


Nasopharyngeal masses in adults—A retrospective analysis of 255 patients to evaluate symptoms, clinical findings, and histological results

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Abstract

Background: Nasopharyngeal tissue hyperplasia is generally associated with adenoids in childhood. In adults, nasopharyngeal masses are occasionally found, but data on symptoms, clinical findings, and histologic results are limited.

Material and Methods: A 10-year retrospective study was conducted, analyzing data from adult patients who underwent nasopharyngeal biopsies. The study included information on case history, preoperative suspected diagnosis, and histology type. Statistical analysis was performed.

Results: Two hundred and fifty-five patients were included, most of them complaining of nasal obstruction, ear pressure, and hearing loss. Biopsy revealed adenoid tissue (64.7%), solid malignancies (15.7%; dominant undifferentiated carcinoma), lymphomas (9.0%), cysts (7.8%), and other benign tumors (2.7%). Malignant neoplasms were predominantly found in male and in elderly patients ($P < 0.0001$). If a malignant tumor was suspected initially, histological examination confirmed this in 75% of the cases. 45% of patients with a malignant nasopharyngeal mass had a unilateral seromucous tympanum.

Conclusions: Persistent nasopharyngeal masses in adults—particularly in elderly men, smokers and those with simultaneous unilateral seromucous tympanum—should undergo a histological examination.

KEYWORDS

adenoid vegetation, adults, histological examination, nasopharyngeal mass, seromucous tympanum

Key points

- Significant findings of the study:
Persistent nasopharyngeal masses in adults—particularly in elderly men,

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smokers, and those with simultaneous unilateral seromucous tympanum—should undergo a histological examination.

- What this study adds:

Data on nasopharyngeal tissue hyperplasia in adults are limited. This study analyzes these points as well as risk factors. In addition, an algorithm for identifying patients at risk for malignant nasopharyngeal disease and diagnostic steps were developed based on the results.

INTRODUCTION

A nasopharyngeal mass refers to an abnormal tissue growth in the nasal part of the pharynx. Histopathological examinations have revealed a diverse range of histological entities in the nasopharynx. In children, adenoid hyperplasia is the most common cause of nasopharyngeal masses. The adenoidectomy, a surgical removal of adenoids, is a common and frequently performed procedure in western countries.^{1,2} The main criteria of adenoid hyperplasia that lead to surgery are obstructive sleep disorder, habitual mouth breathing, and hearing loss.³

Typically, nasopharyngeal tonsil tissue regresses during adolescence. However, nasopharyngeal tissue proliferation is also seen in adults, both symptomatic or asymptomatic, as an incidental finding. For example, the pharyngeal bursa (an embryological residual) occurs in 3% of adults. The closing of the orifice of a nasopharyngeal bursa results in the manifestation of a so called "Thornwaldt cyst"—a most often asymptomatic finding when not infected.¹

Although primarily considered to be a benign condition, nasopharyngeal masses can cause issues due to mechanical obstruction and chronic inflammation. They can lead to (depending on their exact localization in the nasopharynx) local and systemic secondary diseases, such as obstructive sleep disorder, chronic tube dysfunction, middle ear problems like tympanic effusion, otitis media, adhesive process, and the development of cholesteatoma.^{2–4} The simultaneous symptoms epistaxis nasi and enlarged neck lymph nodes occur less frequently and are classified as warning signals.

The nasopharyngeal carcinoma is a comparatively rare malignancy with fewer than 100,000 cases worldwide per year.⁵ The incidence is higher in south-eastern Asia.⁶ Other tumor entities of the nasopharynx are even rarer and comprise, for example, nasopharyngeal adenoid cystic carcinoma and papillary adenocarcinomas, salivary gland anlage tumors, and pituitary adenomas.⁶

Another entity to mention is the juvenile angiofibroma—a rare, principally benign, locally aggressive vascular tumor, which is found almost exclusively in boys and young men (between the ages of 9 and 19 years). Recurrent (unilateral) epistaxis is a frequent symptom. Due to the risk of life-threatening bleeding, a biopsy is contraindicated when juvenile angiofibroma is suspected.⁷

The severity of complaints related to nasopharyngeal masses can vary; macroscopic assessment alone may not reliably determine their nature. The indication for a biopsy or adenoidectomy in adult patients

is usually derived from the children's indications in clinical practice despite the less robust data for adults. The approved indications for adenoidectomy constitute amongst others nasal obstruction, recurrent otitis media, and suspicion of malignancy.⁴ The last mentioned is difficult to define, as according to the natural regress during adolescence, all findings of nasopharyngeal masses in adulthood may be defined as suspect. Diagnosis is therefore often challenging due to the lack of clear indication criteria for nasopharyngeal biopsy in adults, making it difficult to determine the need for biopsy based solely on visual inspection.⁴

For adenoid occurrence in childhood, imaging is typically unnecessary. However, upon suspect of malignancy or in the case of a highly vascularised tumor, further imaging is indicated. Depending on the question, magnetic resonance tomography and/or computed tomography are the favored imaging techniques. Cysts and juvenile angiofibroma are routinely correctly diagnosed with the use of morphological imaging. Contrarily, the nasopharyngeal carcinoma is a histological diagnosis that is often difficult to differentiate radiologically from other neoplasms. In such a case, the role of imaging is the determination of the tumor size.⁸

As aforementioned, the nasopharyngeal mass is an incidental finding in some adult patients and no medical complaints are reported upon or before diagnosis. Especially in such cases, the question arises, whether a biopsy or removal is indicated. Thus, the main objective of the present study was to evaluate the histological types of nasopharyngeal masses and to characterize their related clinical features to improve the knowledge about clinical warning signals and risk factors for malignant diseases of the nasopharynx.

MATERIAL AND METHODS

A 10-year retrospective investigation and analysis of all adult patients (18 years and older; no restriction regarding sex) who had undergone surgical sampling for nasopharyngeal masses in an ORL university hospital department of southern Germany between 2009 and 2019 was conducted. The medical history, symptoms, clinical examination results, and histological findings of the patients were recorded. The clinical examinations and diagnoses were performed by an otorhinolaryngologist of the department when the patient was encouraged to evaluate the prospect of surgery. A mass was clinically suspected as malignant when there was a strong asymmetry, ulcers, a bleeding

diathesis without hints of juvenile angiofibroma, when suspicious cervical lymph nodes were present or in case of any signs of infiltration.

Both patients who underwent a nasopharyngeal biopsy as well as patients who underwent an adenoidectomy were included in the study. The nasopharyngeal biopsy was either performed via transnasal endoscopy (under full anesthesia or local anesthesia) or indirectly via transoral surgery under full anesthesia.

The retrospective analysis was conducted using the department's electronic medical records to gather medical history, reported symptoms, risk factors, clinical examination results, and histological findings. Imaging was only utilized on some patients, especially when there was a high suspicion of malignancy. As this was a minority regarding the total number of patients, the analysis of the radiological findings was not included in the study. Rather, the focus was set on symptoms and clinical data with respect to the histological finding. Data were collected and statistically analyzed using Microsoft Excel (version 16.64), GraphPad Prism (version 9.5.1) and SPSS (version 27). Descriptive and unpaired non-parametric statistical analyses were performed. A *P* value of 0.05 or less was considered statistically significant.

RESULTS

A total of 255 patients, comprising 62% males and 38% females, who were 18 years of age and older, were included in this study. The average age at the time of diagnosis was 42 years (range: 18–87 years). The most often reported symptoms were nasal obstruction (44%), ear pressure (29%), subjective hearing loss (33%), and objective hearing loss (36%). Among the patients, 38% were smokers (as shown in Table 1). The majority of histological diagnoses were adenoid tissue (64.7%), while malignant diagnoses were confirmed in 24.7% of cases. Solid malignancies were detected in 15.7% of cases, lymphomas in 9.0% of cases, cysts in 7.8% of cases, and other benign causes for nasopharyngeal mass in 2.7% of cases. These benign causes included osteomyelitis, juvenile nasopharyngeal angiofibroma, sarcoidosis, inverted papilloma, and haemangioma, each occurring in one case (examples of nasopharyngeal findings shown in Figures 1 and 2).

Out of 149 suspected adenoid cases, 93.3% (*n* = 139) were confirmed by pathological diagnosis. However, in five cases, a carcinoma was detected, while in three cases lymphoma was identified. Additionally, in one case, chronic lymphocytic leukemia (CLL) was detected, with another finding revealing a haemangioma (Figure 1D). For the 31 patients with a suspected cyst, none had malignancies detected in the pathological diagnosis. Of these cases, 61.3% (*n* = 19) were correctly identified as cysts, while the others were adenoids (Figure 1D). In the last group of suspected tumorous masses (*n* = 72), 75% had histological findings that confirmed a malignant tumor, either as carcinoma (*n* = 32) or myeloma/lymphoma (*n* = 19). In the remaining 25% of cases, adenoid tissue (*n* = 13), other benign masses (*n* = 3), and osteomyelitis (*n* = 2) were found.

Amongst the solid malignant neoplasms, 20 cases of undifferentiated carcinoma and 15 cases of squamous cell carcinoma (SCC) were identified (Figure 2C). Additionally, two cases of chordoma, and one case each of sarcoma, adenoid-cystic carcinoma, and sinonasal undifferentiated carcinoma were detected (Figure 2C). With regard to lymphoma findings, there were three cases of Hodgkin lymphoma, four cases of plasma cell myeloma, six cases of diffuse large B-cell lymphoma, nine cases of other non-Hodgkin lymphoma, and one case of CLL (Figure 2B).

The analysis of age distribution revealed a significant concentration of patients in the age range of 30–40, with mostly benign lesions. In contrast, patients with malignant nasopharyngeal masses had a statistically significant higher median age of 54 years compared with

TABLE 1 Table summarizing the patient characteristics including symptoms.

| Characteristics | Number (n) | Percentage |
|-------------------------|-------------|------------|
| Sex | | |
| Male | 158 | 62 |
| Female | 97 | 38 |
| Age | | |
| Median | 41.6 years | |
| Range | 18–87 years | |
| Smoking | | |
| Yes | 97 | 38 |
| No | 158 | 62 |
| Alcohol | | |
| Yes | 23 | 9 |
| No | 232 | 91 |
| Nasal obstruction | | |
| Yes | 111 | 44 |
| No | 23 | 9 |
| not documented | 121 | 47 |
| Ear pressure | | |
| Yes | 75 | 29 |
| No | 64 | 25 |
| Not documented | 116 | 45 |
| Hearing loss subjective | | |
| Yes | 84 | 33 |
| No | 171 | 67 |
| Hearing loss objective | | |
| Yes | 91 | 36 |
| No | 151 | 59 |
| Sensorineural | 1 | <1 |
| Not documented | 121 | 47 |

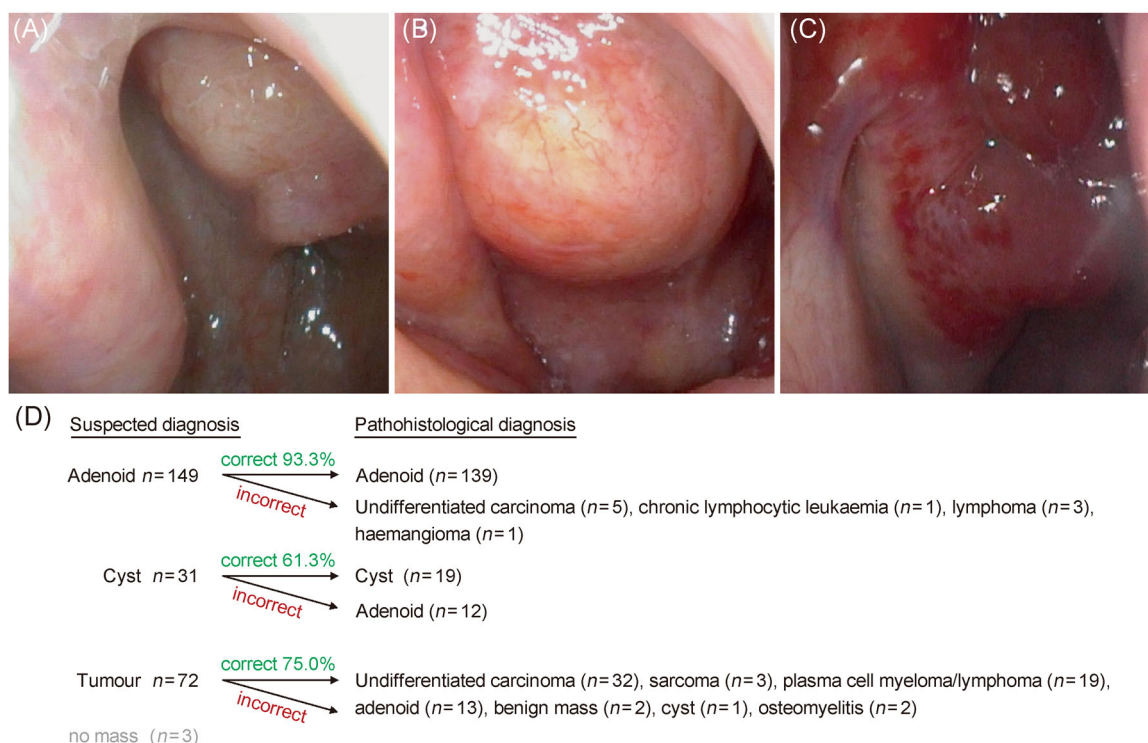


FIGURE 1 Endoscopic findings of adenoid tissue (A), nasopharyngeal cyst (B) and nasopharyngeal tumor (C). Suspected diagnoses and pathohistological diagnoses are shown (D).

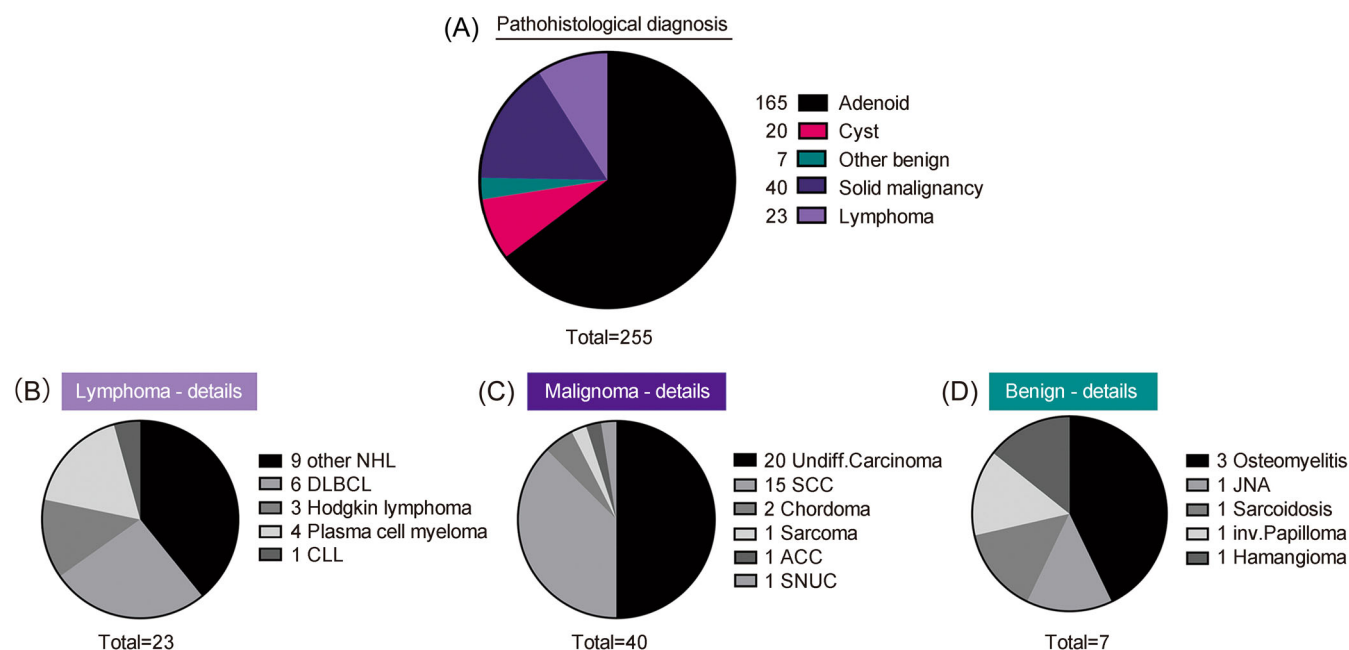


FIGURE 2 Pie charts showing the distribution of overall pathohistological diagnoses (A), lymphomas (B), malignomas (C), and benign diagnoses (D) in absolute numbers and percentages. ACC, adenoid-cystic carcinoma; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; JNA, juvenile nasopharyngeal angiofibroma; NHL, non-Hodgkin lymphoma; SCC, squamous cell carcinoma; SNUC, sinonasal undifferentiated carcinoma.

patients with benign masses who had a median age of 32 years ($P < 0.0001$; Figure 3).

Analysis of the data revealed that the malignancy rate was higher in male patients, with a rate of 28%, compared with that of female patients who had a rate of 20% (Supporting Information: Figure 1).

Furthermore, when patients were grouped by the factors "smoking and excessive alcohol intake," it was found that those without a history of smoking or alcohol consumption had a similar malignancy rate compared to smokers, with rates of 23% and 19% respectively. However, patients who reported excessive alcohol intake or both smoking and alcohol intake had a significantly higher malignancy rate, with rates of 40% and 61% respectively (Supporting Information: Figure 2).

The subjective symptom of hearing-impairment was similar to the objective, measured hearing impairment in cases of benign nasopharyngeal masses. Amongst patients with benign masses, 30% reported a subjective hearing impairment, whilst 32% had this objectively confirmed in the hearing test. Interestingly, among patients with malignant nasopharyngeal masses, 30% reported subjective

hearing impairment, but the objective testing showed a higher rate of hearing impairment in 53% of the cases (Figure 4A). Further analysis of the seromucous tympanum revealed that in 45% of cases, patients with malignancy had a unilateral seromucous tympanum, whereas only 5% suffered from a bilateral seromucous tympanum. In the group of benign masses, 16% had a unilateral seromucous tympanum, and 9% had a bilateral seromucous tympanum (Figure 4B).

Figure 5 presents a proposed algorithm for identifying adult patients at risk for malignant nasopharyngeal disease and the resulting diagnostic steps, based on the study results. The algorithm is intended for Caucasian patients, as risk factors differ in Asian countries.

DISCUSSION

The presence of nasopharyngeal masses in adults poses a clinical challenge in determining their malignant potential. In childhood, these masses are typically benign, but as patients age, there is an increased likelihood of malignancy. Gender differences may also play a role in the presentation and prognosis of nasopharyngeal masses.

The diagnoses of the current study reveal, that many different and rare conditions can arise in the nasopharynx. The initial clinical suspicion (malignant vs. benign) was in the majority of cases correct, however, a relevant number of patients in both groups received an unexpected diagnosis post-histological examination. The diagnosis "juvenile angiofibroma" only played a secondary role in this evaluation, as it usually affects minor patients and can often be diagnosed due to its typical highly vascularized aspects. In this case, a biopsy or adenoidectomy is contraindicated and imaging is the next diagnostic step, which explains the few amount of patients with this diagnosis in this study.

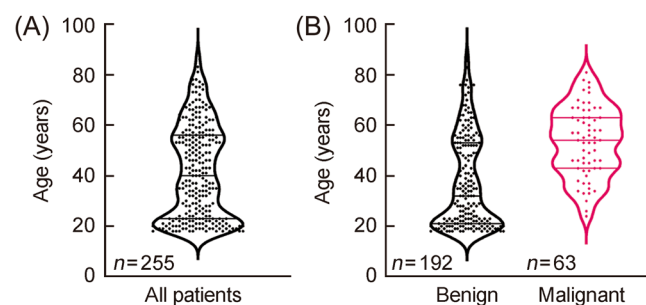


FIGURE 3 Violin plots illustrating age distribution of all patients (A) and regarding benign and malignant nasopharyngeal masses (B).

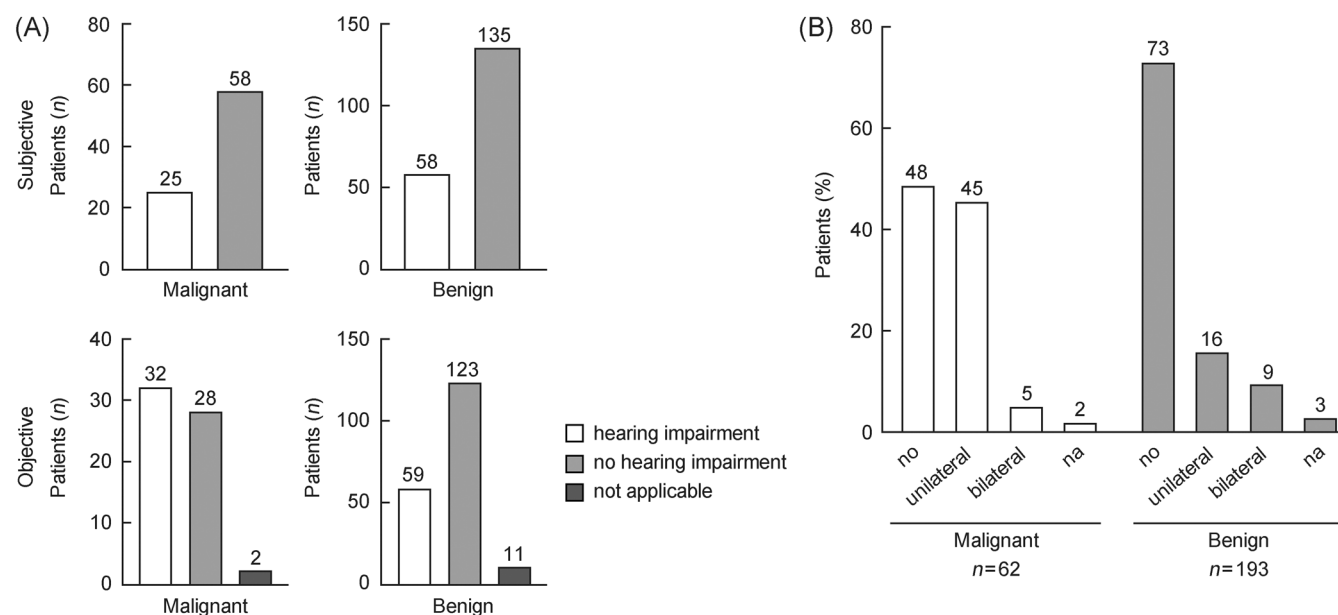


FIGURE 4 Bar graphs presenting subjective and objective symptoms of patients with benign and malignant nasopharyngeal masses (A). Bar graphs depicting existence (no/unilateral/bilateral) of seromucous tympanum of malignant and benign cases with number and percentage of patients (B). na, not available.

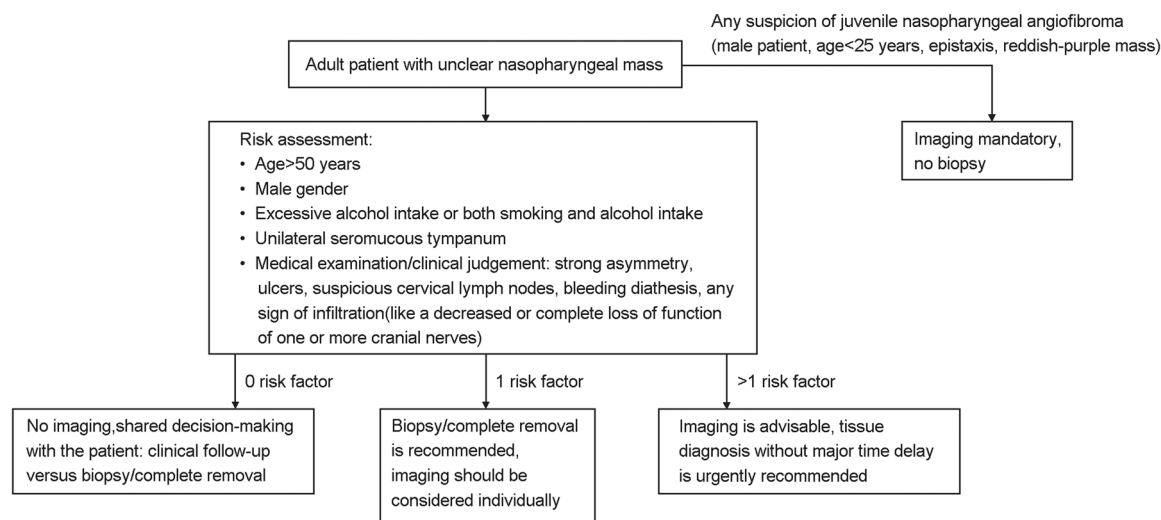


FIGURE 5 A proposed algorithm for identifying patients at risk for malignant nasopharyngeal disease and the diagnostic steps, based on the study results.

The incidence of nasopharyngeal carcinomas is significantly influenced by geographical distribution, with a high prevalence rate in eastern Asia.⁹ Other known risk factors for the development of nasopharyngeal carcinomas are the male gender and regarding the non-keratinizing subtype, there is an association with Epstein-Barr virus infection.^{10–12} The relationship between age and the incidence of nasopharyngeal carcinoma varies between high-risk and low-risk populations.¹³ Beside genetic alterations, other presumed risk factors are tobacco smoking, alcohol, and poor oral health. Dietary factors such as preserved food consumption are also considered to influence the development of nasopharyngeal carcinoma.¹¹

In summary, the results of the present study suggest that in adult patients with unclear nasopharyngeal masses, the factors age, excessive alcohol intake and/or both smoking and alcohol intake, and unilateral hearing impairment are potential warning signs of malignancy.

A retrospective Irish study was performed in 2006 to analyze whether routine nasopharyngeal biopsy in adults presenting with isolated serous otitis media is justified. As all four patients with suspicious-looking nasopharyngeal masses were found to have malignancies, the authors concluded that if a mass is found in the nasopharynx of patients with serous otitis media, it should be biopsied.¹⁴

The male gender was also associated with a tendency towards an increased risk for a malignant condition.

In 2014, Berkiten and colleagues performed a retrospective analysis of 1647 adult patients with nasopharyngeal masses and found also an increased risk of malignancy in elderly patients. Even though their study design was similar to the present study, there are relevant differences regarding the results: Berkiten et al. found benign diseases in 97.4% of the patients, whereas in the present study malignant diagnoses were confirmed in 24.7% of the cases. Not further specified hearing loss and neck mass were associated with malignancy in the study of Berkiten and colleagues.¹⁵

The fact that not only nasopharyngeal carcinoma but also other forms of a solid malignoma or lymphoma were regarded as “malignant diseases” in the current study, the present results are nevertheless coherent with the known risk factors for nasopharyngeal carcinoma. As this monocentric retrospective study was performed in southern Germany with mostly German patients, geographic risk factors can be negated.

As a positive prognostic factor of the current evaluation, it must be mentioned that none of the patients with the preoperative clinical diagnosis of a cyst had a malignant diagnosis after histological examination. In patients with asymptomatic nasopharyngeal cysts, further surgical steps are not mandatory.

One point to discuss is the role of imaging, when nasopharyngeal masses are found in adult patients. When there is any hint for juvenile angiofibroma, imaging is mandatory. In all other cases, the recommendation for imaging must be discussed, considering the value of the additional information of imaging and the avoidance of unnecessary costs on the other hand. In Figure 5, a proposed diagnostic algorithm and risk assessment is presented. When there is a high suspicion of a malignant finding, imaging before surgery should be recommended, to avoid that surgical procedures influence the tumor expansion in imaging. As already mentioned in the introduction, nasopharyngeal carcinoma is a histological diagnosis that is often difficult to differentiate radiologically from other neoplasms. Therefore, imaging cannot replace tissue biopsy.

As the volume of data today is still insufficient, further prospective analyses are needed to confirm or discuss these statements. The current findings highlight the importance of considering patient characteristics, clinical history and symptoms in the evaluation of nasopharyngeal masses to accurately determine their malignant potential. As in over 5% of patients, in which initially adenoids were the suspected clinical diagnosis, a malignant neoplasm was found, it can be summarized that biopsy or adenoidectomy is indicated in all adult patients with unclear nasopharyngeal masses except asymptomatic cysts, especially when at

least one of the above-mentioned risk factors is present. If for any reasons, biopsy is not yet planned or rejected, at least further clinical examinations should be performed and advised. The nasopharynx cannot be directly examined by the patients themselves and rather exclusively by otorhinolaryngologists and if imaging is present then by radiologists. Therefore, a general understanding and awareness—also in other subject areas like general medicine—for indirect signs of nasopharyngeal masses is crucial.

The findings of this study highlight that in adults, malignant nasopharyngeal masses are often accompanied by minor complaints that can easily be overlooked. Such medical complaints include nasal obstruction, ear pressure, and a unilateral hearing impairment. This may lead to a delayed initial diagnosis, progressed stages of disease, and poor prognosis. The delay in diagnosis can result in more advanced tumor stages at first diagnosis, which can significantly impact treatment outcomes and prognosis. Furthermore, the limited surgical options due to the complex anatomy of the nasopharynx with its close relationship to sensitive structures can further complicate the management of malignant masses in this region. Therefore, examination of the nasopharynx should be performed routinely by otorhinolaryngologists, especially when nasal obstruction, ear pressure, hearing loss due to conductive deafness or epistaxis is present.

CONCLUSION

Close attention should be given to older patients, those with a combined alcohol and smoking history or severe alcohol anamnesis, and those presenting with a unilateral hearing impairment—to ensure a timely and appropriate diagnosis and therapy.

AUTHOR CONTRIBUTIONS

Janina Hahn conceived of the presented idea. Melanie M. von Witzleben collected the data. Melanie M. von Witzleben and Adrian von Witzleben analyzed the data and performed the calculations and statistical analysis. Thomas K. Hoffmann contributed to the design and implementation of the research and supervised the project. Melanie M. von Witzleben and Janina Hahn wrote the manuscript. All authors discussed the results and contributed to the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to ethical restrictions.

ETHICS STATEMENT

Ethics approval of the local ethical committee was obtained (application number: 53/22).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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