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Eight years of clinical findings and biopsy results of nasopharyngeal pathologies in 1647 adult patients: a retrospective study

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Abstract. *Eight years of clinical findings and biopsy results of nasopharyngeal pathologies in 1647 adult patients: a retrospective study*. *Objectives*: We performed an 8-year retrospective study to evaluate the presentation, clinical findings and nasopharyngeal biopsy results of adult nasopharyngeal pathologies.
Methodology: This study included 1647 patients (801 males and 846 females) admitted to outpatient clinics. All patients underwent a nasopharyngeal biopsy for a nasopharyngeal mass. In addition, a blind biopsy was taken if there was suspicion of nasopharyngeal carcinoma, even in the absence of a mass lesion. The pathological diagnoses were analysed on the basis of the age, sex and clinical presentation of the patients.
Results: Patient age ranged between 18 and 85 years; the mean was 36 years. Patient age differed significantly between those with benign and malignant disease ($p = 0.000$); the risk of malignancy increased with age. Benign disease was found in 97.4% of the patients. Reactive lymphoid hyperplasia was the most common condition; it was found in 92.71% of benign cases. Undifferentiated nasopharyngeal cancer was the most common malignant disease, being found in 82.95% of all nasopharyngeal malignancies and in 4.43% of all nasopharyngeal disease. The most common symptom was nasal obstruction. The other main symptoms were hearing loss and neck mass. Neck mass was associated with malignancy.
Conclusions: Benign disease of the nasopharynx is more common than malignant pathology in patients with a nasopharyngeal mass. Although adenoidal tissue undergoes regression in the adolescent period, this tissue may present as the chief cause of nasal obstruction in adults. Age and symptoms may predict malignant disease.

Introduction

Nasopharyngeal carcinoma (NPC) accounts for fewer than 2% of all head and neck cancers.[1] The nasopharynx (NP) is difficult to study due to its anatomical structure, and malignant diseases emerging from this region are generally asymptomatic, or easily confused with other diseases. Patients with NPC therefore commonly present at an advanced stage and their prognosis is poor. Consequently, an assessment of reasons for admission is important to ensure early diagnosis and reduce mortality and morbidity.[2]

Materials and methods

This retrospective clinical trial was conducted at the Department of Otorhinolaryngology-Head and Neck Surgery from 1 January 2005 to 1 March 2013. In this study, all admitted patients over 18 years of age with nasopharyngeal masses were scheduled for biopsy. In addition, blind biopsies were conducted in patients with conductive hearing loss and neck mass, even in the absence of any lesion. Patients under 18 years of age and those previously diagnosed and treated for nasopharyngeal pathology were excluded. Ear, nose and throat examination was performed in all patients. All patients were evaluated for NPC risk factors (smoking tobacco use, alcohol consumption, professional toxic exposure, EBV infection), allergic rhinitis and infections.

The data retrieved from the medical records included: patient age, sex, presenting symptoms and histopathology results. Symptoms were divided into six groups: nasal obstruction, otalgia, serous otitis media (OME), neck mass, tinnitus and epistaxis. Patients were divided into three age groups: 18-30, 31-50 and 51-85 years (Table 1).

Topical anaesthesia with 2% lidocaine spray was given to all patients. A rigid or fibre-optic endoscope was used to enter from the two meatus inferiors of

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Table 1
The frequency of benign and malignant diseases by age groups

Age range	**Benign**	**Malign**	**Total**
18-30 years	772 49.5%	5 5.7%	777 47.2%
31-50 years	448 28.7%	26 29.5%	474 28.8%
51-85 years	339 21.7%	57 64.8%	396 24.0%
Total	1559 100.0%	88 100.0%	1647 100.0%

Pearson Chi-Square = 98.091 $p<0.001$.

the nose. The nasal cavity was evaluated for the presence of a deviated septum and currents, and to determine the status of the bottom and middle turbinates, nasopharyngeal mucosa, the Eustachian tube opening, Rosenmuller's fossa and the torus tubarius. Direct punch biopsies were taken by endoscopy with forceps in cases with a nasopharyngeal mass. Histopathological examination was performed with routine haematoxylin-eosin (H & E), Periodic Acid Schiff (PAS) and reticulin staining, as necessary. The lesions were classified as benign or malignant. Histologically proven squamous cell carcinoma was classified using the World Health Organization (WHO) classification.

Statistical Analysis

Statistical analyses of the data were conducted using SPSS ver. 17.0. Descriptive statistical methods (mean and standard deviation, SD), as well as Pearson's chi-square test, were used to compare qualitative data. Results were evaluated using a 95% confidence interval (CI), and the level of significance was set at $p<0.05$.

Results

This retrospective analysis included 1647 patients (801 males and 846 females) with a mean age of 36 ± 17.3 years (range 18-85 years). The average age of male patients was 37.3 ± 17.9 years and that of female patients was 34.8 ± 16.7 years. Fifty-two (59.09%) of the patients were found to have an NPC. Of these patients, 43 (58.9%) had a history of smoking; 21 (24.6%) had a history of alcohol consumption, and professional toxic exposure was a feature in 8 (10.9%). Twenty-eight (31.8%) of the patients with carcinoma had no risk factors. 355 (21.5%) of all patients had allergic rhinitis and 231 (14%) had infections.

Of the 1647 patients, 1559 (94.7%) were diagnosed with benign nasopharyngeal pathology and 88 (5.3%) were diagnosed with malignant pathology.

The average age of patients with benign disease (34.8 ± 16.7 years) differed significantly from those with malignant disease (56.6 ± 15.6 years) ($p<0.001$). In an analysis according to age groups, benign pathology was found in 49.5% of the patients aged 18-30 years, whereas malignant pathology was found in 64.8% of the patients aged 51-85 years ($p<0.001$) (Table 1). In an analysis according to the type of pathology, patients with lymphoma had the highest mean age (63 ± 16.3 years) and those with lymphoid hyperplasia had the lowest mean age (34.6 ± 34.6 years).

A significant difference was detected in the incidences of benign and malignant lesions when the data was broken down according to sex ($p=0.01$): the rate of malignant disease was higher in male patients (65.9%).

Of the 1559 benign lesions, 97.94% ($n=1527$) were classified as lymphoid hyperplasia, 0.7% ($n=11$) were granulomatous inflammation, and 1.36% ($n=21$) were other benign lesions (five Thornwald cysts, one angiofibroma, one haemangioma, three squamous papillomas, two actinomyces, eight nasopharyngeal polyps and one inverted papilloma) (Table 2).

Of the 88 cases diagnosed with malignant disease, 83% ($n=73$) were diagnosed as nasopharyngeal cancer, 14.7% ($n=13$) had lymphomas, and 2.3% ($n=2$) were found to have other malignant lesions (one malignant melanoma and one papillary thyroid carcinoma metastasis) (Table 2).

The diagnostic categories for the majority of patients with NPC were WHO type III (73.97%), followed by type II (19.17%) and type I (6.85%) (Table 3).

Table 4 lists all complaints in patients with nasopharyngeal pathologies. Nasal obstruction (61.08%) was the most common, followed by OME (15.36%) and neck mass (12.44%).

Only 12.44% ($n=205$) of patients had a neck mass. Of these, 37.5% ($n=29$) had a unilateral, and 85.85% ($n=176$) a bilateral, cervical lymphadenopathy. No palpable cervical lymph nodes were found in 87.56% ($n=1442$) of patients. A

Table 2
The mean age and standard deviation based on nasopharyngeal pathology

Nasopharyngeal pathology	Mean	Std. Deviation	Std. Error
Lymphoid hyperplasia	34.65	34.65	0.427
Granulomatous inflammation	47.27	11.551	3.483
Nasopharyngeal carcinoma	55.10	15.226	1.782
Lymphoma	63.08	16.363	4.538
Other malign lesions	73.00	11.314	8.000
Other benign lesions	44.95	16.110	3.602

Table 3
Histological types of the nasopharyngeal carcinomas

NPC Histologic Type	N	%
Keratinising squamous cell carcinomas	5	6.85%
Non-keratinising squamous carcinomas	14	19.17%
Undifferentiated carcinomas	54	73.97%
TOTAL	73	100%

statistically significant difference according to histopathological diagnosis was detected in the presence of a palpable neck mass: the incidence of neck mass in patients with malignant disease was higher than in those with benign disease ($p = <0.0001$).

A significant difference according to histopathological diagnosis was detected in patients with nasal obstruction: the incidence of nasal obstruction in benign disease was significantly higher ($p = 0.016$). Nasal obstruction was found in 62.0% of patients with clinical symptoms of lymphoid hyperplasia and in 49.3% of patients with NPCs.

Of the patients with OME, 9.48% ($n = 82$) had unilateral OME and 90.52% ($n = 171$) had bilateral OME. Of the 253 patients with OME-dependent hearing loss, 241 patients had benign disease and 12 had malignant disease. Of the malignant cases, nine had unilateral, and three bilateral, OME. No significant difference was found in the incidence of benign or malignant disease according to OME status ($p = 0.645$).

No significant difference was detected in terms of the histopathological diagnosis of patients admitted to the clinic with complaints of otalgia, tinnitus or epistaxis. These complaints were not significant in the differential diagnosis of benign and malignant disease ($p > 0.05$).

Discussion

Nasopharyngeal masses are of major concern – particularly in adults – because the risk of malignancy increases with age. A mass filling the nasal cavity and NP may be caused by a common disease (such as adenoid vegetation), infection (such as tuberculosis, cytomegalovirus limited to the NP, or AIDS) or a malignancy. The common causes of adenoid hypertrophy in adults are chronic infection and allergy. Pollution and smoking are also important predisposing factors. Biswas *et al*.[3] reported a 15:1 ratio of benign:malignant nasopharyngeal masses in their study of 30 cases; this compares to 18:1 in our study. However, the age groups were dissimilar: their study included adults and children, whereas we included only adults. Reports of nasopharyngeal lymphoid tissue hypertrophy are becoming more common. In accordance with other reports of nasopharyngeal masses, most patients in our study had lymphoid hyperplasia, and only 5.3% had malignant masses. Age is important in assessing nasopharyngeal masses. Adenoid hypertrophy in adults is rare. The adenoid increases in size up to the age of 6 years, then slowly atrophies and completely disappears at the age of 16 years. Malignant diseases emerge later in life but benign masses are typically identified at a younger age. In our study, the mean age of patients with benign disease was 34.8 ± 16.7 years, while that of patients with malignant disease was 56.6 ± 15.6 years; this difference was significant ($p < 0.001$).

When categorised by age, 49.5% of patients in the 18-30 age group had benign pathology, whereas 64.8% of those in the 51-85 age group had malignant disease ($p = 0.000$).

The sex of patients with nasopharyngeal mass is important. We detected a significant difference

Table 4
The frequency of pathological results according to presenting symptoms

Presenting complaint		Nasal Obstruction	Otalgia	OME	Neck Mass	Tinnitus	Epistaxis	Total
Benign	**Lymphoid hyperplasia**	946 62.0%	104 6.8%	234 15.3%	172 11.3%	57 3.7%	14 0.9%	1527 100.0%
	Granulomatous inflammation	7 63.6%	1 9.1%	1 9.1%	2 18.2%	0 0.0%	0 0.0%	11 100.0%
	Other benign lesions	10 47.6%	0 0.0%	6 28.6%	5 23.8%	0 0.0%	0 0.0%	21 100.0%
	Total	963 61.8%	105 6.7%	241 15.5%	179 11.5%	57 3.7%	14 0.9%	1559 100.0%
Malign	**Nasopharyngeal carcinoma**	36 49.3%	5 6.8%	10 13.7%	21 28.8%	1 1.4%	0 0.0%	73 100.0%
	Lymphoma	6 46.2%	1 7.7%	2 15.4%	4 30.8%	0 0.0%	0 0.0%	13 100.0%
	Other malign lesions	1 50.0%	0 0.0%	0 0.0%	1 50.0%	0 0.0%	0 0.0%	2 100.0%
	Total	43 48.9%	6 6.8%	12 13.6%	26 29.5%	1 1.1%	0 0.0%	88 100.0%

between the rates of benign and malignant lesions according to patient sex ($p=0.01$); malignant disease was more common (65.9%) in male patients.

Patients with nasopharyngeal masses present with various symptoms, including nasal obstruction, neck mass, OME, otalgia, epistaxis, and tinnitus. The medical history and symptoms of the patient must therefore be evaluated. In our study, nasal obstruction (61.08%) was the most common complaint, followed by OME (15.36%) and neck mass (12.44%). The incidence of nasal obstruction in benign disease was significantly higher ($p=0.016$). Stern *et al*.[4] stated that hearing loss may be associated with benign disease. Glynn *et al*.[1] reported that the presence of nasopharyngeal masses and OME was associated with malignancy; the authors cautioned that nasopharyngeal mass should be suspected in a patient complaining of hearing loss. However, whereas the incidence of benign neck mass was significantly higher than that of malignant neck mass ($p=0.000$) in our study, there was no significant difference between benign and malignant disease corresponding to OME status ($p=0.645$). In this study, 9.48% (n=82) had unilateral OME, and 90.52% (n=171) had bilateral OME. Of the 253 patients with hearing loss due to otitis media, 241 had benign and 12 had malignant disease. In these patients with malignant disease, nine had unilateral OME and three bilateral OME.

No significant difference was detected in the histopathological diagnosis of patients admitted to the clinic with complaints of otalgia, epistaxis and tinnitus ($p>0.05$). Symptoms are often similar in nasopharyngeal pathologies, and delays in diagnosis may be due to the lack of specific symptoms. However, because of the higher success rate for the treatment of early-stage disease, early diagnosis is vital. A detailed history, clinical examination and, most importantly, a detailed histopathological examination is essential for accurate diagnosis and timely treatment. Biopsy is important for the diagnosis of both the primary tumour and any post-treatment residual tumour or tumour recurrence.[5] Modern endoscopic methods, advanced imaging techniques and computed tomography (CT) and/or magnetic resonance imaging facilitate the examination of this region and reduce the probability of diagnostic error.[6]

The final diagnosis of NPC is made by biopsy with endoscopic and radiological visualisation. In the presence of adenoid hypertrophy in adults, differential diagnosis of NPC is mandatory. The tumour is often submucosal and biopsy specimens must therefore include both mucosa and submucosa.[7] For this reason, more than one biopsy with a diameter of 2-3 mm is important for diagnosis.[8] In general, bilateral OME suggests adenoid vegetation. However, when OME is unilateral, NPC should be suspected.[2] Endoscopic examination makes it

easier to distinguish between these possibilities. Endoscopy will generally show adenoid hypertrophy as a vegetative mass, whereas NPC will be ulcerated and necrotic.[9] Additionally, CT scans showing the asymmetric thickening of the soft tissue of NP suggest carcinoma, whereas symmetric thickening suggests adenoid vegetation.[10] In the literature, suspicious lymphoid hyperplasia biopsy has been reported many times as NPC.[7]

Adenoid tissue atrophies during adolescence, and the cause of a nasal obstruction is rarely identified in young adults.[7] The presence of lymphoid hyperplasia in the adult nasopharynx, including the persistence of childhood adenoids, is associated with chronic inflammation. Regressed adenoidal tissue may re-proliferate in response to infections and irritans. Epistaxis was seen in benign NP disease in our study at low rates because it was associated with infections and allergic rhinitis generally. Kapusuz *et al*.[11] assessed CT scans from 525 patients with nasal congestion retrospectively and reported that a prevalence rate for adenoid hypertrophy of 26.28%. Hamdan *et al*.[12] reported a 63.6% prevalence rate for adenoid vegetation in the group with nasal obstruction compared to 55.1% in the control group. In our study, the most common symptom was nasal obstruction. A high percentage (97.9%) of lymphoid hyperplasia manifested as nasal obstruction.

Nasopharyngeal tumours can be non-cancerous (benign) or cancerous (malignant). Non-cancerous nasopharyngeal growths are rare and tend to occur in children and young adults. They include tumours or malformations of the vascular (blood-carrying) system, such as angiofibromas and haemangiomas, and benign tumours in minor salivary glands within the NP. In our study, histopathological diagnosis identified only one patient with an angiofibroma and one patient with a haemangioma.

Nasopharyngeal cancer is common among Asians, particularly Chinese. Exposure to salted fish at an earlier age has been shown to be associated with a high risk for NPC in Southern Chinese. Other risk factors include smoking, drinking large amounts of alcohol and occupational exposure to formaldehyde and wood dust.[13] The prevalence of risk factors in the NPC patients [see above] in our study was as follows: tobacco use was seen in 43 (58.90%) cases; alcohol consumption in 21 (24.65%) cases and professional toxic exposure in 8 (10.95%) cases;

NPC is seen most often between the ages of 40-55 years but it also occurs in adolescents. In our study, approximately half of the patients with NPC were over 50 years of age, and the patients were predominantly male. A sex-related tendency is evident: NPC is 2-3 times more common in males than in females.[13] Several types of cancers can develop from the tissues that comprise the NP.[8] Most NPCs are squamous cell carcinomas. Other types of NPCs are more rare and include adenocarcinomas, adenoid cystic carcinomas, lymphomas, melanomas and sarcomas.[14-16] In 1978, NPCs were broken down into three histological categories by the WHO: type I included the typical keratinising squamous cell carcinomas, type II included non-keratinising squamous carcinomas and type III comprised the undifferentiated carcinomas.[17] The type III non-keratinising undifferentiated form is the most common, and is most strongly associated with Epstein-Barr virus infection.[18] The most common form found here was type III. Johannsson *et al*.[19] evaluated malignant nasopharyngeal pathologies over a period of 26 years; NPC was found to be the most common malignant disease (82%), followed by plasmacytoma (4%), lymphoma (3%) and rhabdomyosarcoma (1%). Hopping *et al*.[2] found that NPC was the most common malignancy, followed by lymphoma, which is in keeping with the findings of this study. Common benign conditions included chronic inflammation, lymphoid hyperplasia, Thornwaldt cyst, mucus retention cyst, choanal polyp and normal mucosa. Notably, we found that reactive lymphoid hyperplasia – the most common condition – accounted for 92.71% of all nasopharyngeal disease. Additionally, 97.4% of all nasopharyngeal disease was benign, and NPC was the most common malignant disease (82.95% of all malignant disease and 4.43% of all nasopharyngeal disease), followed by lymphoma.

Conclusion

Benign disease of the NP is more common than malignant pathology. NPC remains the most common malignant disease of the NP. Reactive lymphoid hyperplasia is the most common benign condition. Although adenoidal tissue undergoes regression during adolescence, this tissue may present as the chief cause of nasal obstruction in adults. In the presence of a nasopharyngeal mass,

biopsy should be performed. The symptoms and the macroscopic appearance of nasopharyngeal masses could indicate whether the mass is benign or malignant and if a biopsy is warranted. Early detection is important for accurate diagnosis, and the early and appropriate treatment, of nasopharyngeal pathologies.

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