Nasal Cavity, Paranasal Sinus Cancer and Nasopharyngeal Cancer

Michael Myers M.D.

9/9/15
Regroup for simplicity

1. Maxillary Sinus cancer
2. Ethmoid sinus/nasal Cavity
3. Nasopharyngeal Cancer
Maxillary Sinus Background

1. Most common site amongst the other paranasal sinuses and nasal cavity.

2. Risk factors include occupational exposure ie wood dust, viral such as hpv and EBV-lymphoma, tobacco smoke.

3. Common presenting symptoms include:
1. Most common site amongst the other paranasal sinuses and nasal cavity.

2. Risk factors include occupational exposure ie wood dust, viral such as hpv and EBV-lymphoma, tobacco smoke.

3. Common presenting symptoms include:
   - facial /dental pain, nasal obstruction, and epistaxis
   - cranial neuropathy (especially abnormalities of extraocular movements or trigeminal hypesthesia),
     - chronic sinusitis
     - facial edema,
     - vision loss
     - rhinorrhea,
   - A classic triad of facial asymmetry, palpable/visible tumor in the oral cavity, and visible intranasal tumor
Maxillary Sinus Workup

• History and Physical

• Head and Neck CT with contrast (MRI as needed)

• PET/CT scan for stage III/IV

• Biopsy (transnasal preferred)

• Referral to dentist/prosthetic consultation

• Referral to medical oncologist pending path/surgery
Maxillary Sinus Anatomy

Borders:

Anterolateral: Facial bone
Superior: orbital floor
Inferior: hard palate
Medial: nasal cavity
Posteromedial: Infratemporal fossa
Maxillary Sinus Staging

T1:
Maxillary Sinus Staging

T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone

T2:
Maxillary Sinus Staging

T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone

T2: Bone erosion or destruction including extension into hard palate or middle nasal meatus except extension to posterior wall and pterygoid plates

T3:
Maxillary Sinus Staging

T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone

T2: Bone erosion or destruction including extension into hard palate or middle nasal meatus except extension to posterior wall and pterygoid plates

T3: Tumor invades: 1. post. wall of maxillary sinus 2. subcutaneous tissue 3. floor or medial wall of orbit 4. pterygoid fossa, ethmoid sinuses.

T4a:
Maxillary Sinus Staging

T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone

T2: Bone erosion or destruction including extension into hard palate or middle nasal meatus except extension to posterior wall and pterygoid plates

T3: Tumor invades: 1. post. wall of maxillary sinus 2. subcutaneous tissue 3. floor or medial wall of orbit 4. pterygoid fossa 5. ethmoid fossa

T4a: Tumor involves 1. anterior orbital contents 2. skin of cheek, pterygoid plates, infratempral fossa, cribiform plate, sphenoid or frontal sinuses

T1-T4a is considered resectable
Maxillary Sinus Staging

T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone

T2: Bone erosion or destruction including extension into hard palate or middle nasal meatus except extension to posterior wall and pterygoid plates

T3: Tumor invades: 1. post. wall of maxillary sinus 2. subcutaneous tissue 3. floor or medial wall of orbit 4. pterygoid fossa 5. ethmoid fossa

T4a: Tumor involves 1. anterior orbital contents 2. skin of cheek, pterygoid plates, infratempral fossa, cribriform plate, sphenoid or frontal sinuses

T4b: Tumor involves 1. orbital apex 2. dura or brain 3. middle cranial fossa 4. cranial nerves other than maxillary division V2 of trigeminal nerve 5. nasopharynx 6. clivus
Maxillary Sinus Management
Stage I/II

Surgical Resection
Post Op radiation for high risk features
For SNUC, SNEC, or Small Cell include med onc consult
Maxillary Sinus Management
Stage I/II

Consider post op radiation for:

1. positive margins after re-resection
2. perineural invasion
3. above ohngren’s line with adenoid cystic histology (per NCCN)
Ohngren’s line is used to divide the maxillary sinus into an anteroinferior portion (infra-structure), which is associated with a good prognosis, and a poster superior portion (supero-structure), which has a poor prognosis. The poorer outcome associated with supero-structure cancers reflects early invasion of these tumors to critical structures including the eye, skull base, pterygoids, and infratemporal fossa.
Maxillary Sinus Management
Stage III/IV

1. T3-T4aN0: Surgery -> RT

2. T4b or inoperable: Definitive RT or ChemoRT

3. If bulky tumor requiring orbital exenterating consider preoperative chemotherapy
RT Technique

- IMRT concomitant boost for both definitive and post-op
- Fuse PET/MRI/etc.
- ~70/60/54 in 33 fractions for definitive. 63-66 post op.
- Consider RP, IB and II LN electively based on Brizel et al.
Ethmoid Sinus and Nasal Cavity

Background

1. Ethmoid and Nasal cavity cancers are equally rare and sphenoid and frontal sinus tumors are very uncommon.

2. Nasal cavity is most common site for esthesioneuroblastoma

1. Common presenting symptoms include:
   Nasal congestion, periorbital pain, epistaxis, vision change, mid face numbness.
Work up same as for Maxillary Sinus
Anatomy

Subsites
Nasal Cavity: Septum, wall, floor, vestibule
Ethmoid Sinus: Right and Left
Nasal Cavity and Ethmoid Sinus Staging

Subsites
Nasal Cavity: Septum, wall, floor, vestibule
Ethmoid Sinus: Right and Left

T1:
Nasal Cavity and Ethmoid Sinus Staging

Subsites
Nasal Cavity: Septum, wall, floor, vestibule
Ethmoid Sinus: Right and Left

T1: Tumor limited to one subsite with or without bone destruction.

T2:
Nasal Cavity and Ethmoid Sinus Staging

T1: Tumor limited to one subsite with or without bone destruction.

T2: Tumor involves two subsites or extending to involve and adjacent region within the nasoethmoid complex. Again bone destruction does not matter.

T3:
Nasal Cavity and Ethmoid Sinus Staging

T1: Tumor limited to one subsite with or without bone destruction.

T2: Tumor involves two subsites or extending to involve and adjacent region within the nasoethmoid complex. Again bone destruction does not matter.


T4a: Tumor invades anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
Nasal Cavity and Ethmoid Sinus Staging

T1: Tumor limited to one subsite with or without bone destruction.

T2: Tumor involves two subsites or extending to involve and adjacent region within the nasoethmoid complex. Again bone destruction does not matter.


T4a: Tumor involves 1. anterior orbital contents 2. skin of cheek, pterygoid plates, infratempral fossa, cribriform plate, sphenoid or frontal sinuses

T4b:
Nasal Cavity and Ethmoid Sinus Staging

T1: Tumor limited to one subsite with or without bone destruction.

T2: Tumor involves two subsites or extending to involve and adjacent region within the nasoethmoid complex. Again bone destruction does not matter.


T4a: Tumor involves 1. anterior orbital contents 2. skin of cheek, pterygoid plates, infratempral fossa, cribiform plate, sphenoid or frontal sinuses

T4b: Tumor involves 1. orbital apex 2. dura or brain 3. middle cranial fossa 4. cranial nerves other than maxillary division V2 of trigeminal nerve 5. nasopharynx 6. clivus
Nasal Cavity and Ethmoid Sinus Management Stage I-IVa

Craniofacial resection followed by RT is the preferred treatment.
Nasal Cavity and Ethmoid Sinus
Unresectable or inoperable

Definitive RT or chemoRT
RT Technique

Same as Maxillary sinus except:

- Would cover only RP nodes unless invading into lymphatic rich structures
- Coverage of the incision site for the craniofacial resection is not necessary.
Nasopharyngeal Carcinoma
Anatomy

- Cuboidal shape, slanted roof
- Anterior: Posterior choanae
- Inferior: Free border of the soft palate
- Floor: Superior surface of the soft Palate
- Posterior: Clivus and C1-2 vertebrae
- Superior and Posterior: Irregularly shaped due to pharyngeal bursae, tonsils, hypophysis
Histology

• WHO class 1- Keratinizing squamous cell
  – more common type found in US
  – Class I is worse prognosis
  – Least likely to spread to nodes 60%
• Class 2a- Non-keratinizing squamous cell
  (better local control/worse distant spread)
• Class 2b-
  Undifferentiated/Lymphoepithelioma-
  common in Asia, better prognosis
Natural history...

- Most commonly arises from the mucosal epithelium within the lateral nasopharyngeal recess or fossa of Rosenmüller (a recess behind the entrance of the eustachian tube opening)
- Risk of nodal spread based on histology and T-stage
- WHO class 1 Greater likelihood for uncontrolled local growth, 60% nodal involvement
- WHO class 2b- Most likely to spread to nodes 80-90%
Sites nodal metastases

99 pts... 53% bilateral, 10% N0, Level II most common.

Fletcher and Million 1965
Staging

- **T1**: Tumor confined to nasopharynx
- **T2**: Tumor extends to soft tissue of the oropharynx and/or nasal fossa
  - T2a: Without parapharyngeal extension
  - T2b: With parapharyngeal extension
- **T3**: Tumor invades bony structure and/or paranasal sinuses
- **T4**: Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, or orbit

- **N1**: Unilateral mets in a node 6 cm or less and superior to the SCV fossa
- **N2**: Bilateral mets in a node 6 cm or less superior to the SCV fossa
- **N3**:
  - N3a: Any node greater than 6 cm
  - N3b: Node located in or extends into the SCV

- **M1**: Metastatic disease (Lungs most common site)
Nasopharynx Management

NCCN Guidelines Version 1.2015
Cancer of the Nasopharynx

CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

T1, N0, M0 → Definitive RT to nasopharynx and elective RT to neck

T1, N1-3; T2-T4, any N

Concurrent chemo/RT, followed by adjuvant chemotherapy

or

Concurrent chemo/RT, not followed by adjuvant chemotherapy (category 2B)

or

Induction chemotherapy (category 3), followed by chemo/RT

or

Any T, any N, M1

Concurrent chemo/RT

FOLLOW-UP

Neck: Residual tumor → Neck dissection

Neck: Complete clinical response → Observe

Follow-up (See FOLL-A)

Recurrent or Persistent Disease (See ADV-3)

RT to primary and neck or Chemo/RT, as clinically indicated

Platinum-based combination chemotherapy

See Principles of Radiation Therapy (NASO-A).
See Principles of Systemic Therapy (CHEM-A).
See Discussion on induction chemotherapy.
Can be used for select patients with distant metastasis in limited site or with small tumor burden, for patients with symptoms in the primary or any nodal site.
See Principles of Surgery (SURG-A).

Note: All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Chemoradiotherapy Versus Radiotherapy in Patients With Advanced Nasopharyngeal Cancer: Phase III Randomized Intergroup Study 0099

By Muhyi Al-Sarraf, Michael LeBlanc, P.G. Shanker Giri, Karen K. Fu, Jay Cooper, Te Vuong, Arlene A. Forastiere, George Adams, Wael A. Sakr, David E. Schuller, and John F. Ensley
Enrollment Criteria

1. Histology proven stage III and IV NPC without evidence of metastasis.
2. SWOG performance 0-2.
Arms

- 147 patients evaluated
- Radiotherapy only (n = 69)
- Chemoradiotherapy (n = 78)
Treatment

Radiotherapy:

1. CTV = GTV + 2 cm; 70 Gy (1.8-2.0 Gy/d)
2. Minimum total dose to the neck nodes:
   - 50 Gy for N0
   - 66 Gy for nodes ≤ 2 cm
   - 70 Gy for nodes > 2 cm

Target volume received at least 90% or greater of the mid-depth central axis dose.
Chemotherapy

Concurrent:
Cisplatin 100mg/m² on days 1, 22, 42 during radiotherapy.

Adjuvant:
Cisplatin 80mg/m² and
5-Fu 1,000mg/m²/d every 4 weeks for a total of 3 cycles post radiotherapy.
Progression free survival

The 3-year actuarial PFS were 24% and 69% P < .001
The 3 year overall survival was 47 and 78%, for XRT and ChemoXRT, respectively (P = .005)
Criticisms

- Small study
- Low overall survival for XRT group
- Off protocol treatment
Take home message

• Al-Sarraf was the first randomized study to show an overall survival benefit with concurrent chemoradiotherapy.
The UCSF Experience
(Lee et al IJROBP Vol 53:12-22 2002)
Patient characteristics:

1. N = 67
2. Age = 49 (17-82)
3. Race (82% Asian)
4. Histology (WHO II/III)
Tumor characteristics:

- Histology
- Stage

Table 1. Distribution of patients by the 1997 American Joint Committee on Cancer Staging Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>9</td>
<td>7</td>
<td>10</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>T2</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>T3</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>T4</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>20</td>
<td>24</td>
<td>8</td>
<td>67</td>
</tr>
</tbody>
</table>
Treatment

- 65–70 Gy to GTV including positive neck nodes.

- 60 Gy to CTV (GTV + unspecified margin for microscopic spread)

- 50-60 Gy to clinically negative neck

- Prescription was 1.8 Gy/fraction/day to the CTV.
Treatment

- 33 patients treated with forward planning
- 26 patients had HDR boost.
- 55 (75%) of patients had concurrent cisplatin and adjuvant cisplatin and 5-FU using 0099 protocol.
Results

1. 1 local recurrence at primary site at 25 months after completion of therapy

2. 1 case of neck recurrence at 13 months after completion of radiotherapy.

3. 17 (25%) patients developed distant metastases.
<table>
<thead>
<tr>
<th></th>
<th>Local control</th>
<th>Regional control</th>
<th>Systemic control</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>88%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>97%</td>
<td>98%</td>
<td>66%</td>
</tr>
</tbody>
</table>
Radiation Technique

- Dose: 70/60/54 in 33 fraction (2.12/1.8/1.64)

- I follow RTOG 0615 taking some liberties. The volumes are quite large and require some clinical/critical judgement for the CTV expansion. I have found my residency attending's/mentors invaluable resources when planning years after graduating.