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ORIGINAL ARTICLE

High Incidence of Nasopharyngeal Carcinoma in Asia

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Although nasopharyngeal carcinoma (NPC) is a rare cancer in the United States, it is a leading cause of death in other countries. Dr Titcomb reviews several facts about NPC that can be helpful to underwriters as they encounter this tumor in applicants who reside in, or who are a native of, an area of high incidence.

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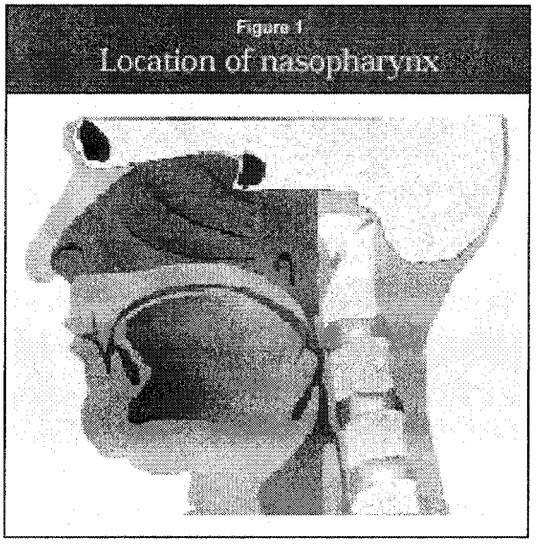
In the United States, the incidence of nasopharyngeal carcinoma (NPC) ranges from 1–2 cases per 100,000 men and 0.4 cases per 100,000 women. However, in other countries and in certain ethnic groups, the tumor is very common. Rates are especially high in Asia. Incidence rates among the Cantonese population of southern China 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.

Similarly high rates are found in the Eskimos of Alaska and Greenland. Intermediate incidence rates are seen in Southeast Asia and the Mediterranean basin. Interestingly, individuals who emigrate from endemic areas retain an increased risk for the disease in later life, albeit somewhat lower than that seen in their native countries.[1–4]

ABOUT NPC TUMORS

The nasopharynx is a cuboidal structure that is bordered by the nasal cavity anteriorly, the base of the skull superiorly, the cervical spine posteriorly, and the upper surface of the soft palate inferiorly. Many important anatomic structures enter or surround it (see the Figure). The eustachian tubes open into the nasopharynx. Many cranial nerves are located nearby. In addition, the nasopharynx is characterized by a rich lymphatic and blood supply. These anatomic factors affect diagnosis, staging, and treatment of the tumor.[3,5]

Nasopharyngeal tumors may occur at any age, but peak incidence is between 50 and 69 years old. The lesions are more common in men. The most frequent presenting symptom is a neck mass. Other symptoms and signs include nasal obstruction with bloody drainage, decreased hearing resulting from serous



Location of nasopharynx.

otitis secondary to eustachian tube obstruction, tinnitus, pain, and cranial nerve palsy.[1,3,5]

Three major etiologic factors with NPC include the following:

1. Individuals with a genetic predisposition are at increased risk, hence the geographic variation in incidence.
2. Dietary factors are also important, in particular, the consumption of salt-cured fish and meat. The belief is that cooking these foodstuffs aerosolizes carcinogenic nitrosamines that are inhaled. Exposure early in life seems to be critical.
3. Infection with Epstein-Barr virus (EBV) occurs in virtually all cases.[1,3,5–8] Most individuals with the disease will have some antibodies to EBV. The most common are immunoglobulin A antibodies to the viral capsid antigen (VCA) and early antigen (EA). However, a variety of others may be detected.[9–11] It appears that the viral DNA is incorporated into the tumor cells.

DIAGNOSING NPC

The diagnosis of NPC is difficult because of its anatomic location. Frequently, the disease is clinically silent until it invades adjacent structures and produces symptoms. Screening with EBV antibodies has been used in endemic areas and can identify higher risk individuals. The incidence of IgA-positive individuals has ranged from 0.6 to 10% of the population in selected areas. The 10-year risk of developing the disease has been estimated to be up to 200 times higher in the antibody-positive group.[8] However, the specificity of the tests is weak and only 1.5–13.6% of those who test positive are found to have the disease. Thus, a positive antibody test does not guarantee a diagnosis of cancer.[7,9] Definitive diagnosis requires biopsy.

There are 3 major histologic types of NPC. Type 1 is keratinizing squamous cell carcinoma (SCC), type 2 is nonkeratinizing SCC, and type 3 is undifferentiated carcinoma. The sporadic NPC lesions that occur in the Western world tend to be type 1, while the endemic variety are usually type 2 or type 3. There is no difference in prognosis between the different tumor types.[1,3,12]

The 3 different staging systems for NPC each use a modification of the T (extent of primary tumor in the nasopharynx), N (degree of nodal involvement), and M (presence of metastasis) system. The burden of disease in different stages ranges from small, localized lesions with no affected nodes to large, locally invading tumors with or without metastases. Nodal involvement, often retropharyngeal and frequently massive, is very common due to the rich lymphatic system in the nasopharynx and its drainage pattern. Distant metastasis, most frequently to bone, lung, and liver, may occur and is more common than with other head and neck cancers. A CT scan and/or MRI of the nasopharynx are usually required to adequately stage the tumor.[1,3]

TREATING NPC

Primary treatment for local or limited regional NPC is with radiation therapy. Because of anatomic limitations and the frequency of nodal involvement, surgery is rarely attempted. Chemotherapy may be used in individuals with extensive local–regional involvement or distant metastases. Local recur-

Mortality ratios from Hong Kong-based study of NPC

	0–5 years	5–10 years
Stages I & II	589%	582%
Stage III	1,476%	460%
Stage IV	2,722%	798%

rences are treated with radiation with or without chemotherapy.[1,3,5]

Adverse prognostic factors include the following:

- More extensive local involvement (higher T stage), especially with cranial nerve palsy or intracranial invasion
- Nodal involvement, especially large nodes
- Bilateral involvement and nodes in the supraclavicular fossa
- Older age at diagnosis
- Gender
- Ear symptoms at the time of diagnosis[1,3,12]
- High lactate dehydrogenase (LDH) levels[13]
- Elevated levels of antibodies to EBV that persist or do not decrease after treatment have been associated with residual or recurrent disease.[9,14]

Survival varies with stage of disease. For stages I and II (locally limited tumor confined to the nasopharynx, no nodal or other metastasis), 5-year survival is approximately 70–80%. Stage III disease (more extensive local involvement or single node metastasis) has a 5-year survival of 40–50%. The 5-year survival with stage IV (invasion of skull or cranial nerves, bilateral or massive nodal involvement, or distant metastasis) is in the 20–40% range.[1–5,12,15,16] In one large Hong Kong-based study of 759 patients, this survival pattern translated into geometric annual average mortality ratios presented in the Table.[12]

SUMMARY

Nasopharyngeal carcinoma is a common cancer in individuals who reside in, or who have emigrated from, certain geographic areas (southern China, Southeast Asia, Mediterranean basin). An individual from an endemic area who has elevated IgA antibodies to EBV should be considered to have NPC until an examination rules out the diagnosis. A negative evaluation does not eliminate the possibility of later development of the disease. Occurrence of nasal obstruction with a bloody discharge, recurrent serous otitis/otitis media in an adult, or the development of a painless neck mass or cranial nerve palsy in an individual from an endemic area should all raise suspicions about NPC. Radiation therapy is the primary treatment for NPC. Treatment with surgery or chemotherapy should raise suspicions of regionally extensive or recurrent disease. The morbidity and mortality risk is significant with NPC. Survival rates vary with the stage of the disease and are best for smaller tumors without nodal involvement.

The burden of disease in different stages ranges from small, localized lesions with no affected nodes to large, locally invading tumors with or without metastases.

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