

## What is the Diagnostic Role of Adenoid Hypertrophy and Adult-Onset Otitis Media with Effusion in Clinically Asymptomatic Nasopharyngeal Carcinoma?\*

OI Ozdamar, GO Acar, M Tekin

### ABSTRACT

**Objectives:** To verify the role of adenoid hypertrophy (AH) and otitis media with effusion (OME) in adult patients, in relation to the diagnosis of clinically asymptomatic nasopharyngeal carcinoma (NPC).

**Methods:** One hundred and six adult patients were enrolled in this retrospective study. Of 256 cases who underwent nasopharyngeal biopsy for suspected nasopharyngeal malignancy in our clinic between January 2009 and July 2014, this subset met our criteria. We divided the patients into two groups—patients with AH only and those with synchronous presence of OME, and AH.

**Results:** Two patients out of 68 (2.9%) in the first group (only AH) and one patient out of 38 (2.6%) in the second group had NPC. There was no statistically significant difference.

**Conclusion:** We found that asymmetric AH in adult patients seems an important risk factor for NPC, and we strongly suggest that biopsy be done to rule out nasopharyngeal carcinoma, whether or not they synchronously have OME even in the absence of other clinical symptoms that would arouse suspicion of a nasopharyngeal malignancy, such as neck mass, epistaxis and cranial nerve impairment.

**Keywords:** Adenoid hypertrophy, adult, nasopharyngeal carcinoma, otitis media with effusion

### INTRODUCTION

Nasopharyngeal carcinoma (NPC), arising in the epithelium of the nasopharynx, is a rare malignant tumour in the United States and Europe that occurs in only 1 per 100 000 population, with a male predominance by a ratio of about two to one; however, the incidence is approximately 30-times higher in Taiwan, Hong Kong and southern China (especially the Guangdong province) which is accepted as an endemic region (1).

Although otitis media with effusion (AO-OME) is a disease that is believed to be unique to childhood it can be seen in any age group. Possible causes of AO-OME are adenoid hypertrophy (AH), nasal problems, acute respiratory tract infection, acute otitis media and secondary smoke (2, 3). The rare diagnosis of AO-OME

in adults compared to children, may be an early sign of a NPC and warrants further evaluation for underlying malignant disease, especially if it is in one ear.

Nasopharyngeal carcinoma can cause OME through the following proposed pathogenic mechanisms: (a) obstruction of the Eustachian tube directly from a mass effect of the tumour and (b) tumour invasion of tensor veli palatini muscle that results in obstruction or dysfunction of Eustachian tube (4). So, a flexible, endoscopic, nasopharyngeal examination of adult patients with AO-OME is required to rule out a malignancy.

In this study, our aim was to verify the role of AH and OME in adult patients as a harbinger of clinically asymptomatic NPC, in a geographic area that is non-endemic for the disease, by comparing biopsy results of two study

\*This study was presented as a poster presentation in 29th Politzer Society Meeting, November 13 to 17, 2013, Antalya, Turkey. From: Department of Otorhinolaryngology—Head and Neck Surgery, Goztepe Training and Research Hospital, Istanbul Medeniyet University, Istanbul, Turkey.

Correspondence: Dr O Ozdamar, Department of Otorhinolaryngology—Head and Neck Surgery, Goztepe Training and Research Hospital, Istanbul Medeniyet University, Erkin cd. No: 1 Goztepe, 34730 Istanbul, Turkey. Email: osmanilkay73@yahoo.com

groups: group 1—patients who had only symmetrical or asymmetrical AH, and group 2—patients who synchronously had symmetrical or asymmetrical AH and OME.

## SUBJECTS AND METHODS

The retrospective research protocol was approved by the local Clinical Research Ethics Committee. One hundred and six patients who underwent a nasopharyngeal biopsy, with/without insertion of grommet ventilation tube to one or both ears between January 2000 and July 2014 at a tertiary healthcare centre, were analysed in this retrospective study.

All of the patients were older than 18 years old, ranging from 18 to 76 years. They were confirmed to have AH by magnetic resonance imaging (MRI) and flexible nasopharyngoscopy; however, a suspected lesion was not identified in any patient. Patients without MRI were excluded from the study to ensure that patients were not included who might have had submucosal tumour detectable by imaging methods. Thus, only patients with clinically asymptomatic NPC by means of physical examination and imaging methods were included. Otomicroscopic examination, tympanometry and pure-tone audiometry were performed for each patient who had OME. All of the patients had undergone nasopharyngeal biopsy to exclude NPC.

We divided the patients into two groups according to synchronous presence or absence of OME, and AH. In the first group, there were 68 patients, who only had AH. In the second group, there were 38 patients, who had OME in addition to AH. The patients with OME underwent myringotomy and insertion of grommet ventilation tube as a standard treatment (Table 1).

Table 1: Distribution of AH, with and without OME, in patients, and side of ventilation tube insertion

	Patients number	VT side s
Group 1 (AH w/o OME)	68	None
Group 2 (AH w OME)	38	
Right		11
Left		14
Bilateral		13
Total	106	38

AH = adenoid hypertrophy; OME = otitis media with effusion; VT = ventilation tube.

### Patients with AH

In the group of adult patients who had solely AH, AH was either symmetrical and generalized, or asymmetrical

in which only one side of the nasopharynx was hypertrophied. All of the patients underwent nasopharyngeal biopsy under general anaesthesia. Malignancies other than NPC were excluded.

Thirty-one patients were male and 37 patients were female. The mean age of the patients was 43.2 years, with a range of 18–78 years. The cases who had signs and symptoms related to a high suspicion of malignancy, such as epistaxis, pathologic lymphadenopathy in the neck, or a malignant lesion detected at the nasopharyngeal area with flexible fiberoptic examination and/or MRI, were excluded from the study. Only patients who were apparently normal, except with asymmetrical or generalized, symmetrical, non-specific AH, were included.

### Patients with AH and OME

In the group of adult patients who had OME in addition to AH, AH was either symmetrical and generalized, or asymmetrical, in which only one side of the nasopharynx was hypertrophied.

Twenty-two patients were male and 16 patients were female. The mean age of the patients was 46.6 years, with a range of 18–72 years. As in the first group, the cases with signs and symptoms highly suggestive of malignancy were excluded from the study. Only patients who were apparently normal, except for non-specific AH with synchronous OME, were included.

### Statistical analysis

Data were analysed using a commercially available statistics software package (SPSS 15 for Windows). The Pearson's Chi-squared and Fisher's exact tests were used to analyse discrete variables to compare the two groups. In all analyses, values of  $p < 0.05$  were considered statistically significant.

## RESULTS

Two patients out of 68 in the first group had an NPC (both of them had non-keratinizing squamous cell carcinoma, WHO type II). The carcinoma ratio was 2/68 (2.9%). In the second group, one patient out of 38 (2.6%) was detected with an NPC (non-keratinizing squamous cell carcinoma, WHO type II). There was no statistically significant difference between the groups ( $p > 0.05$ , see Table 2). Overall, three out of 106 (2.8%) patients who underwent nasopharyngeal biopsy were diagnosed with a nasopharyngeal carcinoma.

Table 2: Comparison of patients with only AH (group 1) and patients with AH and OME (group 2)

	Value	df	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson's Chi-square	0.008	1	0.927		
Continuity correction	0.000	1	1.000		
Likelihood ratio	0.009	1	0.926		
Fisher's exact test				1.000	0.708
Linear-by-linear association	0.008	1	0.927		
Number of valid cases	106				

AH = adenoid hypertrophy; OME = otitis media with effusion; NPC = nasopharyngeal carcinoma; RLH = reactive lymphoid hyperplasia; VT: ventilation tube.

In group 1, 55 patients had symmetrical, generalized AH and the remaining 15 patients had asymmetrical AH; seven had it in the right side and six had it in the left side. Nearly, half of the patients (33/68; 48.5%) had no symptoms, and AH in these subjects was detected incidentally on MRI that was performed by the neurology and neurosurgery clinics for other purposes, mainly differential diagnosis of chronic headache. These cases were referred to our clinic, and all of the patients underwent a flexible endoscopic examination. The other 35 patients (51.5%) attended our clinic for nasal obstruction and postnasal dripping, and AH was detected with an endoscopic examination of the nasopharynx; however, a suspicious lesion was not established in any patient. Magnetic resonance imaging (MRI) findings were also seemingly normal except for the AH in all of the patients.

Two out of 68 (2.9%) cases were shown to have carcinoma of the nasopharynx with biopsy results. Both of them had asymmetric AH that was right-sided with an unremarkable medical history in one female patient and left-sided in the other male patient. The female patient was consulted to our clinic for AH as an incidental finding on the MRI. On the other hand, the male patient presented to our clinic for nasal obstruction, which was progressive for the last six months. The patient had undergone a septoplasty for septal deviation in the same surgical session. None of the patients' pathologic results (those who had symmetric generalized AH in the nasopharynx) showed NPC (see Table 3).

In group 2, 25 patients (25/38; 65.8%) had symmetrical, generalized AH and the remaining 13 patients (13/38; 34.2%) had asymmetrical AH, in which seven were in the right side, and six were in the left side. All of the patients had attended our clinic for the complaints of hearing loss, aural fullness and tinnitus with/without nasal obstruction. Adenoid hypertrophy was detected

with an endoscopic examination of the nasopharynx; however, a suspicious lesion was not established in any patient. Magnetic resonance imaging findings were also seemingly normal, except for the non-specific AH with synchronously present OME in all of the patients. One out of 38 (2.6%) cases was revealed to have carcinoma of the nasopharynx on biopsy. The patient was a male who had a left-sided, asymmetric AH. The patient attended our clinic for nasal obstruction, which was progressive for the last six months, and a left-sided, asymmetric AH was detected through an endoscopic examination of the nasopharynx. None of the patients' pathologic results (those who had symmetric, generalized AH in the nasopharynx), were NPC (see Table 3).

Table 3: Distribution of patients in relation to side of AH and biopsy results

Patients	Symmetrical AH		Asymmetrical AH		Total
	NPC	RLH	NPC	RLH	
Gender	MF	MF	MF	MF	MF
Patients with AH (Group 1)	None	24 29	1 1	6 7	31 37
Patients with AH and OME (Group 2)					
Right VT	None	4 2	None	3 2	7 4
Left VT	None	3 3	1 0	4 3	8 6
Bilateral VT	None	7 6	None	None	7 6
Total					22 16

AH = adenoid hypertrophy; OME = otitis media with effusion; NPC = nasopharyngeal carcinoma; RLH = reactive lymphoid hyperplasia; VT = ventilation tube, M = male; F = female.

## DISCUSSION

Nasopharyngeal biopsy performed in otorhinolaryngology practice under general or local anaesthesia is not an uncommon surgical intervention in patients with suspected malignant disease of the nasopharynx. Nevertheless, the high rates of negative biopsy results question the validity of its routine implementation, which is a waste of time and cost in these circumstances. We found that asymmetric, adenoid hypertrophy in adult patients seems an important risk factor, and we strongly suggest that biopsy is needed to rule out nasopharyngeal carcinoma, whether they synchronously have OME or not, although, in the absence of other clinical symptoms, nasopharyngeal malignancy may still be present.

Two well-documented, important clinical features of NPC are firstly a high incidence in some geographic areas, such as China, Southeast Asia and North Africa, which have an incidence of up to 30-times more than low-incidence geographical areas including the United States and Europe; and secondly, there is a high incidence

in some races of persons that dwell in high-occurrence geographic areas (5). In these patients, nasopharyngeal biopsy could be performed to rule out a malignancy in clinically suspect situations, because early detection of an NPC can improve a patient's prognosis and quality of life.

Hsieh *et al* (6) evaluated a large number of patients who underwent nasopharyngeal biopsy for suspected NPC, and they assessed various clinical symptoms and signs (such as nasopharyngeal mass, neck mass, epistaxis, OME, headache, cranial nerve involvement) for relationship with the biopsy results by dividing the patients into cancerous and non-cancerous groups. They detected statistically significant differences for nasopharyngeal mass, neck mass, epistaxis and age between the groups after multivariable regression analysis. The only significant variable in the cancerous group for newly diagnosed NPC was neck mass. They found that nasopharyngeal mass had the highest sensitivity (90.7%), but lowest specificity (28.4%) due to a high rate of clinical misdiagnosis of nasopharyngeal lymphoid hyperplasia as NPC when examined with conventional white-light. On the other hand, an important clinical feature of this malignant disease is the possibility of a submucosal tumour underlying normal looking mucosa, which requires taking a biopsy, including submucosal deep tissue, up to a few millimetres (7).

Narrow-band imaging (NBI), a novel, optical technique to visualize nasopharynx, was also introduced in addition to conventional white-light endoscopes (8, 9). Narrow-band imaging (NBI) and conventional endoscopes were compared for differentiation rates of AH and NPC diagnosis in 79 consecutive, adult patients (9). They concluded that NBI was superior to the white-light endoscope for the detection of benign AH, but not that of NPC. However, NBI was not performed in our cases when we evaluated patients' files and electronic charts. Otitis media with effusion of childhood is mostly bilateral, and has numerous causes, except for tumours; however, it may be an early sign of an NPC in adults, when it is nearly always a unilateral occurrence. This warrants performing an endoscopic examination of the nasopharynx to exclude a nasopharyngeal malignancy. However, Gaze *et al* (10) detected nasopharyngeal neoplasm in adults with the only symptom being OME at an incidence of 1.4%. Similarly, they found an incidence of 1.5% in the second group of adult patients who had nasopharyngeal tumour presenting with only complaint of OME. It was concluded that the expected rate to disclose a diagnosis of NPC with isolated OME in adult

patients, as presented in the literature, was between 0.4% and 5.7%, depending on population studied (4, 10–12). They suggested using clinical judgement with other clinical findings to determine whether an endoscopic nasopharyngeal examination was necessary or not in these patients.

Deeb and Ashktorab (13) concluded that bilateral AO-OME cases were usually caused by benign clinical conditions; however, unilateral cases needed nasopharyngoscopy to rule out nasopharyngeal malignancy. Glynn *et al* (14) presented 85 adult patients with isolated serous otitis media who underwent nasopharyngeal biopsy; serous otitis media was unilateral in 59 (69%) patients and bilateral in 26 (31%) patients. They detected NPC in three of 59 unilateral OME cases; one of the 26 bilateral serous otitis media cases was lymphoma.

We agree that adult patients with unilateral OME need an endoscopic examination of the nasopharynx to rule out a malignancy. Additionally, OME which is not improved with medical treatment or spontaneously, needs an endoscopic examination of the nasopharynx. For this reason, we excluded the patients in whom OME was improved with medical treatment or spontaneously and who did not need ventilation tube insertion.

All of the mentioned studies were performed in low-incidence geographic areas. Our results for prevalence of NPC in AH without/with OME are higher for both of our study groups, at 2.9% and 2.6%, respectively. A possible explanation may be that AH is present in all our patients. This difference was not statistically significant ( $p > 0.05$ ). Ho *et al* (4) detected that five patients out of 87 with only OME were diagnosed with NPC, for a prevalence of 5.7% (5/87). They did not specifically mention AH detected by an endoscopic nasopharyngeal examination and/or MRI technique, but indicated that there were "no other apparent symptoms and signs suggestive of NPC". They concluded that the high prevalence of NPC was the result of endemicity for the disease in their population.

Magnetic resonance imaging of the nasopharynx is not only important for detection of a malignancy but also for the staging of NPC. Cui *et al* (15) found that MRI is superior to clinical detection of trigeminal nerve involvement in the untreated NPC patients. Tumour might invade deep anatomic structures, such as skull base, trigeminal nerve, cavernous sinus, intracranial region, by extending superiorly and laterally (14). Therefore, MRI is necessary in suspected cases with normal-looking nasopharyngeal mucosa, with or without adenoid hypertrophy.

## CONCLUSION

We detected that asymmetric adenoid hypertrophy in adult patients seems an important risk factor requiring biopsy to rule out NPC, whether or not it is present synchronously with OME. We conclude the following regarding clinically asymptomatic NPC in a low-incidence geographic area for the disease:

- (1) Asymmetric AH in adult patients indicates a high risk for NPC. We strongly suggest that this finding requires a biopsy to detect a malignancy earlier if it is present.
- (2) A narrow-band imaging (NBI) endoscopic examination of the nasopharynx, coupled with conventional white-light endoscopic examination, has a higher chance of detecting benign adenoid lymphoid hypertrophy according to recently published studies (8, 9); therefore, it might decrease unnecessary nasopharyngeal biopsies.
- (3) Generalized symmetric AH, as with OME in adult patients, indicates a relatively low risk for NPC. There is need for a biopsy of the nasopharynx (in the absence of other signs and symptoms) to rule out malignancy in these patients, if a neck mass or a tumourous lesion is detected on endoscopic examination of the nasopharynx. It seems that other factors are important, including clinical justification and experience of the surgeon. Patient-related factors are also important, such as age, gender, medical history, *etc.* Adult onset-otitis media with effusion (AO-OME) in non-endemic, geographic regions and in ethnic populations known to have low incidence of the malignancy for the malignancy, is more commonly due to benign diseases, such as allergic conditions and chronic infections.

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