Nasopharyngeal Carcinoma (Lymphoepithelioma; Transitional Cell Carcinoma; Epidermoid Carcinoma)

(NPC) is a poorly differentiated primary malignancy of the nasopharyngeal epithelium. Although rare, NPC accounts for 1/3 of all nasopharyngeal neoplasms in children, occurring mostly in adolescents and young adults.

This malignancy can appear at any site of the upper respiratory tract, but most commonly occurs in the lateral wall of the nasopharynx. It is associated with Epstein-Barr virus (EBV) infection, exposure to smoke or to chemical pollutants.

NPC is more common in Southeast Asia than in the US and Europe. In the Chinese population, there appears to be a genetically-determined risk; and ingestion of salted fish (often a staple food for Southeast Asians) also appears to be linked to this disease.

The World Health Organization classifies nasopharyngeal carcinoma into three subtypes:

Type I - squamous cell carcinoma, typically found in older adult
Type II - non-keratizing carcinoma, also typically found in adults, and associated with EBV infections
Type III - undifferentiated carcinoma, common in childhood, and associated with EBV infections

Clinical Signs and Symptoms:

Nasopharyngeal carcinoma tends to present late and is more often diagnosed because of its metastatic features rather than the effects of the primary tumor. (A – 2) Cervical lymphadenopathy often is the first and only presenting symptom. Other symptoms may include nasal obstruction, epistaxis, earaches, deafness, or difficulty of hearing, tinnitus, post nasal discharge and cranial nerve palsies involving the oculomotor (III), trigeminal (V), or abducens (VI) nerve. Patients may also present with neck swelling and tumors in the neck.
Metastatic spread is often to the adjacent lymph nodes, lungs, vertebrae, long bones, or liver. Bone pain and symptoms associated with tumor-related visceral organ dysfunction may be present. Metastatic NPC may present with a peculiar paraneoplastic syndrome of marked osteoarthropathy with joint swelling, clubbing, bone and joint pain.

**Diagnostic Workup:**

- Lymph node biopsy is often diagnostic for NPC
- Nasopharyngoscopy to determine presence of a nasopharyngeal mass
- CT of the head and neck that includes views of the brain, with special attention to the base of the skull
- MRI might better define the extent of the primary tumor
- CT of the chest and abdomen to detect possible metastases
- Bone scan to detect possible metastases
- Serum assays of EBV titers and full EBV serology (including IgA and IgG anti-VCA). Also, it is recommended that the EBV DNA levels in peripheral blood be measured since they correlate with total tumor burden and can be used to monitor treatment and recurrence.
- Staging using the American Joint Committee on Cancer (AJCC) TNM classification system

**Treatment:**

The nasopharynx is a difficult area to access by surgery; and by the time of presentation nasopharyngeal carcinoma has usually spread to adjacent areas and lymph nodes. Surgery is done initially to obtain a sampling (biopsy) of the tumor, either from the involved lymph node or the primary site. Supportive procedures such as myringotomy or tympanostomy are done to relieve ear symptoms.

The primary therapeutic modality is irradiation of the nasopharynx, posterior nasal cavity, posterior maxillary sinus, base of the skull, and cervico-supraclavicular lymph nodes. Xerostomia is a major treatment side-effect since the recommended dose is 6000 to 7000 cGy.

Other treatment-related late effects include fibrosis of the neck and trismus (tonic contraction of the muscles of mastication). Patients who receive large doses of radiation should be followed up and monitored for hypothyroidism and second malignancies.

Recent studies suggest the advantage of chemotherapy in addition to radiation in achieving excellent survival rates and long-term disease-free survival for patients with advanced disease. This is what is called “chemoradiation”; patients receive chemotherapy and radiation therapy concurrently. Most head and neck cancers, including nasopharyngeal carcinoma, are responsive to several cytotoxic agents, such as cisplatin (Platinol), fluorouracil (5-FU), methotrexate (Mexate), and bleomycin.
Future Directions:

Increased survival rates have been demonstrated with multimodal therapy of radiation and chemotherapy. Current treatment studies are focused on the EBV- nasopharyngeal carcinoma association and the use of biologic modifiers such as interferon, or the development of EBV-specific cytotoxic lymphocytes.

Helpful Weblinks:

EMedicine.com
This website contains a manuscript including pathology, treatment modalities and current state of knowledge regarding nasopharyngioma
http://www.emedicine.com/ped/topic1553.htm

Union Hospital, Hong Kong
Nasopharyngeal Carcinoma Screening Package
This website contains outlined information about NPC and good tips for early detection.
http://www.union.org/eng/b4-1-15.php

New England Journal of Medicine, Waltham, MA
This article describes the relationship of EBV virus serologic markers to NPC in Taiwan

General Practice Notebook – Nasopharyngioma
http://www.gpnotebook.co.uk/simplepage.cfm?ID=1872363526

The National Cancer Institute – Nasopharyngeal Cancer PDQ

Related www.Cure4Kids.org seminars

Seminar #21 Nasopharyngeal Carcinoma in Children
Carlos Rodriguez-Galindo, MD, Kathleen J. Helton, MD, Jesse J. Jenkins, III, MD and Matthew J. Krasin, MD
http://www.cure4kids.org/seminar/21

Seminar #164 Nasopharyngeal Carcinoma in Children (In Portuguese)
Carcinoma nasofaringeano em crianças e adolescentes
Carlos Rodriguez-Galindo, MD, Kathleen J. Helton, MD, Jesse J. Jenkins, III, MD and Matthew J. Krasin, MD
http://www.cure4kids.org/seminar/164
APPENDIX

A – 1 Nasopharyngeal Carcinoma

Axial schematic illustration of a nasopharyngeal carcinoma. Most commonly, the tumor is located in the lateral wall of the nasopharynx around the ostium of the Eustachian tube, the fossa of Rosenmuller. Spread may occur:

directly:
  - anteriorly (nasally)
  - inferiorly (pharyngeal)
  - superiorly (sphenoidal)
  - posteriorly (region of first cervical vertebra)
  - laterally (parotid gland; IX, X, XI, XII cranial nerves)

lymphatic: upper deep cervical lymph nodes

haematogenous: spinal column, lung and liver

Neurographics, Oakbrook, IL
www.neurographics.org/2/2/2/Fig10.shtml

General Practice Notebook
http://www.gpnotebook.co.uk/simplepage.cfm?ID=1925906422&linkID=23471&cook=no
A – 2  Cervical Lymphadenopathy is usually the presenting symptom of NPC

![Image of a patient's neck]

IPTQ website
www.iptq.com/cases/nose&throat_ca1.htm

A – 3  Lymph node chain at risk for metastatic spread

![Diagram of neck with highlighted lymph nodes]

Ipsilateral Nodal Groups
Schematic illustrations demonstrate the ipsilateral and contralateral nodal groups most likely at risk for developing nodal metastases from nasopharyngeal carcinoma. Note that only the most common nodal groups are highlighted on each side using the following color scheme: red > 45%, dark blue = 15%-45%, purple < 15%.

A – 4 Osteoarthropathy – Clubbing

**A – 5 AJCC Staging System for Nasopharyngeal Carcinoma**

<table>
<thead>
<tr>
<th>Value</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumor confined to the nasopharynx</td>
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</tbody>
</table>
| T2    | Tumor extends to soft tissue of oropharynx and/or nasal fossa  
|       | T2a: Without parapharyngeal extension  
|       | T2b: With parapharyngeal extension |
| T3    | Tumor invades bony structures and/or paranasal sinuses |
| T4    | Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, or orbit |
| N0    | No regional lymph node metastasis |
| N1    | Unilateral metastasis in lymph node(s) measuring ≤ 6 cm in greatest dimension above the supraclavicular fossa |
| N2    | Bilateral metastasis in lymph node(s) measuring ≤ 6 cm in greatest dimension above the supraclavicular fossa |
| N3    | Metastasis in a lymph node(s)  
|       | N3a: > 6 cm in greatest dimension  
|       | N3b: Extension to the supraclavicular fossa |
| M0    | No distant metastasis |
| M1    | Distant metastasis |

Stage I  
- T1  
- N0  
- M0

Stage IIA  
- T2a  
- N0  
- M0

Stage IIB  
- T1  
- N1  
- M0  
- T2a  
- N1  
- M0  
- T2b  
- N0-1  
- M0

Stage III  
- T1  
- N2  
- M0  
- T2  
- N2  
- M0  
- T3  
- N0-2  
- M0

Stage IVA  
- T4  
- N0-2  
- M0

Stage IVB  
- Any T  
- N3  
- M0

Stage IVC  
- Any T  
- Any N  
- M1