

Ten years of experience in clinicopathologic characteristics, treatment and outcome of patients with nasopharyngeal pathologies in Yazd, IranFariba Binesh¹, Ahmad Shajari², Somayeh Abdollahi³, Nasim Behniafard⁴

¹ M.D. of Pathology, Professor, Department of Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

² M.D. of Pediatric Nephrology, Assistant Professor, Department of Pediatrics, Yazd Branch, Islamic Azad University, Yazd, Iran

³ General Practitioner, Yazd, Iran

⁴ M.D., General Practitioner, Otorhinolaryngology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

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Abstract

Introduction: Although there are some studies regarding the clinical characteristics and outcome of nasopharyngeal tumors, one such study from Iran has not been reported to date. This study aimed to evaluate the clinical features, treatment, and consequences of nasopharyngeal lesions.

Methods: In this cross sectional study, we conducted a retrospective review of patients who were diagnosed with nasopharyngeal pathologies and treated at Shahid Sadoughi Hospital and Shahid Ramazanzadeh Radiotherapy Center in Yazd, Iran, over a period of 10 years (from 2005 to 2014). The variables in the study were the patient's hospital registration number, date, name, age, gender, address, topography, clinical symptoms, morphology, stage, types of treatment, and survival for each subject. Survival data were analyzed using Kaplan-Meier estimates, and multivariate analysis was performed using the Cox regression method. Statistical analyses were performed using IBM-SPSS, version 22.

Results: In the study, there were 123 patients, 85 males and 38 females, who had nasopharyngeal lesions. The mean age at diagnosis was 41.51 ± 20.33 years. There were 83 patients with malignant neoplasms and 40 patients with non-malignant lesions. The most common malignant tumor was nasopharyngeal carcinoma, and the most common benign lesion was angiofibroma. Survival analysis was performed for the 83 patients who had malignant neoplasms, and survival was found to be 94.5 ± 4.32 months. There were significant differences in survival based on the stage of the disease, histological type, and the type of treatment ($p = 0.001, 0.02, \text{ and } 0.003$, respectively).

Conclusion: In our institutional study, malignant tumors were more common than benign lesions. Patients with nasopharyngeal carcinoma presented relatively late and at an advanced stage. Regular follow-up is necessary for early detection, recurrence, or metastases of malignant tumors.

Keywords: Nasopharynx, Mass, Clinicopathology, Survival, Outcome

1. Introduction

Nasopharynx is the part of the pharynx that lies behind the nasal cavity and above the soft palate. It has anterior, posterior, and lateral walls (1). Masses in the nasopharynx form a heterogeneous group of lesions with a broad spectrum of histopathological features. In other words, a variety of benign and malignant pathologies can be seen in this anatomical area. The nasopharynx is not easily available, and the initial presentation of nasopharyngeal lesions varies widely, with malignant lesions rarely remaining localized to the nasopharynx. Neck mass, nasal obstruction, epistaxis, and diplopia are the common presenting symptoms. Although the presenting aspect and advanced imaging methods help in reaching an assumptive diagnosis, histopathological examination remains the mainstay of

Corresponding author:

Dr Nasim Behniafard, Otorhinolaryngology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Tel: +98.353183368, Fax: +98.3538224100, Email: nbehniafard@gmail.com

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determining the final diagnosis. Thus, a careful histological workup is essential for a correct diagnosis and proper intervention. The absence of differentiation of benign and malignant lesions at initial exhibition leads to significant lag in the initial diagnosis and therapy. As one reviews the literature, it is clear that there are some studies regarding the clinical features, treatment, and outcome of nasopharyngeal tumors (2-4). Our pathology ward is a referral center in Yazd Province and also for the south and southeast areas of the country. As a result, although this study is an institutional base research, it has epidemiological value. As stated earlier, it is important to know the range of non-neoplastic lesions in this region and to differentiate them from neoplastic lesions. However, to the best of our knowledge, no definitive study on clinico-pathology and outcome of nasopharyngeal lesions from this region of Iran has been reported to date. So, the aim of this study was to define the ascertained clinicopathological features and treatment results of these lesions in a major tertiary care hospital located in central Iran.

2. Material and Methods

2.1. Research design and setting

In this cross sectional, retrospective project, the medical records of the patients from 2005 to 2014 were reviewed at Shahid Sadoughi Hospital and Shahid Ramazanzadeh Radiotherapy Center in Yazd, Iran. The medical charts of all patients diagnosed with nasopharyngeal lesions treated were retrieved.

2.2. Instruments and data collection

Sampling was done by taking a census. As study variables, we recorded the patient's hospital registration number; date of admission; and personal information, including age, gender, address, anatomical site, clinical complaint, histological diagnosis, stage of disease, therapeutic approach, and survival. The data were obtained via the patients' records and by phone. We should add that histopathological diagnosis was based on Hematoxylin & Eosin-stained slides, and the immunohistochemistry (IHC) method was used in cases in which it was necessary.

2.3. Ethics of research

This work was conducted in accordance with the Declaration of Helsinki (2000). This study was approved by the Ethics Committee of Islamic Azad University of Medical Sciences, central Yazd branch (Ref No.: 10510101921015, June 2014), after which the forms for recording demographic data were completed.

2.4. Statistical analyses

Overall survival (OS) was calculated from date of diagnosis until death or the date of the last follow-up. The patients were staged according to the tumor, node, and metastasis (TNM) staging system. Cases without histopathological biopsy confirmation were excluded. Survival data were analyzed using Kaplan-Meier estimates, and multivariate analysis was performed using the Cox regression method. A p-value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM® SPSS® Statistics, version 22 (IBM® Corp., Armonk, NY, USA).

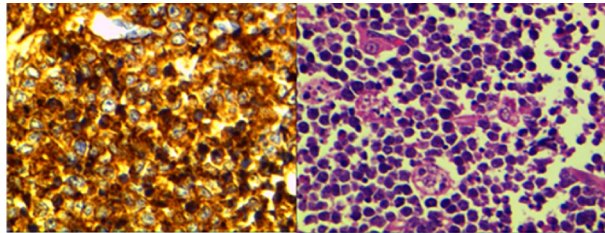
3. Results

We reviewed the records of approximately 110,000 patients who were referred to the Shahid Sadoughi Pathology Department in Yazd, Iran, over a 10-year period. There were 123 patients with nasopharyngeal lesions. The ages of the patients ranged from 45 days to 85 years. The mean age of the patients was 41.5 ± 20.33 years. There were 85 males and 38 females (M:F ratio = 2.2:1). Of the 123 cases, there were 83 patients with malignant neoplasms and 40 patients with non-malignant lesions. The frequencies of the different types of lesions and presenting symptoms are listed in Table 1. The most common malignant tumor was nasopharyngeal carcinoma, and the most common benign lesion was angiofibroma (Figure 1). The most common presenting symptoms were neck swelling (36.6%) hearing loss (33.3%), nasal obstruction (30.1%), and epistaxis (23.6%). Among the patients, 9.5% were in stage I, 28.6% were in stage II, 40.5% were in stage III, and 21.4% were in stage IV. On initial diagnosis, 24.4% of the patients underwent surgery alone, while 3.3% of the patients received chemotherapy alone, 0.8% received radiotherapy alone, and 0.85% received both chemotherapy and surgery. Among the patients, 47.2% received both chemotherapy and radiotherapy, and 15.4% received a combination of radiotherapy, chemotherapy, and surgery. Some of the patients, i.e., 8.1%, elected to have no treatment at all. The most common type of treatment in malignant tumor was combined chemotherapy and radiotherapy, while surgery was the most common therapeutic modality for benign lesions. At the end of the study, 99 patients were alive. There were 22 deaths due to malignant tumor and two deaths due to unrelated causes. The average survival for our patients was 94.5 ± 4.32 months (95% CI: 86.03-102.97 months). Figure 2 shows that, during the period from 0 to 85 months, the OS had decreased and then was constant. According to this study, most patients who were diagnosed with nasopharyngeal lesions were referred to the center

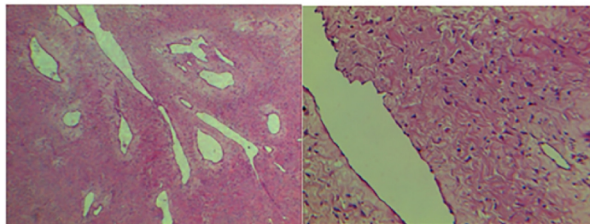
in 2009, 2012, and 2013. Male patients had a lower OS rate than female patients, although this difference failed to reach statistical significance ($p = 0.38$).

Table 1. Frequency of different types of lesions according to histology and the presenting symptoms

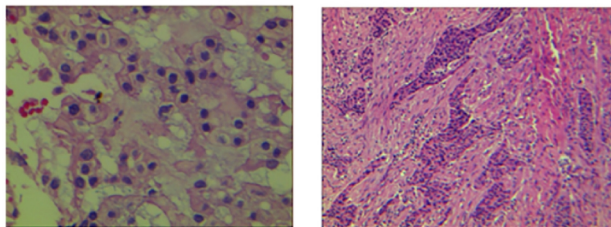
Variables		n	%
Diagnosis	Nasopharyngeal carcinoma	69	56
	Chordoma	2	1.6
	Adenoid cystic carcinoma	1	0.8
	Malignant lymphoma	8	6.5
	Osteosarcoma	1	0.8
	Neuroblastoma	1	0.8
	Lymphoid hyperplasia	10	8.1
	Angiofibroma	16	13
	Polyp	1	0.8
	Inflammation	9	7.3
	Cyst	2	1.6
	Teratoma	2	1.6
	Dysplasia	1	0.8
	Symptoms	Cervical mass	45
Epistaxis		29	23.6
Nasal obstruction		37	30.1
Hearing loss		41	33.3
Cranial nerve palsy		5	4.1
Anosmia		6	4.9
Headache		17	13.8
Diplopia		5	4.1
Other symptoms		22	17.9



Malignant lymphoma CD20 (IHC Stain) & (H&E Stain)



Angiofibroma (H&E Stain)



Chordoma (H&E Stain)

Nasopharyngeal Carcinoma

Figure 1. Microscopic features related to some of the types of lesions

Younger patients (ages 0-29) survived longer than the older patients (age > 50). However, this difference was not statistically significant ($p = 0.28$). Survival was worse in patients who presented with a cervical mass, hearing loss, and without nasal obstruction, but, again, the differences failed to reach statistical significance ($p = 0.33, 0.95,$ and $0.013,$ respectively). The best OS was observed in patients with benign lesions (all of them were alive), lower stages (stage II), and those who underwent surgery alone ($p = 0.001, 0.02,$ and $0.003,$ respectively) (Figure 3). There was an association between age and epistaxis (more common in younger patients), nasal obstruction (more common in younger patients), and hearing loss (observed more often in older patients) ($p = 0.00, 0.018,$ and $0.026,$ respectively). In addition, we noted an association between the type of tumor and the frequency of a mass in the neck (more common in malignant tumor), epistaxis (observed more often in benign lesions), and hearing loss (more common in malignant tumors) ($p = 0.00, 0.001,$ and $0.07,$ respectively).

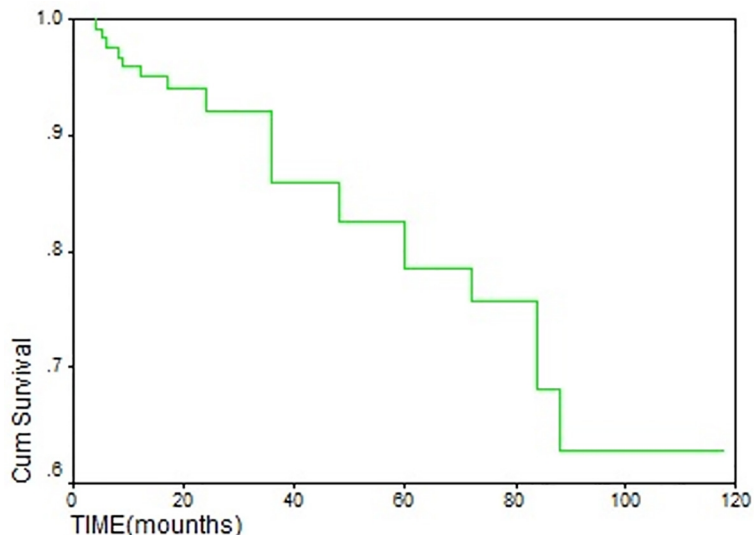


Figure 2. Overall survival of patients with nasopharyngeal tumors

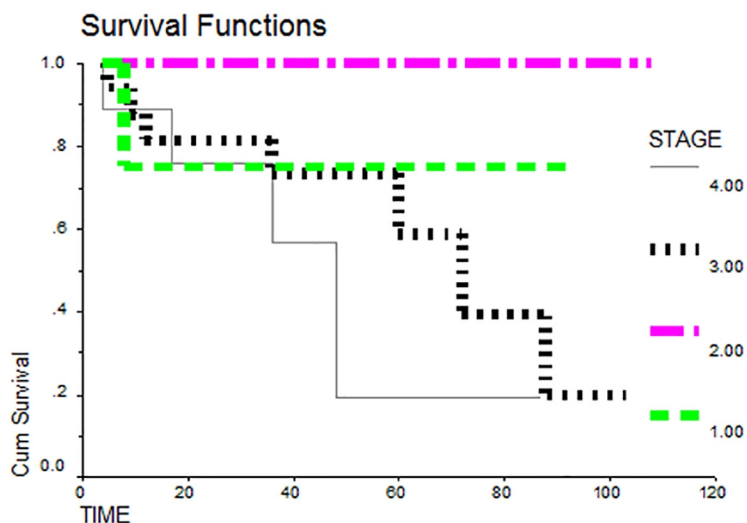


Figure 3. Overall survival according to stage

4. Discussion

Nasopharyngeal masses in adults present a bewildering problem because of the fear of malignancy. The purpose of this study was to analyze the clinicopathological pattern and survival of patients who had nasopharyngeal lesions in Yazd, Iran. The mean age of the patients at the time of diagnosis was 41.51 ± 20.33 years. The peak age of presentation was different in various studies. For example, in Tondon's study, a younger peak age of presentation was recorded (20-29) than in our study (5). In another study, the mean age of the patients was 26.8. Patients' ages

ranged from 18 to 85 in Berkiten's study (2). The age range in one recent study was similar to that in our study (less than 1 to 76) (3). In the present study, there were 85 males and 38 females. In Khan's study, presentations among males outnumbered those among females by 2.3 to 1 (6). In another study, these masses had predilection for males with a male to female ratio of 1.98:1, similar to a study by Zafar et al. (3, 4). However, a Nigerian study and a study in Nepal indicated female preponderance (7, 8). In our study, the common presentation of nasopharyngeal masses were neck swelling (36.6%), aural difficulties (33.3%), nasal obstruction (30.1%), and epistaxis (23.6%), which was in agreement with other studies (2, 7). Mention should be made that serous otitis media resulting in deafness is an accepted index of nasopharyngeal obstruction, and the possibility of a nasopharyngeal malignancy must be considered in patients, especially adults. Careful evaluation under anesthesia and biopsy of the nasopharynx is routinely undertaken in many centers to rule out nasopharyngeal malignancy in these patients. In one study (9), 4.7% of the adults with conductive hearing loss secondary to serous otitis media were found to have a malignancy on nasopharyngeal biopsy. Thus, these authors suggested a high index of suspicion of a nasopharyngeal malignancy in adults presenting with serous otitis media. In the current study, there were 83 patients with malignant neoplasms and 40 patients with non-malignant lesions. However, in one study, non-neoplastic lesions made up 81.6% of the total cases of nasal cavity, paranasal sinuses, and nasopharynx (3). Similarly, a high portion of non-neoplastic lesions also was noted in the study by Zafar et al. (4), showing 89% of non-neoplastic lesions. In another research, benign disease was detected in 97.4% of the cases (2). In addition, in one research, the histology of nasopharyngeal masses of HIV positive and HIV negative patients were compared. Most nasopharyngeal masses in HIV positive patients were benign. Malignancies were significantly more common in the HIV negative group than in the HIV positive group (10). On the contrary, Maruyama et al. (11) believed that most tumors that occur in the nasopharynx are malignant, which was in concordance with our results. We encountered only one case of osteosarcoma and adenoid cystic carcinoma and two cases of chordoma, which are uncommon tumors. In the present study, eight cases of non-Hodgkin's lymphoma were reported, accounting for 6.5% of all of the tumors, confirmed by IHC. Olfactory neuroblastoma is a rare neuroectodermal tumor that arises from the olfactory sensory epithelium in the upper nose. We found a single case of olfactory neuroblastoma, in agreement with Parajuli et al. (8). Fibroma, neurofibroma, and papilloma are the most commonly encountered benign tumors in the nasopharynx. This was not true in the present study. In our study, the most common benign lesion was angiofibroma. Juvenile nasopharyngeal angiofibroma is the most common benign tumor of the nasopharynx (12). It makes up less than 1% of all nasopharyngeal tumors. The tumors peak in the second decade of life, and they are observed more commonly in male adolescents (12). In Dinesh Garq's study (3), most of nasopharyngeal masses were of adenotonsillar hypertrophy, in disagreement with Biswas et al. (13), who found that antrochoanal polyp to be the most common nasopharyngeal masses. In another study (2), reactive lymphoid hyperplasia was the most common lesion; it was detected in 92.71% of benign cases. In Khan's study, the histopathological examination of 240 cases presenting with a mass in the nasal cavity, para-nasal sinuses, and nasopharynx indicated that there were 144 cases (60%) of tumor-like lesions, and tumors constituted 96 cases (40%). Of 56 cases of benign masses, the most common type was angiofibroma, followed by inverted papilloma (6). In another study, non-tumoral nasopharyngeal lesions were more common than neoplastic masses (94.6% versus 5.4%) (3). The majority of these were of adenotonsillar hypertrophy (3). We observed nine cases of non-specific inflammation, but there were no cases of tuberculosis or fungal infection. However, Zafar (4) reported six cases of TB or fungal infection. This difference might be due to higher prevalence of tuberculosis in some parts of the world. In the current study, the most common malignant tumor was nasopharyngeal carcinoma. It is said that squamous cell carcinoma is the most common type of nasopharyngeal tumors. Non-Hodgkins lymphoma is ranked second. Other epithelial tumors, such as adenocarcinoma and cylindroma, are uncommon. Rhabdomyosarcoma is the most prevalent nasopharyngeal malignancy in children (14). Nasopharyngeal carcinoma has a propensity to affect relatively young people; the loss of working life due to nasopharyngeal carcinoma is serious. The geographical differences in its incidence and mortality are indicative of the universal differences in the prevalence of risk factors. Genetic vigilance, early-age exposure to some carcinogens, and latent EBV infection are suggested to be three major etiological factors (15). In one research, undifferentiated nasopharyngeal cancer was the most common malignant disease, being diagnosed in 82.95% of all nasopharyngeal malignancies and in 4.43% of all nasopharyngeal lesions (2). The study conducted by Khan et al. (6) included 40 malignant cases, and the most common lesion was squamous cell carcinoma, followed by nasopharyngeal carcinoma. Among our patients, 9.5% were in stage I, 28.6% in stage II, 40.5% in stage III, and 21.4% in stage IV. The nasopharynx is not easily attainable, and, at the time of diagnosis, the disease is in an advanced stage. Commonly, patients present with advanced disease that has metastasized to the lymph nodes in the neck. Therefore, there is an obvious need for early diagnosis and treatment method to reduce the fatality of nasopharyngeal carcinoma. Screening could be used to diagnose precancerous lesions and also early invasive cancers. Abdullah et al. (16) reported the feasible agents of late presentation of nasopharyngeal carcinoma include

lag in searching medical consultation, perplexing character of presenting symptoms, bothersome nature of clinical evaluation, and quiet spread of the tumor. Surgical excision is the principal manner of treatment in most of non-neoplastic and benign neoplastic lesions and wide surgical cutting, radiotherapy or chemotherapy in malignant tumors. Since complete surgical excision is impossible owing to close vicinity to base of skull, radiation therapy has been the principal method of treatment, and chemoradiation is the preferable procedure for advanced stages. In our study, the most common type of treatment in malignant tumor was combined chemotherapy and radiotherapy, and surgery was the most common therapeutic modality that was applied in benign lesions. The average survival for our patients was 94.5 ± 4.32 months (95% CI: 86.03-102.97 months). The median survival time of nasopharyngeal carcinoma varies between 12.9 and 26.8 months (17, 18). But a variable survival outcome is frequently discovered in clinical practice. The overall survival in a study conducted in Malaysia was 31.30 months (19), and the reasons for different survivals in patients with nasopharyngeal carcinoma in different studies are described diversely (20). It seems that different therapeutic approaches, heterogeneous environmental and genetic risk factors, and the dynamic nature of the applied staging system are effective. Among these, the advanced stage of the disease at the time of diagnosis is an important cause of lower survival in much of the research. In a study conducted by Chee EePhua et al. (21), it was shown that patients in stage I had the best survival (81.8%) and those in stage IV had the worst (25.9%). Treatment modalities are very important. Radiation therapy has been the mainstay of treatment, and chemoradiation is the preferred method for advanced stages. Although in the current study, stage III was the most common stage, the relatively high survival in our patients might be due to the higher number of patients in our study who received concurrent chemo-radiation compared to other studies. In the current study, survival was worse in patients presenting with cervical mass, hearing loss, and without nasal obstruction. In addition, we noted an association between the type of tumor and the frequency of neck mass (more common in malignant tumor), epistaxis (more seen in benign lesions), and hearing loss (more common in malignant tumors). Our study and other similar studies showed that complete clinical and histopathological connection helps the physician to classify the nasopharyngeal lesions into various non-neoplastic and neoplastic types. But final histopathological examination provides a definitive diagnosis. Our experience suggests that hearing loss or cervical mass are uncommon in patients with benign nasopharyngeal lesions and medical practitioners should be vigilant concerning the possibility of malignancy.

5. Conclusions

Malignant diseases of the nasopharynx were more common than benign pathology in our patients with a nasopharyngeal mass. Age and symptoms may predict malignant disease. Regular follow up is necessary for early detection, recurrence, or metastases of malignant tumors. In the presence of clinician-based competence and despite the technical limitations in Iran, malignant nasopharyngeal tumors are being treated optimally with the need for development of a better knowledge among the public concerning the importance of the early diagnosis of malignant tumors.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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