Nasopharyngeal Cancer: Clinical and Research Update

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Disclosures

Clinical Trial Support:
  • Genentech
  • Bristol-Myers-Squibb (pending)
  • Merck (pending)

Honoraria:
  • Astra-Zeneca (expert panel)
Boundaries of the Nasopharynx

- Like a “cube” with 6 sides
- Front
  - back of nasal cavity
- Back
  - upper spine
- Upper
  - “clivus” (base of brain)
- Lower
  - palate
- Two side walls
  - Eustachian tube opening
  - fossa of Rosenmuller
Spread of Cancer from the Nasopharynx

• Cancer can spread any of the 6 directions
  – Most common:
    • Forward into the nose
    • Down to the throat
    • Into base of skull
  – Sometimes:
    • Further up into brain
  – Rarely:
    • Out of the ears
    • Back into the spine
Nasopharyngeal carcinoma

- NPC is rare in Europe and the U.S.
- NPC is extremely common in southern China and Hong Kong, where the rate is 25 times higher than the West (18% of all cancer)
- NPC has been called "the Cantonese cancer"
- NPC is also common in Taiwan, Singapore, Malaysia, Thailand, and Vietnam; also Africa, Mediterranean, and among the Alaska Inuit
Incidence in various countries

• < 1% of all cancers in U.S. (2/100,000)

• Incidence in Males/100,000/yr:
  Hong Kong 28  Alaska 17.2
  Connecticut 0.6  Singapore 16.8
  Japan 0.4
Incidence of NPC Worldwide

Globocan, IARC 1989
San Francisco Bay Area

• In San Francisco, we have a high proportion of southern Chinese/Hong Kongese immigration
• There is a similar pattern of migration to Southeast Asia, Canada, and Australia
• Usually people are diagnosed with NPC at age 50-60 but they can be very young (teens-20s)
• Siblings or children of NPC patients are at higher risk
• The ethnic predisposition for NPC carries into the second generation after immigration
Age-Standardized Mortality Rates From NPC in California

(P. Buell, Cancer Res. 34:1189-1191, 1974)
Risk factors

• Smoke from wood fires (polycyclic hydrocarbons)
  – chronic nasal infection, poor hygiene, poor ventilation
• Occupational exposure to dust, smoke, inhalants
• Salted fish (nitrosamines) → RR 5.6
• Smoking, Alcohol
• Formaldehyde
• Radiation exposure
• AND…. GENETICS + EBV…. 
Role of Epstein Barr Virus (EBV)

- EBV is a common virus
- 95% of people in U.S. are exposed by 30–40 years of age
- The World Health Organization does not have preventative measures because it is so easily spread and is worldwide
- Very rarely does Epstein-Barr virus lead to cancer
Early symptoms of NPC

- Lump in the **neck**
- Nasal obstruction or “congestion” or trouble breathing; bleeding from **nose**
- Deep ear pain or “stuffy **ears**” or sudden hearing problem or ringing/buzzing

- Sore throat/difficulty swallowing
- Pain in mouth or throat or neck
- Facial numbness or changes in vision
ENT or OHNS

• History and physical examination
  – Examination with nasal endoscopy

• Biopsy of cancer mass: cupped forceps from nose, or thin needle from neck

• MRI or CT scan

• PET/CT

• Bloodwork
What NPC looks like on MRI scans: early to advanced stage
Biopsy of a nasopharynx mass
Fine needle aspiration biopsy from enlarged neck node

Biopsy needle inserted into lymph node and sample removed
Spread from nasopharynx to the lymph nodes of the neck

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<td>169 = 87%</td>
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Ipsilateral

Contralateral

Nasopharynx
Spread from nasopharynx to the lymph nodes of the neck

• Lymph node involvement at diagnosis
  – 90% have one side of the neck
  – 50% have both sides of the neck
  – This is why we do not recommend surgery (cannot get it all out)

• From lymph nodes, cancer can spread to bones, liver, lungs
Treatment modalities

• Radiation + chemotherapy
• Chemotherapy is given for another 2-3 months after chemoradiation
• Surgery is only done if nasopharynx or neck that does not respond to chemoradiation
  – Do not start with a neck surgery!
  – Many other cancers of mouth and throat start with surgery – NPC Is unique!
NPC should be treated with intensity modulated radiation therapy (IMRT)
IMRT shapes the radiation from many angles → combining all of the shapes avoids the eyes and brain
High levels of Epstein Barr Virus in the blood predicts the outcome of the treatment

Pretreatment

1 week after RT completion

Lin, NEJM 2004;350:2461
NRG-HN001: National EBV Testing Study for Newly Diagnosed NPC

Intermediate or higher stage of disease

REGISTER

IMRT + cisplatin

EBV (-)

EBV (+)

No more treatment

Cisplatin + 5FU x3

Gemcitabine + paclitaxel x3

National cooperative group study
National Quality of Life Co-Chair: Dr. Yom, UCSF
T Cell sees the Cancer Cell - But interaction of PD-1 and PD-L1 deactivates the T Cell
T Cell sees the Cancer Cell - Blocking PD-1/PD-L1 interaction allows the T Cell to activate
UCSF-Singapore PD-1 Inhibition Study for Newly Diagnosed NPC

Intermediate or higher stage of disease

REGISTER

PD-1 inhibitor x 1 → IMRT + cisplatin + PD-1 inhibitor x 4*

PD-1 inhibitor x 7

* Patients will be tested for EBV, T cells, immunologic markers

Principal Investigator: Dr. Yom, UCSF
Collaborators: NCC and NUH Singapore
Randomized Phase II Study of Pembrolizumab vs Chemotherapy for Metastatic NPC

Eligibility:
- R/M NPC
- EBV+ by EBER IISH
- Platinum Pretreated
- ECOG 0 or 1

Stratification:
- Liver mets vs none

Randomized 1:1

Pembrolizumab 200 mg (MK-3475) Q3W

D/C Study Treatment
- 1. PD, or
- 2. Unacceptable Toxicity, or
- 3. Completed Treatment

Survival Follow-up

SOC
- Investigator’s choice of one of the following:
  - Docetaxel, Gemcitabine, Capecitabine

*Second Course of Pembrolizumab
Subjects randomized to Pembrolizumab who completed 2 years of treatment with confirmed response, may be eligible for retreatment with up to 1 additional year of Pembrolizumab at the time of recurrence in Survival Follow-up

Multi-center international study
Site PI: Dr. Algazi, UCSF
Adoptive T Cell Phase III Study for Metastatic NPC

Phase III Clinical Trial of Gemcitabine and Carboplatin followed by Epstein-Barr Virus-specific Autologous Cytotoxic T Lymphocytes vs Gemcitabine and Carboplatin

- **EBV+ NPC**
- Metastatic
- No prior metastatic therapy

Multi-center international study
Site PI: Dr. Algazi, UCSF
We welcome any collaborations to advance research in NPC at UCSF