/Hospital, Hyderabad, Telangana. Institutional Ethical committee clearance was observed from Gandhi medical college with no IEC/GMC/2022/11/10.

Demographic and clinical parameters were retrieved from medical records. After being preserved in 10% buffered formalin, specimens underwent tissue processing. The tissue sections were examined under a microscope after routine paraffin embedding and staining in five-micron sections with hematoxylin and eosin. All cases of Nasopharyngeal carcinomas with microscopic diagnosis underwent immunohistochemical analysis for Pancytokeratin.

RESULTS

The total number of surgical biopsies of the nasopharynx during the study period from January 2013 to December 2019 was 136 cases, and the total number of Nasopharyngeal carcinoma cases was 28. The year-wise incidence of total number of nasopharyngeal biopsies and the incidence of NPC's are mentioned in [Table1].

With an average of 4 cases per year, 28 out of 136 (20.6%) cases were diagnosed with Nasopharyngeal carcinoma during the study session. The highest incidence was observed in 2016, at 29.4%, and the lowest incidence was found in 2017 at 14.3%. When the gender-wise incidence was observed, the NPC incidence was three times higher in males, i.e., 21 (75%), compared to females with 7 (25%) cases, which is 3:1 male-to-female ratio. Age varied from 10 to 70 years, with the highest occurrence seen in the 10 to 20 year age range, at 25%, and the 51 to 60 year age range, at 21.4% [Table 2].

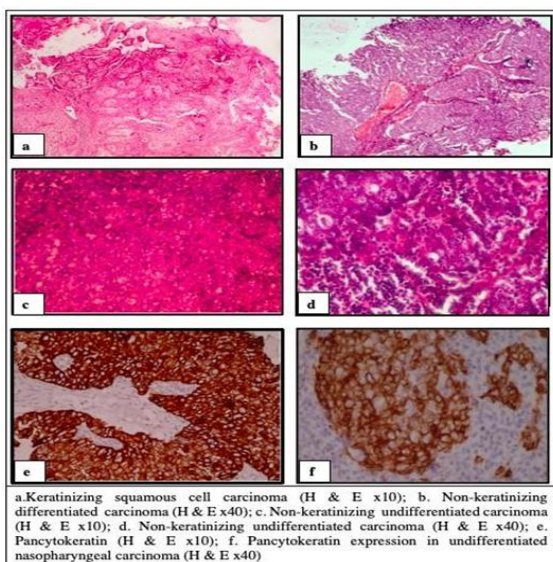
Clinical symptoms

The clinical symptoms or presentation of NPC was found to vary in patients, where the most common clinical presentation was cervical lymphadenopathy observed in 18 patients (64.3%), followed by nasal blockage in 04 cases (14.29%), ear blockage in 03 cases (10.7%) followed by nasal bleeding, ear and squint each was seen in 1 patient (3.6%), which was depicted in [Table3].

Histology

According to WHO classification (2017), nasopharyngeal carcinoma is classified into keratinizing squamous cell carcinoma, non-keratinizing differentiated carcinoma, non-keratinizing undifferentiated carcinoma and basaloid squamous cell carcinoma. The most common histological type in the present study was non-keratinizing undifferentiated carcinoma, with 17 cases (60.7%), followed by keratinizing squamous cell carcinoma in 8 patients (28.57 %). Only 3 (10.7%) Nonkeratinizing differentiated carcinoma were detected. [Table 4]

Among 8 instances of keratinizing squamous cell carcinoma, it was found to be more prevalent in the age group of 51-70 years, representing 6 cases (75%). In 2 cases (66.6%) with non-keratinizing differentiated carcinoma, the age range with the highest prevalence was 31–50 years. Twenty out of 28 cases were non-keratinizing carcinomas with varied prevalence between differentiated and undifferentiated among various age groups. When non-keratinizing undifferentiated carcinoma was analyzed according to the age group in 17 cases, maximum number of cases were seen in childhood and adolescence, with 11 cases (64.75). Typically, elderly adults were found to be prevalent for Keratinizing squamous cell carcinoma. In our study, no cases were diagnosed as basaloid squamous cell carcinoma. [Table 5]



Pancytokeratin

Pancytokeratin expression was done on 28 cases of histologically diagnosed nasopharyngeal carcinoma. Membrane and cytoplasmic staining was considered a positive result. All cases showed cytoplasmic and membrane positivity. Pancytokeratin positivity in non-keratinizing undifferentiated carcinoma of the nasopharynx helped to rule out the Amelanotic melanoma, small round cell tumors like Lymphoma, and Embryonal Rhabdomyosarcoma.

Table 1: Year-wise incidence of nasopharyngeal carcinomas

Year	Total no. of nasopharyngeal biopsies	Total no. Of nasopharyngeal carcinomas	Percentage
2013	22	04	18.2%
2014	24	05	20.8 %
2015	19	04	21.05 %
2016	17	05	29.4 %
2017	21	03	14.3 %
2018	15	04	26.6 %
2019	18	03	16.7 %
Total	136	28	20.6 %

Table 2: Age group distribution in nasopharyngeal carcinoma

Age group (in years)	No. of Patients	Percentage
10-20	07	25 %
21-30	05	17.85%
31-40	02	7.14%
41-50	05	17.85 %
51-60	06	21.4 %
61-70	03	10.71%
Total	28	100%

Table 3: Clinical presentation of Nasopharyngeal carcinoma

Presenting complaints	No. Of cases	Percentage
Cervical lymphadenopathy	18	64.3%
Nasal blockage	04	14.29%
Ear blockage	03	10.7%
Nasal bleeding	01	3.6%
Ear ache	01	3.6%
Squint	01	3.6%
Total	28	100%

Table 4: Histological types of nasopharyngeal carcinoma

Histological type	No. of cases	Percentage
Keratinizing squamous cell carcinoma	08	28.6 %
Non-keratinizing Differentiated	03	10.7 %
Undifferentiated	17	60.7 %
Basaloid squamous cell carcinoma	0	0
Total	28	100%

Table 5: Different types of NPC incidence among age groups

Age group	Keratinizing squamous cell carcinoma	Non-keratinizing differentiated carcinoma	non-keratinizing undifferentiated carcinoma
10-30 yrs	0 (0%)	1 (33.3%)	11 (64.7%)
31- 50 yrs	2 (25%)	2 (66.6%)	3 (17.64%)
51-70 yrs	6 (75%)	0 (0%)	3 (17.64%)
Total	8 (100%)	3 (100%)	17 (100%)

DISCUSSION

Nasopharyngeal carcinoma is different from other head and neck tumors as it affects mostly in younger people and has more chances for developing metastasis.^[10] The nasopharynx is not easily visualized using Fibroscopy or a mirror examination with or without general anesthesia. The Fossa of Rosen Muller is the most probable location for NPC. A cervical neck mass that is asymptomatic, a nasal obstruction, otitis media, and epistaxis are the symptoms of nasopharyngeal carcinoma. As a result of nonspecific symptoms and signs postponing the diagnosis, a clinical presentation at an advanced stage of the disease takes place. The way nasopharyngeal carcinoma shows itself can vary depending on the position of the tumor in relation to the cranial nerves, the base of the skull, the eustachian tube, and the parapharyngeal space. Before the carcinoma crosses the first stage, individuals exhibit very mild symptoms. Near the bottom of the skull, the passageway for the nasopharynx is located. Because of the tumor's proximity to the skull, its capacity for infiltration, NPC may appear as the base of the skull erosion brought on by the tumor's superior expansion, as well as the widespread nature of the symptoms. NPC is thought to have a bad prognosis when cranial nerve involvement and erosion of the skull base are present.^[4]

The origin of NPC is significantly influenced by genetic and regional factors. Both non-keratinizing differentiated and undifferentiated forms of NPC exhibit a high correlation between Epstein-Barr virus (EBV) expression and nasopharyngeal carcinoma. In nasopharyngeal keratinizing squamous carcinomas, human papillomavirus (HPV) has been identified.^[12] Intraepithelial dysplasia or in-situ carcinoma are unusual precursors of carcinoma that are used to identify NPC.

In the present study, the age group was ranging from 10 -70 years. Despite the fact that NPC incidence tends to rise with age, the incidence was found to be maximum in late adolescence and during the fifth or sixth decades by which a bimodal distribution tendency has been observed which is similar to other studies.^[4,13,14] Nasopharyngeal carcinoma usually strikes at two age peaks in North Africa, which is between 10 -20 years old and between 45 - 55 years old. Similarly, 45 - 55 years is the peak age for NPC in Eskimos and Chinese.^[14,15] Further, the ratio of men to women in our study was 3.3:1, which was equal to Van et al.,^[4] and Thompson et al.,^[10]

The majority of the individuals in our study were found to have clinical symptoms with cervical lymphadenopathy (64.3%) which is comparable to Bernadette et al., study^[11] (65%) and Lin et al., (70%).^[16] In our study, nasal blockage (14.29%) and ear blockage (10.7%), nasal bleeding (3.6%), ear

ache (6%), and other neurological symptoms, i.e. Squint (3.6%) were found to be the common symptoms. In Umar et al,^[17] the study showed the other clinical observations were epistaxis (42.1%), nasal complaints (68.4%), audiological symptoms (57.9%), and neurological problems (such as diplopia (47.36%), voice changes, and headaches).

In this study, there were 8 cases of keratinizing squamous cell carcinoma (28.57%) nonkeratinizing differentiated carcinoma was seen in 3 cases (10.7%) and 17 cases (60.7%) of nonkeratinizing undifferentiated carcinoma observed. In our study, non-keratinizing undifferentiated carcinoma was seen in the maximum number of cases which is in line with other studies.^[1,18] Keratinizing squamous cell carcinoma was detected in 8 cases in the present study. Six out of eight cases (or 75%) were observed between the ages of 50 and 70. The monoclonal keratin antibodies (AE1/AE3) have been used in surgical pathology to identify epithelial tumors and have emphasized their diagnostic value in nasopharyngeal carcinoma. The majority of carcinoma types may be recognized by positive staining and the absence of markers associated with other kinds, making a collection of monoclonal antibodies especially useful. Despite epithelial membrane antigen being a reliable epithelial marker in this study, it has been found in small percentage of lymphoid malignancies also, therefore it cannot be utilized solely as an epithelium-specific marker.^[12]

Pancytokeratin was done in all histologically diagnosed nasopharyngeal carcinomas. Pancytokeratin was found to be positive in 28 out of 28 cases (100%). These results are especially pertinent to clinical practice because nasopharyngeal samples tend to be tiny and significantly distorted by crushed artifacts. The ability of these monoclonal antibodies to consistently work in materials that have undergone standard processing is a significant advantage given that the malignant nature of nasopharyngeal biopsies is frequently discovered after the sample has been evaluated after fixation and paraffin embedding. Pathologist can now successfully add immunocytochemistry to the conventional histological examination using such a panel of monoclonal antibodies to differentiate whether a nasopharyngeal tumor is a carcinoma or a lymphoma, embryonal rhabdomyosarcoma, amelanotic melanoma with its consequent impact on the patient's care and perspectives.^[8]

Since it is simple to identify squamous cell carcinomas as the majority of head and neck malignancies, histological identification is not particularly difficult. The nasopharynx is an exception, where most of the tumors are undifferentiated, that can be difficult to differentiate from other neoplasms.^[8] Therefore, Pancytokeratin expression was helpful to confirm the diagnosis of NPC and to differentiate them from lymphoma, embryonal rhabdomyosarcoma and amelanotic melanoma.

CONCLUSION

Nasopharyngeal carcinoma develops from the surface-covering nasopharyngeal mucosa and has light microscopy or ultrastructural features of squamous differentiation. Due to its proximity to the skull base and infiltrating ability, nasopharyngeal carcinoma presents as an asymptomatic cervical lymphadenopathy (metastasis), a disease which poses difficulties in diagnosis and management. NPC was found to be more common in males with a higher incidence in 10-30 & 50-70 yrs. Metastatic cervical lymphadenopathy is the most typical clinical presenting feature. Nasopharyngeal non keratinizing undifferentiated type is most common in young adolescents, whereas nasopharyngeal keratinizing squamous cell carcinoma is predominant in elderly. Squamous cell carcinomas are the most common type of carcinoma of the head and neck area. An exception to this rule is nasopharyngeal carcinoma, where a significant number of tumors are undifferentiated malignancies that can be hard to tell apart from other neoplasms. Pancytokeratin expression helps differentiate nasopharyngeal carcinoma from other poorly differentiated nasopharyngeal tumors.

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