Management of Lymph Nodes in Aggressive Non-Melanoma Skin Cancer

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OUTLINE
Overview of NMSC
Define Aggressive
Primary Ablation
Management of Lymph Nodes
  - Extent of Lymphadenectomy
  - Data on Risk of Occult Disease
  - Radiation / Chemotherapy Indications

Non-Melanoma Skin Cancer
80% - Basal Cell Carcinoma
20% - Cutaneous Squamous Cell Carcinoma
< 1% - Others:

Disclosures
None
Non-Melanoma Skin Cancer

80% - Basal Cell Carcinoma
20% - Cutaneous Squamous Cell Carcinoma
< 1% - Others: Dermatofibrosarcoma, Malignant fibrous histiocytoma, Adnexal malignancy, Merkel cell carcinoma

1.3 million cases/year in U.S. (More than all other cancers combined)

Primary Care / Dermatology
75% NMSC in the head and neck

Chen GJ 2006
Aggressive Head and Neck NMSC

< 5% of all cases
- 6000 cases of regional metastases / year
- 2500 deaths / year

Clinical Features of Aggressive NMSC

Treated By: Otolaryngology / Head and Neck Surgery
(and Dermatology / Plastic Surgery / General Surgery)
**Clinical Features of Aggressive NMSC**

- Size: >2 cm
- Location (Lip / Ear / Mask-Zone)
- Rapid Growth
- Radiation History
- Immunosuppression (cSCC)
- Recurrence

**Etiologies of High Risk Location**

- Projecting anatomy - More UV
- Thinner skin - Easier spread
- Embryologic fusion plates - Easier spread
- Abundance of nerves - Increased PNI
- Resection hesitancy - Closer margins

**Histopathologic Features of Aggressive NMSC**

**BCC**
- Infiltrative (Morpheaform)
- Sclerosing
- Mixed infiltrative
- Micronodular
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**cSCC**
- Poorly differentiated
- Spindle cell
- Desmoplastic
- Acantholytic

Thickness (4 mm, Clark IV)

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Both:
- Lymphovascular invasion
- Perineural invasion
- Positive margins

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**WORK UP**

Biopsy (Full thickness)

Physical Exam
(+ Nasopharyngolaryngoscopy)

Consider Imaging (CT, MRI, U/S?)

- cSCC > BCC
- Non palpable lymphadenopathy
- Subdermal infiltration
- Nerve involvement
- Bone erosion

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**Primary Treatment Of ANMSC**
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Identify aggressive subtypes

Ablation of primary with margins / Reconstruction:

Mohs (if no SQ)

or

Classic excision (w/ margins)
Primary Treatment Of ANMSC

Identify aggressive subtypes

Ablation of primary with margins / Reconstruction:

Mohs (if no SQ)
or
Classic excision (w/ margins)
- BCC: 0.4 cm
- cSCC: 1 cm
(Choo 2005)

Nonoperative / Cosmesis?
Consider XRT
Aggressive NMSC
Higher Risk for Regional Metastases

Management of Lymph Nodes in Aggressive NMSC

NODAL DRAINAGE PATTERNS

NODAL DRAINAGE PATTERNS
LYMPH NODE MANAGEMENT

If + Lymph Nodes Present (Exam / Radiology)

Perform Lymphadenectomy
All Intervening Lymphatic Beds

Posterolateral Neck Dissection
or
Parotidectomy / Neck Dissection
or
Neck Dissection

(Lentsch 2001)
If PE/Imaging: parotid positive and neck negative:

Parotidectomy and cervical lymphadenectomy:
- Apparent parotid metastases:
  - 20-44% occult neck metastases
  

What about the likelihood of occult LN disease and the need for elective regional lymphadenectomy?

Parotid and neck metastases do worse than parotid disease alone:
- 61% vs 79% 5 year DSS (p=0.027) (n=322)
  
  (Andruchow 2006)
Aggressive Basal Cell Carcinoma

Usually only locally destructive
<0.05% metastasis to regional nodes

BCC Becomes Dangerous With:
- Neglect
- Recurrence
- Immunosuppression

Aggressive BCC Lymph Node Management

Very little pure data
Extrapolated from cSCC
Very rare metastases (< 0.05%)
**Aggressive BCC Lymph Node Management**

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Aggressive BCC = Increased Recurrence

Consider imaging
Tumor Board referral / discussion
If very aggressive and N0
  – consider elective appropriate regional lymphadenectomy

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**Aggressive cSCC Lymph Node Management**

Perform imaging of lymph node beds

- N0: Strong consideration
  – Elective regional lymphadenectomy

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**Data on Aggressive cSCC LN Metastases**

Not many prospective studies exist

Many risk factors are interdependent not analyzed in multivariate analyses.

Most risk factor data shows risk for recurrence/DSS

Some data on risk for occult nodal disease

Authors often equate risk of recurrence with risk for occult disease

NCCN: High risk = increased recurrence / metastases

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Size

- > 2cm: 30% vs 9% regional mets 72% vs 95% DSS
  Rowe 1992

- > 4cm: 4.5 x Decreased DSS
  Clayman 2005

H-Zone:

  Increased BCC recurrence
  (p<0.01; n=2314)

  Silverman 1991

Higher regional mets (n=11)

Netterville 1998

Ear and lip:

  9 and 14% vs 5% regional mets

Recurrent ear and lip:

  45% and 31% vs 25% regional mets

Rowe 1992
Sentinel Lymph Node Biopsy

Used in malignant melanoma and breast carcinoma

Potential use in ANMSC

Indications For Adjuvant Radiation

Size: > 4 cm
Recurrence
Poor differentiation, Spindle cell
Close/Positive margins
PNI
Multiple levels of LN spread
ECS
INCREASE LOCOREGIONAL CONTROL
And Possibly Survival
IPSILATERAL XRT ONLY NECESSARY
Chemotherapy

Cisplatin +/- 5FU, Bleomycin, Doxycyclin

Indications:
Positive Surgical Margins
Multiple LNs
ECS

Extrapolated from mSCC
Small studies / Anecdotal

CONCLUSIONS
Most NMSC is treatable with primary ablation

Small subset – Aggressive (< 5%)

Identify aggressive characteristics

Have a strong consideration for
  - Imaging
  - Elective lymphadenectomy (cSCC)

If P+ / N+ : Appropriate lymphadenectomy + adjuvant tx

Necessity Benefit of elective lymph node treatment?
  - More data (especially prospective) needed
    - SLN Biopsy

THANK YOU
Extent of Elective Lymphadenectomy

Posterior scalp:
- Occipital
- Postauricular
- LN Levels 5a, 2, 3

Face/anterior scalp:
- Superficial parotidectomy
- LN Levels 1, 2, 3

Lips/MidFace:
- LN Levels 1, 2, 3
- (Perifacial LNs?)
- (Uni vs Bilateral)

Intraoperative: + LN -> Extend Lympadenectomy

Evidence for Use Of Radiation

If lymph nodes positive -> Adjuvant XRT improved local regional control:

If regional metastases:
Surgery and XRT better than surgery alone

80% vs 57% recurrence-free
73% vs 54% 5 year survival (p=0.004)

Parotidectomy 63%, XRT 46%, Combined 89%
(Taylor 1991)

Perineural invasion: XRT increased LC, DSS, OS
(Lai 2002)

Contralateral XRT not necessary
Contralateral LN very rare:


**2010 AJCC STAGING FOR BCC/SCC**

All skin (not just H/N) excluding eyelid skin

- **T1** - < 2cm
- **T2** - > 2cm (or 2+ high risk features)
- **T3** - Facial Bone
- **T4** - Spine / Skullbase

- **P1 / N1** - < 3cm
- **P2 / N2** - 2+ LNs and/or > 3cm and < 6cm
- **P3 / N3** - > 6 cm (or 7th nerve / Skullbase)

- **M1** - Any distant metastasis

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**Aggressive cSCC Lymph Node Management Evidence**

Superficial parotidectomy is adequate (vs total)  
(Total only to remove apparent disease)

- Most parotid lymph nodes are lateral to the facial nerve  
  (Hong 2005)

- Radical parotidectomy / Facial nerve excision

- No decreased recurrence
- No increased survival
Perineural Invasion
Increased Regional/Distant Mets (Breuninger 1990)
OS 60% vs 80%, DSS 65% vs 95%, RFS 65% vs 85% (Moore 2004)
Perineural Invasion (5-14%) (Leibovitch 2005, Williams 2001)

Histology
Spindle cell, Desmoplastic, Basosquamous, Acantholytic
Poor Differentiation (lymphatic/perineural invasion in 50% (Cassarino 2006)

Positive Margins
50% risk (Huang CC, 2004)

The following had 30-47% recurrence
>2cm, 4mm thickness, Perineural invasion,
Poor differentiation

Aggressive cSCC Lymph Node Management Evidence

Elective cervical lymphadenectomy extent:
- Levels 1, 2, 3 – SOHND
  (Barzilai 2005)
- 35% of elective neck dissections had occult pathology
  (Obrien 2001)

Imaging indicated:
- Only 20% of parotid disease apparent on physical exam.
  (Lai 2002, Audet 2004)
- Parotid and neck have high risk of occult metastases.
  (Moore BA 2005)
OTHER/RARITIES

Dermatofibrosarcoma
2-3cm margins or Mohs
+ margins -> radiation

Merkel Cell Carcinoma / Adenexal Malignancy
2-3 margins or Mohs
+ margins -> radiation
Elective regional lymphadenectomy

Risk Factors For Regional Metastases in NMSC

> 2 cm
Invasion into SQ
Lymphovascular invasion
From a scar
Inflammation
Recurrent

Evidence for Use Of Radiation

ANMSC RISK FACTORS

UV Light
Ionizing Radiation
Actinic Keratosis
Previous BCC or SCC
FH
Scar
 Syndromes (XP, Albinism, Gorlin)
HPV
Ear / Lip

Hematologic Malignancy (CLL)
AIDS
Organ Transplant

More progression/mortality
(Martinez 2003)
Aggressive Histopathologic Features Evidence

**IMAGING**

- Ultrasound
  - No radiation
  - Lymph Node Evaluation
  - No evaluation of nerve involvement/areas deep to bone

- CT scan Neck With Contrast
  - Lymph Node Features:
    - Maximum Axial Diameter: Level 1 or 2: >1.5cm, Rest: >1cm
    - Heterogeneous Enhancement
    - Necrosis
    - Rounded Contour
    - Loss of Fatty Hilum
    - #, ECS, >3cm-Worse Prognosis
    - Expansion of Nerve Canals

**IMAGING**

- MRI

- PET
IMAGING

MRI
  Lymph Nodes
    T1: post-contrast/fat-suppressed: nodal necrosis
    T2: heterogeneous
  Perineural Spread (enhancement/thickening/loss of fat plane)
  Intraorbital/Intracranial Extension

PET
  Limited Role
  10% impact on initial staging

Regional Follow-up

80% of nodal metastases in NMSC develop within 9 months of treatment. (Chu 2003)

Rare for regional and distant mets to show up at the same time. (Veness 2005)