Pathology Registry of Malignant Tumors of Nasopharynx from 2001-2005 at Ain Shams University Hospitals

Thesis

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By

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Introduction

Cancer of the nasopharynx is a disease with a remarkable geographic and racial distribution worldwide ***(Jemal et al., 2011).*** Except for a handful of populations, this is a rare human malignancy ***(Yang et al., 2005).*** In most regions, the incidence rate of nasopharyngeal cancer is 1.2 per 100,000 for both sexes ***(Ferlay et al., 2010).***

In the U.S.A., the incidence of nasopharyngeal cancer ranges from 1–2 cases per 100,000 men and 0.4 cases per 100,000 women ***(Clifton and Titcomp, 2001).*** In Egypt, nasopharyngeal cancer contributed 0.39% of total malignancies in the National Cancer Institute (NCI) ***(Mokhtar et al., 2007).***

Although, it is a leading cause of death for large population in Southeast-Asia and to lesser extent in Northern Africa ***(Rosai, 2004),*** It accounts for about 18% of all cancers among Cantonese population of Southern China ***(Clifton and Titcomb, 2001).***

Regardless of race and geography, the commonest form of nasopharyngeal cancers are those arising from the epithelial cells lining the nasopharynx; referred to as nasopharyngeal carcinoma (NPC); which constitute 75–95% of nasopharyngeal cancers in low-risk populations and virtually all nasopharyngeal cancers in high-risk populations ***(Yu and Yuan, 2002)***.

Age distributions of NPC show distinct features across different populations. Bimodal age distribution was noticed in several low to intermediate risk populations; a small peak occurs in late childhood and a second peak occurs in people aged 50-60 years. Male to female ratio is approximately 2:1 ***(Bray et al., 2008).***

In the current WHO clasification, nasopharyngeal carcinoma has three histological subtypes: squamous cell carcinoma, nonkeratinising carcinoma and basaloid squamous cell carcinoma ***(Chan et al., 2005).***

Besides nasopharyngeal carcinoma, a broad range of neoplasms can arise in the nasopharynx, from epithelial to lymphoid, mesenchymal and neurogenic ***(Ganzer and Arnold, 2010).*** Nasopharyngeal non-Hodgkin's lymphoma accounts for 2.5 % of all extranodal NHL ***(Chan et al., 2005).*** Hodgkin's lymphoma only rarely shows primary involvement of the nasopharynx ***(Moghe et al., 2001).***

NPC has many interacting risk factors involved in its development, mainly, Epstein-Barr virus (EBV) ***(Abdulamir et al., 2008).*** The near constant association of EBV with NPC irrespective of ethnic background indicates a probable oncogenic role of the virus in the genesis of this tumor ***(Raab-Traud, 2002).***

In high risk areas preserved and fermented food consumed in weaning and early childhood has been incriminated as risk factor ***(Chan et al., 2005).*** Other risk factors include cigarette smoking, occupational exposure to smoke, dust and formaldehyde ***(Hildesheim et al., 2001).***

Crush artifacts are common in nasopharyngeal biopsies, making it difficult to determine whether the observed distorted cells represent carcinoma or merely lymphoid cells. Immunostaining for cytokeratin is of great help in reaching a diagnosis of nasopharyngeal carcinoma ***(Chan et al., 2005).***

The mainstay of treatment for NPC is radiation therapy (***Chan et al., 2005).*** The presenting stage is the most important prognostic factor ***(Sze et al., 2002).***

Aim of the work

Registry of different types of malignant tumors of the nasopharynx received at the pathology laboratories of Ain Shams University Hospital and Ain Shams Specialized Hospital during the period of 5 years (2001-2005) with full registration of the clinico-pathological data from the files.

Anatomy of the nasopharynx

The nasopharynx is the narrow tubular passage behind the nasal cavity. Its sloping roof and posterior wall are formed by the basi-sphenoid, basiocciput and the first cervical vertebra. Anteriorly, it communicates with the nasal cavity via the choanae. The orifices of Eustachian tubes are in the lateral walls, and each is shielded superiorly and posteriorly by a comma-shaped elevation called the torus tubarius. Immediately above and behind the torus tubarius is a pharyngeal recess called the fossa of Rosenmüller. The nasopharynx tapers inferiorly, and continues as the oropharynx from the level of the soft palate *(figure 1)* ***(Goh and Lim, 2009).***

The nasopharynx constitutes part of the Waldeyer ring. The later is formed by a ring or group of extranodal lymphoid tissues at the upper end of the pharynx which consists of the palatine tonsils, the pharyngeal tonsils (adenoids), the base of tongue (lingual tonsils) and the adjacent submucosal lymphatics *(figure 2).* Nasopharyngeal tonsils (adenoids) lie along the posterior and lateral walls of the nasopharynx ***(Wenig, 2009).***

Since the nasopharynx is in close proximity to many different anatomic structures, tumors arising in the latter sites can also present clinically as a nasopharyngeal mass ***(Breda et al., 2008).***

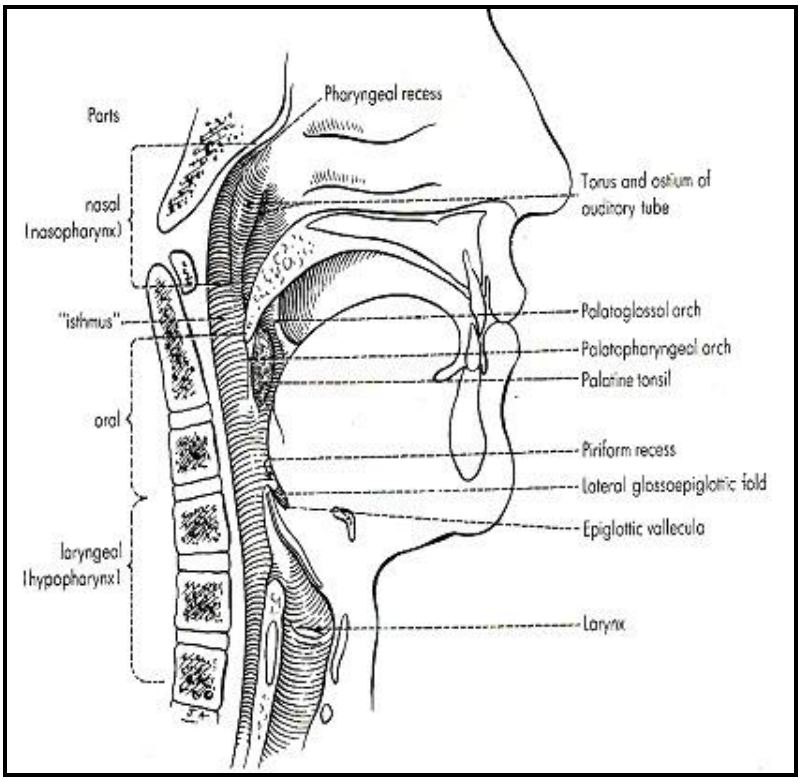

Figure (1): Anatomical subdivisions and "contents" of the pharynx ***(Wenig, 2009).***

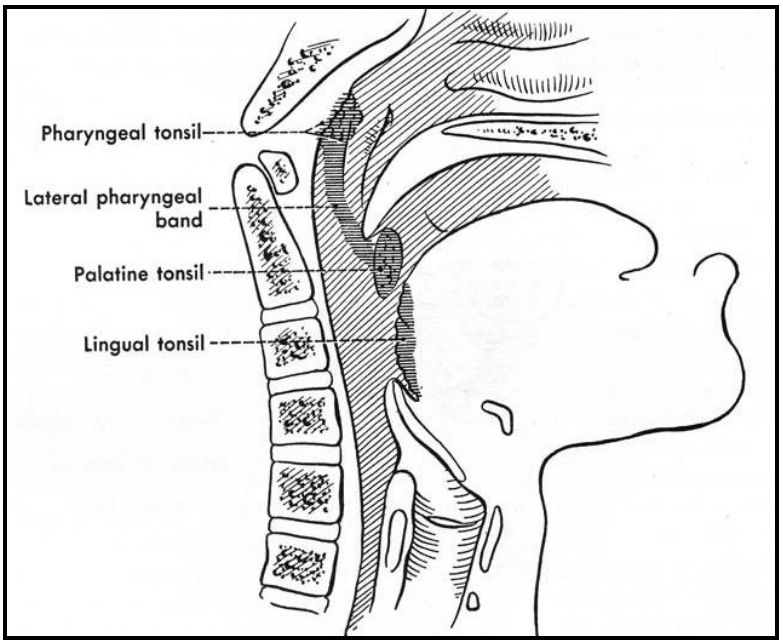

Figure (2): Waldeyer's tonsillar tissues ***(Wenig, 2009).***

Histology of the nasopharynx

Nasopharyngeal mucosa is covered by respiratory-type ciliated epithelium, but variable amounts of squamous epithelium are common. The mucosa exhibits invaginations, forming crypts that abut the underlying stroma. The stroma is rich in lymphoid tissue that often includes reactive lymphoid follicles. The surface or crypt epithelium is commonly infiltrated by many small lymphoid cells, which expand and disrupt the epithelium to produce a reticulated pattern. Some seromucinous glands are present, but they are not as abundant as in the nasal mucosa ***(Ganzer and Arnold, 2010).***

Classification of tumors of the nasopharynx

WHO histological classification of tumors of the nasopharynx *(Barnes et al., 2005).*

Malignant epithelial tumors

- Nasopharyngeal carcinoma
  - Nonkeratinizing carcinoma
  - Keratinizing squamous cell carcinoma
  - Basaloid squamous cell carcinoma
- Nasopharyngeal papillary adenocarcinoma
- Salivary gland-type carcinomas

Benign epithelial tumors

- Hairy polyp
- Schneiderian-type papilloma
- Squamous papilloma
- Ectopic pituitary adenoma
- Salivary gland anlage tumor
- Craniopharyngioma

Soft tissue neoplasms

- Nasopharyngeal angiofibroma

Haematolymphoid tumors

- Hodgkin lymphoma
- Diffuse large B-cell lymphoma
- Extranodal NK/T cell lymphoma
- Follicular dendritic cell sarcoma/tumor
- Extramedullary plasmacytoma

Tumors of bone and cartilage

- Chordoma

Secondary tumors

Soft tissue tumors in general are relatively uncommon in the head and neck region and the proportion of all soft tissue sarcomas that arise in this region is no more than 5–10%, although the proportion is somewhat higher in children ***(Bree et al., 2010)***. The spectrum and clinicopathological features of nasopharyngeal soft tissue tumors are similar to those of other sites in the upper aerodigestive tract except for angiofibroma, which typically presents in the nasopharynx. In children and adolescents the vast majority of soft tissue malignancies are rhabdomyosarcomas ***(Chan et al., 2005).*** Soft tissue tumors that have been mentioned in WHO classification of tumors to occur along other sites of upper aerodigestive tract include:

Malignant tumors

- Fibrosarcoma
- Malignant fibrous histiocytoma
- Leiomyosarcoma
- Rhabdomyosarcoma
- Angiosarcoma
- Malignant peripheral nerve sheath tumor
- Liposarcoma
- Kaposi sarcoma
- Synovial sarcoma

Borderline and low malignant potential tumors

- Desmoid-type fibromatosis
- Inflammatory myofibroblastic tumor
- Glomangiopericytoma (Sinonasal-type haemangiopericytoma)
- Extrapleural solitary fibrous tumor

Benign tumors

- Myxoma
- Leiomyoma
- Haemangioma
- Schwannoma
- Neurofibroma
- Meningioma
- Rhabdomyoma
- Lymphangioma
- Granular cell tumor

(Barnes et al., 2005)

Likewise, WHO mentioned that tumors of bone and cartilage of the nasopharynx has the same spectrum and clinicopathological features as that of other sites in the upper aerodigestive tract, except for chordoma, which typically presents in the nasopharynx ***(Chan et al., 2005);*** and that includes:

Malignant tumors

- Chondrosarcoma
- Mesenchymal chondrosarcoma
- Osteosarcoma
- Chordoma

Benign tumors

- Giant cell lesion
- Giant cell tumor
- Chondroma
- Osteoma

- Chondroblastoma
- Chondromyxoid fibroma
- Osteochondroma (exostosis)
- Osteoid osteoma
- Osteoblastoma
- Ameloblastoma
- Nasal chondromesenchymal hamartoma

(Barnes et al., 2005)

Although primary mucosal melanoma is extremely rare in the head and neck, it can occasionally arise in the Eustachian tube orifice in the nasopharynx ***(Yang et al., 2009).***

Malignant epithelial tumors

Nasopharyngeal carcinoma

Definition

Nasopharyngeal carcinoma is a non-lymphomatous, squamous-cell carcinoma that occurs in the epithelial lining of the nasopharynx. This neoplasm shows varying degrees of differentiation ***(Wei and Sham, 2005).***

Synonyms

Lymphoepithelioma, lymphoepithelioma like carcinoma, lymphoepithelial carcinoma, Schmincke type lymphoepithelioma, Regaud type lymphoepithelioma, transitional cell carcinoma, intermediate cell carcinoma, anaplastic carcinoma, undifferentiated carcinoma with lymphoid stroma, vesicular nucleus cell carcinoma, squamous cell carcinoma (WHO-1), nonkeratinizing carcinoma (WHO-2), undifferentiated carcinoma (WHO-3) ***(Chan et al., 2005).***

Localization of the tumor

Nasopharyngeal carcinoma is frequently seen at the pharyngeal recess (Rosenmüller's fossa) posteromedial to the medial crura of the eustachian tube opening in the nasopharynx ***(Wei and Sham, 2005 and Brennan, 2006).***

Histogenesis

Nasopharyngeal carcinoma arises from the surface or crypt epithelium of the nasopharyngeal mucosa. In some cases, the tumor appears to arise from the basal layers of the stratified squamous epithelium, a finding further supported by the strong immunoreactivity for p63 in both the tumor and normal basal cells ***(Thariat et al., 2009).***

The suggested precursor of the basaloid squamous cell carcinoma (BSCC) is a totipotent primitive cell located in the basal cell layer of the surface epithelium, or in the proximal ducts of minor salivary glands ***(Ereno et al., 2008).***

Epidemiology

Global incidence and mortality

Nasopharyngeal carcinoma (NPC) shows a distinct racial and geographical distribution ***(Chang and Adami, 2006).*** It constitutes 75–95% of nasopharyngeal cancers in low-risk populations and virtually all nasopharyngeal cancers in high-risk populations**.** Most cancer registries only present incidence data for cancer of the nasopharynx as a whole. Therefore, nasopharyngeal cancer rates, which, for most populations, are indistinguishable from their respective NPC rates, are used to compare worldwide incidence of NPC as well ***(Yu and Yuan, 2002).***

In most regions, the incidence rate of nasopharyngeal cancer is 1.2 per 100,000 for both sexes ***(Ferlay et al., 2010).*** However, dramatically elevated rates are observed in the Cantonese population of southern China (including Hong Kong); incidence rates among them are as high as 25–50 cases per 100,000 and may account for 18% of all cancers in that area. It is the leading cause of death among Cantonese young people ***(Clifton and Titcomp, 2001).***

Intermediate rates are observed in several indigenous populations in Southeast Asia, and in natives of the Arctic region, North Africa, and the Middle East ***(Chang and Adami, 2006).*** Within these populations, there is a remarkable heterogeneity among ethnic lines ***(Yu and Yuan, 2002).*** In Central and Southern Africa countries, where infection-related cancers are predominant, the well known excess risk for nasopharyngeal carcinoma is confirmed, with rates reaching the level of 5.4 per 100,000 in men and 1.9 per 100,000 in women, which is 10 times higher than in Europe ***(Zanetti et al., 2010).*** In the U.S.A., the incidence of nasopharyngeal carcinoma (NPC) ranges from 1–2 cases per 100,000 men and 0.4 cases per 100,000 women ***(Clifton and Titcomp, 2001)***

Mokhtar et al. (2007) reported that during the years 2003-2004, in the surgical pathology unit of the department of pathology at the Egyptian National Cancer Institute (NCI), primary malignant solid tumors, represented 42% of all received cases through this period. Whereas primary malignant