NASOPHARYNGEAL CARCINOMA:
A CONCISE CLINICO-RADIOLOGICAL APPROACH TO ADVANCED DISEASE

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AGENDA

• Our Patient: Clinical Presentation
• Clinicopathological Features of Nasopharyngeal Carcinoma
• Role of Radiology in NPC
• Systematic Approach to CT/MR in NPC
• Review of Relevant Anatomy – The Foramina, The Fossa, & The Bones
• Our Patient: Radiological findings
  • CT Sinus w/o contrast
  • MR Skull Base w/ contrast
• Applying the Systematic Approach
OUR PATIENT: CLINICAL PRESENTATION

• 61yo Chinese gentleman from Guangdong province, Southern China.

• He presented with intermittent R nasal bleeding for 6-7 months, on a background of nasal congestion of 1 year’s duration, which was initially attributed to seasonal allergies.

• No pain, hearing loss, change in smell, or neck swelling.

• Slight decrease in appetite, and lost 5-6lbs in the last 20 days.

• Ex-smoker of 20 pack-years. No family history of cancers.

• Physical exam was unremarkable.
OUR PATIENT: CLINICAL PRESENTATION

• Nasoendoscopy was done.
• A right large, obstructive mass obstructing the posterior choanae was found.
• CT and MR were done, which found a large right nasopharyngeal mass suggestive of nasopharyngeal cancer.
• Mass was biopsied, which confirmed histopathologically the diagnosis of nasopharyngeal cancer (non-keratinizing, EBER+).
CLINICOPATHOLOGICAL FEATURES OF NPC
NASOPHARYNGEAL CA

- 70% of NPCs are advanced (Stage III or IV) at diagnosis.
  - Occurs in the posterior nasal space, with symptoms only occurring with advanced and locally invasive disease.

- Unique epidemiological distribution.
  - Highest incidence in Southern China, Hong Kong, Singapore, and Southeast Asia (up to 25 cases per 100,000 people).
  - Common in ethnic Chinese from the south of China (e.g. Cantonese, Hokkiens).
  - Rare in the United States (<1 case per 100,000 people).
EPIDEMIOLOGY

- Most commonly occurs among 31 – 60yo (80%).

- Bimodal age distribution
  - Second decade of life
  - Sixth decade of life.

- M:F = 3:1
ETIOLOGY

15.5% of NPC patients had a first-degree relative who had the same condition.

NPC expresses Epstein-Barr encoded ribonucleic acids (EBERs) within NPC cells.

It is believed that EBV is not the initiating event in NPC, but rather potentiates tumorigenesis via latent infection of a predisposed nasopharyngeal epithelial cell.

HLA-A2, HLA-Bw46, HLA-B17, HLA-Bw58, HLA-DR3, HLA-DR9 are significantly more prevalent in NPC patients.

Diets high in nitrosamines or preservatives, such as salted fish, eggs, and vegetables.

From Tan KS, Loh KS. (2015). Cummings Otolaryngology, 6E: Chapter 96 – Benign and Malignant Tumours of the Nasopharynx.
CLINICAL PRESENTATION

- Most common presentation in NPC is the presence of a neck lump (60%), due to metastatic disease in the cervical lymph nodes.
  - Typically Level V and Level II.
- Second most common presenting symptom is blood in saliva or sputum (40%).
- Third most common presenting symptom is deafness (30%), due to conductive hearing loss from OME secondary to Eustachian tube dysfunction.
- Fourth-most common presenting symptom is epistaxis (23%). Not as common as the tumor is located in the postnasal space.
- Other symptoms include: nasal obstruction (17%), tinnitus (14%), and cranial nerve palsies (9.5%).
  - Of cranial n. palsies, most common nerves affected in descending order of frequency are the 6th, 5th, 12th, and 9th/10th nerves.
CORRELATING CLINICAL PRESENTATION TO ANATOMY
Obstruction of Eustachian tube opening in nasopharynx, resulting in OME and conductive hearing loss.

From Netter’s Clinical Anatomy, 5e
RELATING ANATOMY TO CLINICAL PRESENTATION

**NP mass**
- Extension through sphenoid bone intracranially.
- Intracranial extension, CN palsy, cavernous sinus involvement.
- Epistaxis, nasal obstruction, anosmia
- Extension to soft palate.
- Dysphagia

**Extension through choanae into nasal cavity**

**Extension through choanae into nasal cavity**

**Frontal sinus**

**Sphenoidal sinus**

**Nasal septum**

**Choanae (posterior nasal apertures)**

**Lateral process of nasal septal cartilage**

**Major alar cartilage**

**Nasal vestibule**

**Anterior nasal spine**

**Incisive canal**

**Oral cavity**

**Tongue**

**Soft palate**

**Falx cerebri**

**Dura mater**

**Sella turcica**

**Pharyngeal tonsil**

**Torus tubarius**

*From Netter’s Clinical Anatomy, 5e*
Any Chinese adult male presenting with a neck lump, blood-stained sputum, and unilateral deafness has **NPC until proven otherwise**
DIAGNOSIS OF NPC

- Gold standard is biopsy of mass with histopathologic confirmation.
  - Usually an office procedure performed via a rigid nasoendoscope under LA.

- **WHO Classification of Nasopharyngeal Carcinoma.**
  - **Type I** – keratinizing carcinoma (i.e. SCC)
  - **Type II** – non-keratinizing carcinoma
  - **Type III** – basaloid squamous cell carcinoma* (90%)
ROLE OF RADIOLOGY IN NPC
ROLE OF RADIOLOGY IN NPC

- Crucial in the workup and management of nasopharyngeal carcinoma.

- Staging
  - To delineate extent of local tumour invasion.
  - To assess for distal involvement e.g. nodal metastasis, bone involvement.
  - To guide patient management.

- Surgical planning
  - For recurrent cases of NPC.
ROLE OF RADIOLOGY IN NPC

- Diagnosis?
  - Gold standard in diagnosing NPC remains **nasoendoscopic biopsy**.
  - King et al. (2011) found that **MR had a sensitivity of 100%** for cancer detection, that was **significantly higher than that of endoscopy** (90%, $P < .01$) and comparable to that of endoscopic biopsy (95%, $P = .12$).

- MR may help identify cancers missed at endoscopy and endoscopic biopsy
## MENU OF TESTS

<table>
<thead>
<tr>
<th>LOCOREGIONAL ASSESSMENT</th>
<th>SYSTEMIC ASSESSMENT</th>
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<tbody>
<tr>
<td><strong>CT scan</strong></td>
<td><strong>Bone scintigraphy (Tc-99 disphosphonate)</strong></td>
</tr>
<tr>
<td>• Visualizes well soft-tissue of nasopharynx.</td>
<td>• Highest pick-up rate. Consistent with skeleton being the most common distant site of metastasis in NPC.</td>
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<tr>
<td>• Particularly useful in delineating clival and skull base erosions.</td>
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<tr>
<td><strong>MRI</strong></td>
<td><strong>F-18 FDG-PET</strong></td>
</tr>
<tr>
<td>• Increasing popular.</td>
<td>• Highly-sensitive for nodal and distal metastases; can be used to detect tumor recurrence.</td>
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<tr>
<td>• Imaging modality of choice for NPC.</td>
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<tr>
<td>• Superior definition in detecting soft-tissue changes.</td>
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<tr>
<td>• Superior delineation of intracranial involvement.</td>
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<td><strong>Bone scintigraphy (Tc-99 disphosphonate)</strong></td>
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<tr>
<td><strong>CT Thorax or CXR</strong></td>
<td><strong>CT Abdomen or U/S Liver</strong></td>
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OUR PATIENT:
RADIOLOGICAL TESTS DONE

• 13 Jan 2016 – CT sinus w/o contrast
• 9 Feb 2016 – MR skull base w&w/o contrast
• 9 Feb 2016 – MR soft-tissue neck w&w/o gado
• 11 Mar 2016 – FDG tumor imaging (PET-CT)
• 18 May 2016 – CXR (PA and Lateral)
• 16 Aug 2016 – FDG tumor imaging (PET-CT)
• 14 Nov 2016 – FDG tumor imaging (PET-CT)
• 11 May 2017 – CT sinus w/o contrast for surgical planning
SYSTEMIC APPROACH TO READING CT/MR IN NPC

PART I: CONFIRMING NPC
SYSTEMIC APPROACH TO CT/MR IN NPC (I)

• To confirm the presence of nasopharyngeal carcinoma.

• CT Features include:
  • Soft-tissue mass that is centered around the fossa of Rosenmüller (posterolateral recess of the pharyngeal wall).
  • Heterogenously enhancing tumour mass

• MR Features include:
  • T1: isointense to muscle
  • T2: isointense/hyperintense to muscle on fat saturation (eliminate fat signal, only contrast lighting up); look for fluid in middle ear.
FOSSA OF ROSENMÜLLER – KEY TO NPC

- Posterolateral or pharyngeal recess.
- Located posterior to the torus tubarius.
- Most common site of origin for NPCs.
- Can be visualized on nasoendoscopy, CT, and MR.

From RANZCR Part 1 Wikia
http://ranzcrpart1.wikia.com/wiki/Nasopharynx:Rosenm%C3%BChler_fossa
FOSSA OF ROSENMÜLLER – KEY TO NPC

From Amanda Person, Pinterest
https://www.pinterest.com/pin/4222193377383966

View of naso-pharynx via scope placed through left nostril.

- Fossa of Rosenmüller
- Torus Tubarius
- Salpingo-pharyngeal fold
- Salpingo-palatine fold
- Levator fold (levator veli palatini)
- Eustachian tube orifice (ostium pharyngeum)
- Posterior floor of nose = dorsal soft palate

Nasopharynx – Surface Anatomy
FOSSA OF ROSENMÜLLER – KEY TO NPC

From Cumming’s Otolaryngology, 6E.

Nasopharyngeal mass from the Fossa of Rosenmüller occupying the entire postnasal space.
FOSSA OF ROSENMÜLLER

Torus tubarius

Eustachian tube opening

Fossa of Rosenmüller

From headneckbrainspine.com
SYSTEMIC APPROACH TO CT/MR IN NPC (II)

- Important to assess bony and key intracranial structures for involvement.

### 6 QUADRANT APPROACH

<table>
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<tr>
<th>SUPERIORLY</th>
<th>INFERIORLY</th>
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<tr>
<td>Cavernous sinus</td>
<td>Oropharyngeal involvement</td>
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<tr>
<td>Pterygopalantine fossa</td>
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THE FORAMINA, THE FOSSA, & THE BONES
The foraminal foramina are important as they provide a route for tumors in intracranial extension.
THE FORAMINA

Foramen rotundum

- Runs inferolaterally in an oblique path.
- Joins the middle cranial fossa with the pterygopalatine fossa.

Contains:
- Maxillary nerve (V2) of the trigeminal nerve.
Foramen ovale

- One of two foramina in the greater wing of sphenoid bone.
- Most common route of intracranial spread in NPC.

Contains:
- Mandibular nerve (V3) of the trigeminal nerve.
- Emissary veins to cavernous sinus
- Accessory meningeal artery
- Lesser petrosal nerve (br. of glossopharyngeal nerve)

From headneckbrainspine.com
Foramen spinosum

- One of two foramina in the greater wing of sphenoid bone.

Contains:
- Middle meningeal artery and vein.
- Meningeal branch of the mandibular nerve (supplies the dura mater).
The Foramina

Foramen lacerum

- Situated anteromedial to the carotid canal.
- Common route of intracranial spread in NPC.
- It is a potential space – filled with cartilage after birth.

Contains:
- Vidian artery
- Vidian nerve
The pterygopalantine fossa is a crucial region that connects many intracranial passages.

If involved, be highly suspicious for V2 nerve and Vidian nerve involvement.
THE FOSSA

Pterygopalantine fossa

- Deep to the infratemporal fossa, medial to the pterygomaxillary fissure.

Connects to:
- Foramen rotundum
- Vidian canal
- Sphenopalatine foramen
- Pterygomaxillary fissure

From Khonsary SA et al. (2013).
https://openi.nlm.nih.gov/detailedresult.php?img=P MC3858801_SNI-4-422-g006&req=4
Important to assess the extent of local disease.
THE BONES

Sphenoid bone

- Body of the sphenoid.
- 2 greater wings
- 2 lesser wings
- Pterygoid processes
THE BONES

Clivus

• Part of the basilar occipital bone.

Important relations:
• Abducens nerve (CN VI) passes along the clivus along its course.
OUR PATIENT:
CT SINUS W/O CONTRAST
Blue arrows: Foramen rotundum.

Yellow arrows: Vidian nerve canal

Green arrows: Lateral pterygoid

Sclerosis of pterygoid bone can be seen.

From PACS. BIDMC
Blue arrows: Eustachian tube

Yellow arrows: Torus tubarius

Green arrows: Fossa of Rosenmüller

Right nasopharyngeal mass seen with obliteration of FOR.
Right 3.8 cm x 3.2 cm nasopharyngeal mass seen with obliteration of FOR.

Extension of mass into R choanae can be seen.

Nasopharyngeal mass seen also extends over the midline in the posterior nasal space.
Yellow arrows: Pterygopalatine fossa.

Effacement of fat on the right when compared to left, with loss of fat-attenuation. This is suggestive of R pterygopalatine fossa involvement.
Blue arrows: Pterygoid process of sphenoid bone.

Sclerosis of the right pterygoid bone more than the left, suggestive of local extension to the sphenoid bone.
Blue arrows: Foramen lacerum
Yellow arrows: Foramen ovale
Green arrows: Foramen spinosum
Purple arrows: Carotid canal
Blue arrows: Foramen rotundum
Yellow arrows: Middle ear cavity
Green arrows: Mastoid air cells

Opacified middle-ear cavity and mastoid air cells on the right, consistent with nasopharyngeal carcinoma.
Right 3.8 cm x 3.2 cm x 2.7 cm nasopharyngeal mass seen in posterior nasal space.
Erosion and infiltration of clivus is seen.
Normal left pterygopalatine fossa
Sclerosis of adjacent pterygoid process and sphenoid bone.
OUR PATIENT: 
MR SKULL BASE W/ CONTRAST
Right heterogenous isointense nasopharyngeal mass is seen.
Effacement of the right pterygopalantine fossa fat is better visualized on MR.
Blue arrows: fluid opacification of R maxillary sinus

Yellow arrows: Fluid opacification of R mastoid air cells, secondary to nasopharyngeal mass
Blue arrows: V2 branch of the trigeminal nerve

Yellow arrows: Vidian nerve

Thickening and enlargement of the right V2 and Vidian nerve is seen, suggestive of perineural spread.
Extension of tumor through the foramen ovale into the cavernous sinus is seen. Involvement of the V2 nerve is also seen.
## APPLYING THE SYSTEMIC APPROACH

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Possible differentials?
PUTTING IT ALTOGETHER – TNM STAGING

T: Tumor invasion
- T1 – confined in nasopharynx only
- T2 – extends into soft tissues
- T3 – extends into bony structures or paranasal sinuses
- T4 – extends into intracranially / cranial nerve / infratemporal fossa / orbit

N: Nodal involvement
- N1 – unilateral, <6cm
- N2 – bilateral, <6cm
- N3 - >6cm or involvement of supraclavicular fossa.

M: Metastases
- M0 – no distal metastases
- M1 – distal metastases present

On CT/MR,
T: invasion of intracranial content and adjacent bony structures.

On FDG PET-CT,
N: bilateral nodal involvement <6cm maximal diameter above supraclavicular fossa.
M: no distal metastases.

∴ T4 N2 M0

✓ Stage 4 non-keratinizing nasopharyngeal carcinoma
## Prognosis by Stage

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<th>Stage</th>
<th>Relative 5-year Survival Rates</th>
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<tr>
<td>I</td>
<td>72%</td>
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<tr>
<td>II</td>
<td>64%</td>
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<tr>
<td>III</td>
<td>62%</td>
</tr>
<tr>
<td>IV</td>
<td>38%</td>
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- T4 N2 M0
- Stage 4 non-keratinizing nasopharyngeal carcinoma

From American Cancer Society, cancer.org
MANAGEMENT OF NASOPHARYNGEAL CARCINOMA

- Multidisciplinary management
- Dental clearance
  - Essential as radiation field involves the oral cavity.
  - Any decaying, unhealthy teeth are extracted to prevent osteomyelitis during radiotherapy.
- Audiological investigations – pure-tone audiograms

- Definitive therapy
  - Radiotherapy
    - Stage I and II – radiotherapy ONLY.
    - Stage III and IV – chemoradiotherapy.
    - Recurrent disease – surgical resection.
REFERENCES


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