



# Pathologic Evaluation of Routine Nasopharynx Punch Biopsy in the Adult Population: Is It Really Necessary?

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**Objectives.** To retrospectively evaluate the patients who underwent nasopharyngeal biopsy with imaging and biopsy results, who have or don't have symptoms for nasopharyngeal pathology and to determine the ratio of the nasopharyngeal cancer cases and other pathologic conditions.

**Methods.** In this retrospective study, 983 patients who underwent endoscopic nasopharyngeal biopsy for symptomatic nasopharyngeal lesions were included. All pathological results, benign or malign was recorded and classified due to the patients' presenting symptoms such as symptomatic for nasopharyngeal pathology or asymptomatic. Computed tomography (CT) or magnetic resonance imaging (MRI) reports were also recorded separately as group A for malignancy or group B for not malignancy.

**Results.** Forty-five (4.6%) of 983 biopsies were malignant. In this group, there is no statistically significant difference between symptomatic and asymptomatic group. For malignant pathologies, the sensitivity of MRI was found 88.2% and CT was 61.5%.

**Conclusion.** For early diagnosis of nasopharyngeal cancer, all patients admitted to Ear, Nose and Throat (ENT) referral clinics should be examined endoscopically irrespective of their complaints and suspicious cases should be investigated by imaging especially by MRI. If MRI report clearly indicates Thornwaldt cyst or reactive lymphoid hyperplasia and this result is compatible with endoscopic findings, biopsy may not be necessary. Apart from these cases, all suspected lesions should be biopsied.

**Keywords.** Nasopharyngeal Neoplasms; Biopsy; Multidetector Computed Tomography; Magnetic Resonance Imaging

## INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a unique disease with clinical behavior, epidemiology and histopathology that is different from that of the other squamous cell carcinomas of the head

and neck [1,2]. This cancer is highly malignant with extensive infiltration, early lymphatic spread and notorious predilection for distant metastasis [3]. Despite growing incidence and awareness in the relevant populations, because of its silent, deep-seated location, majority of the patients already have advanced disease at the time of diagnosis [3,4]. NPC patients most commonly have a unilateral neck lump in 50%–70% of patients, from cervical lymph node metastasis; the tumor may not be clinically apparent at the time of presentation. Eustachian tube obstruction may produce persistent unilateral hearing loss or otitis media [2]. Other presenting symptoms include epistaxis, nasal obstruction or less frequently cranial nerve palsies [2-5].

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Nasopharyngeal endoscopy is the initial investigation of choice for the detection of NPC with the definite diagnosis of NPC being confirmed by means of endoscopic biopsy of the site of the primary tumor [6]. Imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) have been used for the diagnosis and staging of NPC [5,6]. The presence of high level anti-Epstein-Barr Virus (EBV) antibodies with NPC are well known. Serologic markers for EBV infection, such as antibodies to EBV immunoglobulin A or EBV DNA gene products have also been used for screening [7].

Despite all the advances in imaging and screening techniques, the current gold standard of clinical NPC detection is nasopharyngoscopy combined with biopsy of suspicious lesions.

Suspicion of NPC based on the presence of metastatic cervical lymph nodes or unilateral serous otitis media can be relatively easy. For early diagnosis improves survival and prognosis, the diagnosis of NPC patients before abovementioned marked symptoms emerge is important. Because of this, all patients admitted to reference center, should be examined endoscopically irrespective of their complaints and suspicious cases should be investigated by imaging and biopsy. In this research, we retrospectively investigated the patients who underwent nasopharyngeal biopsy with imaging and biopsy results, who have or don't have symptoms for NPC and determined the ratio of the NPC cases and other pathologic conditions with or without obvious symptoms.

## MATERIALS AND METHODS

Nine hundred eighty-three patients (600 males and 383 females) aged from 10 to 85 years old (mean age, 39.7 years) who underwent endoscopic nasopharyngeal biopsy for suspicious nasopharyngeal lesion and whose required data were obtained from their files included in this retrospective research between 2010 and 2014 years, in Ankara Atatürk Training and Research Hospital ENT Clinic. Review of medical records was approved by the Institutional Review Board (IRB No: 2015186). All pathological results, benign or malign was recorded. Results were classified due to the patients presenting symptoms such as symptomatic group (343 patients) for nasopharyngeal pathology

or asymptomatic group (640 patients). Patients presenting with symptoms caused by the presence of a tumor mass in the nasopharynx (epistaxis, nasal obstruction, and discharge) symptoms associated with dysfunction of the Eustachian tube (hearing loss), symptoms associated with the superior extension of the tumor (headache, diplopia, facial pain, and numbness) and neck masses were included in the group of symptomatic for nasopharyngeal pathology and all other patients were included in the group of asymptomatic (diagnosed incidentally) detected by routine nasal endoscopy.

Amongst all patients who underwent nasopharyngeal biopsy we have obtained 765 of CT or MRI results (199 MRI and 566 CT). MRI was mainly used for looking to soft parts of nasopharynx and its around. But CT scan was performed in these conditions: (1) Incidental nasopharyngeal radiological finding on brain, paranasal or maxillofacial CT; (2) History of claustrophobia or placed cardiac pacemaker, vascular stent, artificial joints or any metallic piece; and (3) Being over table's weight limit. All imaging techniques were performed with or without intravenous contrast. If a patient had a history of severe asthma, chronic renal failure or allergic reactions due to contrast materials or unknown drugs, noncontrast imaging techniques were preferred. For each pathological diagnosis group, CT or MR imaging reports were recorded separately as group A for malignancy or group B for benign findings. Radiological findings for malignancy were; all asymmetric nasopharyngeal thickenings with or without contrast enhancement or invasion or destruction of surrounding tissues, and the cases reported as clearly malignant by the radiologist. All diffuse thickenings and reactive lymphoid hyperplasia and Thornwaldt cysts were recorded as group B.

All nasopharyngeal biopsies were performed under local anesthesia with tetracaine 4% and decongestion with oxymetazoline hydrochloride 0.05%. A four-quadrant nasopharyngeal biopsy was taken using a punch forceps. The biopsy specimens were immersed in formalin and then embedded in paraffin. Sections cut from paraffin blocks were stained with hematoxylin and eosin. If there was a suspicious finding in an imaging technique, nasopharyngeal thickening was re-biopsied to confirm the result. Frozen biopsy was not performed in none of our patients.

All statistical analyses were performed by IBM SPSS ver. 22.0 (IBM Co., Armonk, NY, USA). Chi-square tests and Student *t*-test were performed to evaluate for statistical significance. A *P*-value of 0.05 or less was regarded as statistically significant.

## RESULTS

Nine-hundred and eighty-three nasopharyngeal biopsies were performed during the study period. There were 383 females (39%) and 600 males (61%) whose median age at the time of the procedure was 39 years (range, 10 to 85 years). Forty-five

### HIGHLIGHTS

- Nearly half of the patients who were diagnosed malign nasopharyngeal pathology presented with asymptomatic.
- All patients should be examined endoscopically regardless of presenting symptoms.
- Magnetic resonance imaging was valuable for sensitivity when compared to endoscopic biopsy.

(4.6%) of the 983 pathologies were malignant. Twenty-nine (3%) of the 45 malignant pathologies were NPC and remaining 17 (1.6%) were other malignant pathologies.

Pathological reports of the benign and malign biopsies according to patients presenting symptoms and their distribution ratios are shown in Table 1. In malign pathologies group, there is no statistically significant difference between symptomatic and asymptomatic group ( $P>0.05$ ). However, there is a statistically significant difference between symptomatic and asymptomatic group in benign pathologies group ( $P<0.001$ ).

The results of CT or MR imaging reports for benign or malign lesions with each pathological diagnosis group and their suspicious for malignancy or not are shown in Table 2. For malignant pathologies the sensitivity of MRI was found 88.2%, and CT was 61.5%. For benign pathologies the specificity of MRI was found 98.8%, and CT was 97.7%. In CT groups; there is a stati-

cally significant difference between group A and B in benign pathologies ( $P<0.001$ ). However, there is no statically significant difference in malign pathologies ( $P>0.05$ ). In MRI groups; there are statically significant differences between group A and B in benign and malign pathologies ( $P<0.05$  in both groups). The most common finding for malignancy in both CT and MRI was asymmetric nasopharyngeal thickening. The most common clinical manifestation for malignancy was a nasopharyngeal mass (16/45) in a routine endoscopic examination, followed by a cervical mass (15/45), serous otitis media (10/45) and epistaxis (4/45).

## DISCUSSION

Though NPC is a rare disease on a world scale, and accounts for 0.7% of all cancers according to global cancer statistics, from the International Agency for Research on Cancer, there were over 84,000 new NPC cases in 2008 [8,9]. With evolution of treatment, this lethal cancer carries an excellent prognosis and maybe curable especially if detected early but most of the patients presented with stage III to IV disease with negatively affected the cure rate and increased the mortality rate [3,7,10].

Imaging is an essential tool in the management of nasopharyngeal cancer. MRI is superior to CT in this regard because of the lack of artifact from dental fillings, the availability of high-resolution coronal and sagittal imaging, and the exquisite lesion contrast relative to the brain, extracranial fat, and muscle. However, destruction of cortical bone (such as that of the skull base) is more easily visualized, and best evaluated by CT. Though MRI is currently the best technique to achieve an accurate diagnosis, CT may initially help to assess the nasopharyngeal lesion because it allows rapid image acquisition and is able to image bone, soft tissue and blood vessels all at the same time and costs

**Table 1.** Distribution of pathological diagnosis associated with presenting symptoms

Pathological diagnosis	Symptomatic group	Asymptomatic group	P-value
	No. (%)	No. (%)	
Malign pathologies	29 (64.4)	16 (35.6)	<0.001
Nasopharyngeal cancer	18 (40.0)	11 (24.4)	
Lymphoma	11 (24.4)	4 (8.9)	
Plasmocitoma	-	1 (2.2)	
Benign pathologies	314 (33.5)	624 (66.5)	<0.001
Reactive lymphoid hyperplasia	293 (31.2)	551 (58.7)	
Thornwaldt cyst	10 (1.1)	50 (5.3)	
Squamous metaplasia	7 (0.7)	10 (1.1)	
Granulomatous inflammation	3 (0.3)	6 (0.6)	
Actinomycosis	1 (0.1)	3 (0.3)	
Hamartoma	-	3 (0.3)	
Amyloidosis	-	1 (0.1)	

**Table 2.** Detailed imaging results of CT and MRI between group A (for malignant findings) and group B (for benign findings)

Pathological diagnosis	CT (n=566)		P-value	MRI (n=199)		P-value
	Group A	Group B		Group A	Group B	
Malign pathologies	16 (61.5)	10 (38.5)	>0.05	15 (88.2)	2 (11.8)	<0.001
Nasopharyngeal cancer	11 (42.3)	2 (7.7)		13 (76.4)	1 (5.9)	
Lymphoma	5 (19.2)	8 (30.8)		1 (5.8)	1 (5.9)	
Plasmocitoma	-	-		1 (5.8)	0	
Benign pathologies	108 (20.1)	432 (79.9)	<0.001	17 (9.3)	165 (90.7)	<0.001
Reactive lymphoid hyperplasia	99 (18.3)	392 (72.6)		12 (6.6)	139 (76.4)	
Thornwaldt cyst	4 (0.7)	27 (5)		0	22 (12.1)	
Squamous metaplasia	3 (0.6)	7 (1.3)		2 (1.1)	2 (1.1)	
Granulomatous inflammation	22 (0.4)	392 (0.6)		1 (0.5)	1 (0.5)	
Actinomycosis	0	27 (0.4)		1 (0.5)	0	
Hamartoma	0	1 (0.2)		1 (0.5)	1 (0.5)	
Amyloidosis	-	-		-	-	

Values are presented as number (%).

CT, computed tomography; MRI, magnetic resonance imaging.

less than MRI (about half the price of MRI). In our study, 285 patients who were not convenient for MRI (patients with cardiac pacemakers, tattoos and metal implants, anxiety caused by claustrophobia and cost-effectiveness issues and getting faster results) were performed CT. In 314 patients, nasopharyngeal findings were incidentally found or discovered by other CTs (brain, maxillofacial, and paranasal).

Though serological screening programs for high-risk populations can be available, current gold standard of NPC detection is nasopharyngoscopy combined with biopsy of suspicious lesions [4,11,12]. Our research clearly showed that nearly half of the patients who were diagnosed malign nasopharyngeal pathology presented with asymptomatic. Therefore, especially in referral ENT centers, all patients should be examined endoscopically regardless of presenting symptoms. In the literature, the sensitivity of endoscopy for NPC has been reported nearly as 90% [5,6]. This ratio may be true for the patients whose symptoms are highly suspicious for NPC. According to our research, this sensitivity rate is very high for the patients presenting with asymptomatic. In our research, malignant pathology was spotted in 4.6% of all of the specimens. In order to avoid unnecessary biopsies, imaging techniques (especially MRI) should be used for suspicious lesions. All minor bulging and asymmetries should be examined radiologically. Various radiological techniques can be used for the evaluation of nasopharyngeal lesions (CT, MRI, angiography and PET/CT) [13-16]. Amongst these, MRI is currently the best technique to achieve an accurate diagnosis. According to King et al. [6], nasopharyngeal MRI offers 95% accuracy for the detection of primary NPC. In our research, MRI offers 88.2% sensitivity. This ratio was even lower for CT reports (61.5%). Our low accuracy rate may be due to noncontrast MRI or CT scans performed in patients with a history of severe asthma, known allergy to contrast materials and renal disease. According to Liu et al. [13], malignant lymphoma is the second most common neoplasm of head and neck with Waldeyer's ring being the most common extra nodal site. Typically, nasopharyngeal non-Hodgkin's lymphoma is characterized as symmetrical and diffuse exophytic tumor that can extend into the nasopharyngeal airway rather than infiltrating deeply into the parapharyngeal region [13]. In contrast, NPC tends to be an asymmetrical tumor that has a propensity to undergo extensive invasion both laterally and in depth and so spread superiorly into the skull base, rather than inferiorly into the oropharynx [13]. Because of the diffuse and symmetrical nature of these tumors with noncontrast technique, our MRI and CT accuracy rate may be low. Moreover, it is hard to differentiate the NPC from the lymphoma on noncontrast radiological basis. On the other hand, in our research, the sensitivity of MR and CT imagings for Thornwaldt cysts were 100% and 87.1% respectively, and for reactive lymphoid hyperplasia were 92.1% and 79.9%, respectively. In additionally, approximately, 5% of cancers were missed at endoscopic biopsy due to symmetric nasopharyngeal lesions

or lack of deep biopsies; all of these cancers were identified at MR imaging. In this study, MRI was valuable for sensitivity when compared to endoscopic biopsy (88.2% and 84.4%, respectively). Biopsy has a disadvantage when taken a biopsy in a mistake region of nasopharynx which may be result as a reactive lymphoid hyperplasia.

In our study, the main limitation is that we did not compare the contrast and noncontrast technique. Noncontrast MRI for detection of low-grade nasopharyngeal cancers may be unnoticed when compared to contrast MRI.

In conclusion, MRI has the potential to be an initial diagnostic test for the detection of nasopharyngeal malignancy. MRI depicts subclinical cancers missed at endoscopy or endoscopic biopsy and identifies patients who do not have NPC and who therefore do not need to undergo invasive sampling biopsies and has an advantage in guiding biopsy in order to determine the site of the biopsy. Only the suspected lesions which are approved by MRI with contrast should be biopsied.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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