

ARROCase: Occult Primary of the Head and Neck

Anna Lee, PGY-3

Faculty: David Schreiber, MD

Department of Radiation Oncology

SUNY Downstate Medical Center

Dept. of Veterans Affairs, New York Harbor Health System

Case: History

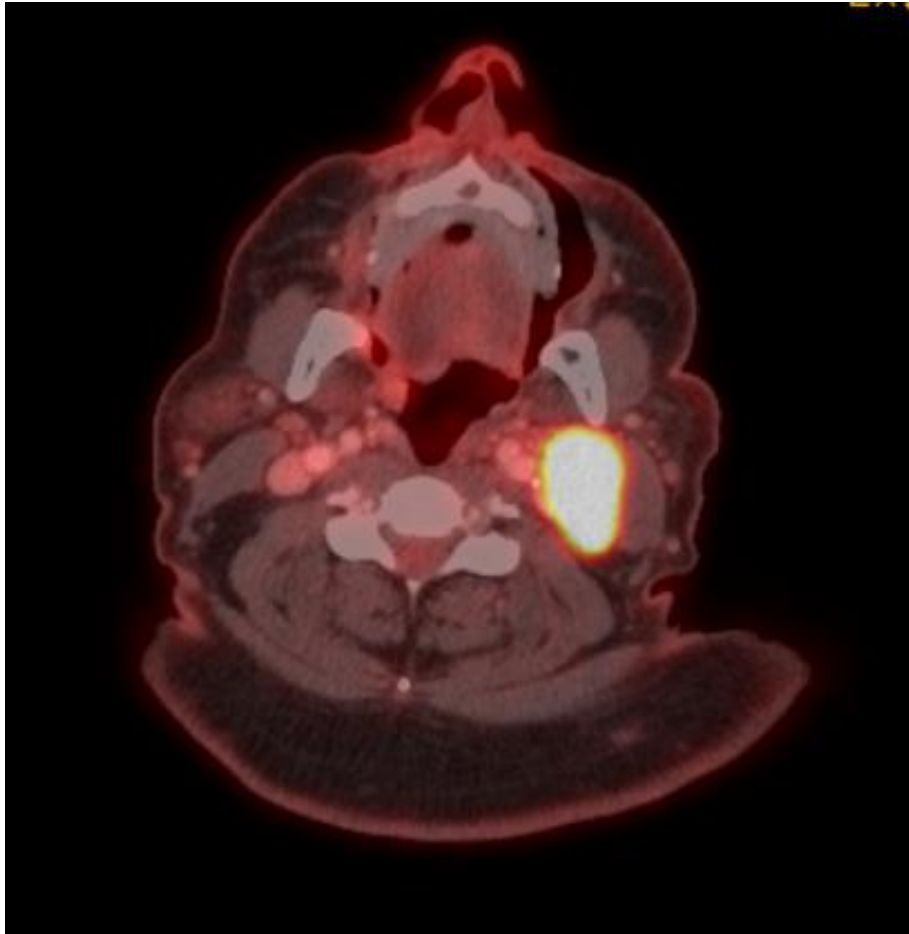
- 62yo male with slow growing, painless left neck mass for 7 months
- ROS negative except for decreased appetite and minimal weight loss

Case: History

- PMH: left knee arthroscopic surgery, tubulovillous adenoma on c-scope
- PSH: left knee arthroscopy 1981
- FH: colon cancer - cousin
- SH: 40PY smoking history, quit 3 years ago; 6-12 beers/day; h/o cocaine use; no IVDA; works as a mover
- NKDA
- No prior chemo or radiation therapy

Case: Imaging

Enlarged
jugulodigastric lymph
node, 3.9cm x 2.5,
max SUV 15.9



Workup & Evaluation

- H&P including complete head and neck exam, skin exam and fiberoptic exam
- Radiographic Studies
 - Chest imaging
 - CT of the head and neck
 - If equivocal, MRI
 - FDG PET-CT
- Laboratory Studies
 - CBC, CMP, TSH
- Dental, nutrition, speech and swallow evaluations

Workup & Evaluation

- Direct Endoscopy and Directed Biopsies
 - EUA, pan-endoscopy and directed biopsies of OPX and any sites with clinical suspicion
 - FNA preferred over core needle biopsy of the cervical node
 - Lower likelihood of seeding
 - HPV, EBV testing suggested for squamous cell carcinoma or undifferentiated histology
 - EBV testing, if positive, would suggest closer evaluation of nasopharynx
 - Tonsillectomy +/- lingual tonsillectomy
 - Consider thyroglobulin, calcitonin, PAX8, TTF1 staining for adenocarcinoma or undifferentiated tumors

Case: Pathology

- Direct laryngoscopy and nasal endoscopy, left palatine and lingual tonsillectomy, BOT biopsies, left neck node dissection of levels II-IV (1/37+)
- Pathology for positive level IIA node:
 - Squamous cell carcinoma, poorly differentiated
 - no ECE
 - p16 positive
 - EBV negative
- Primary areas of clinical concern all negative

Occult Primary of the H&N

- ~3-5% of all H&N cancers are of an unknown primary
- OPX is the presumed site of origin
 - Tonsils and base of tongue (80%)
- ~10% of pts present with bilateral neck disease
- T0 (not Tx) is the assigned T stage if no primary is found

AJCC Staging System: Occult Primary

Table 1

**American Joint Committee on Cancer (AJCC)
TNM Staging Classification for the Lip and Oral Cavity
(7th ed., 2010)**

(Nonepithelial tumors such as those of lymphoid tissue, soft tissue, bone, and cartilage are not included)

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma <i>in situ</i>
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
T4a	Moderately advanced local disease* (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, that is, chin or nose (oral cavity) Tumor invades adjacent structures (eg, through cortical bone [mandible or maxilla] into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
T4b	Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

*Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4.

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
N2	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N2a	Metastasis in single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension
N2b	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
N3	Metastasis in a lymph node more than 6 cm in greatest dimension

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

Histologic Grade (G)

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

[Continued...](#)

Overall Stage IVA (pT0pN2aM0)

Case: Management

- This patient received:
 - RT only with IMRT to 60Gy in 30 fractions to the left neck
 - 54Gy in 2Gy x 27 fractions to the right neck and 1.8Gy x 30 fractions to the OPX
 - NPX was not included as pathology was EBV negative

Radiation Planning

- Simulation:
 - Supine with neck extended, immobilize with thermoplastic mask
 - Consider mouthpiece, wire scars, consider bolus near skin
 - IV contrast if no contraindications
 - Fuse diagnostic imaging
- Radiation Dose/Fractionation:
 - High risk areas: 66Gy in 30fx or 70Gy in 35fx
 - Intermediate risk areas: 60Gy in 30fx or 63Gy in 35fx
 - Low risk areas: 54Gy in 30fx or 56Gy in 35fx

Radiation Technique

- IMRT preferred, with image guidance if available

Radiation Contouring

- GTV = gross disease based on exam and imaging
- CTV high risk = GTV + margin for subclinical disease (5-10mm)
- CTV intermediate risk:
 - Central: CTV for central structures, nodal stations and HPV/EBV. Historically included entire pharynx and larynx
 - Neck: Bilateral IB-V and RP if bilateral neck involvement. Ipsilateral IB-V and RP if only ipsilateral neck involvement
- CTV low risk = uninvolved contralateral II to IV nodes (cannot omit)
- PTV = CTV + 3-5mm margin, depending on image guidance

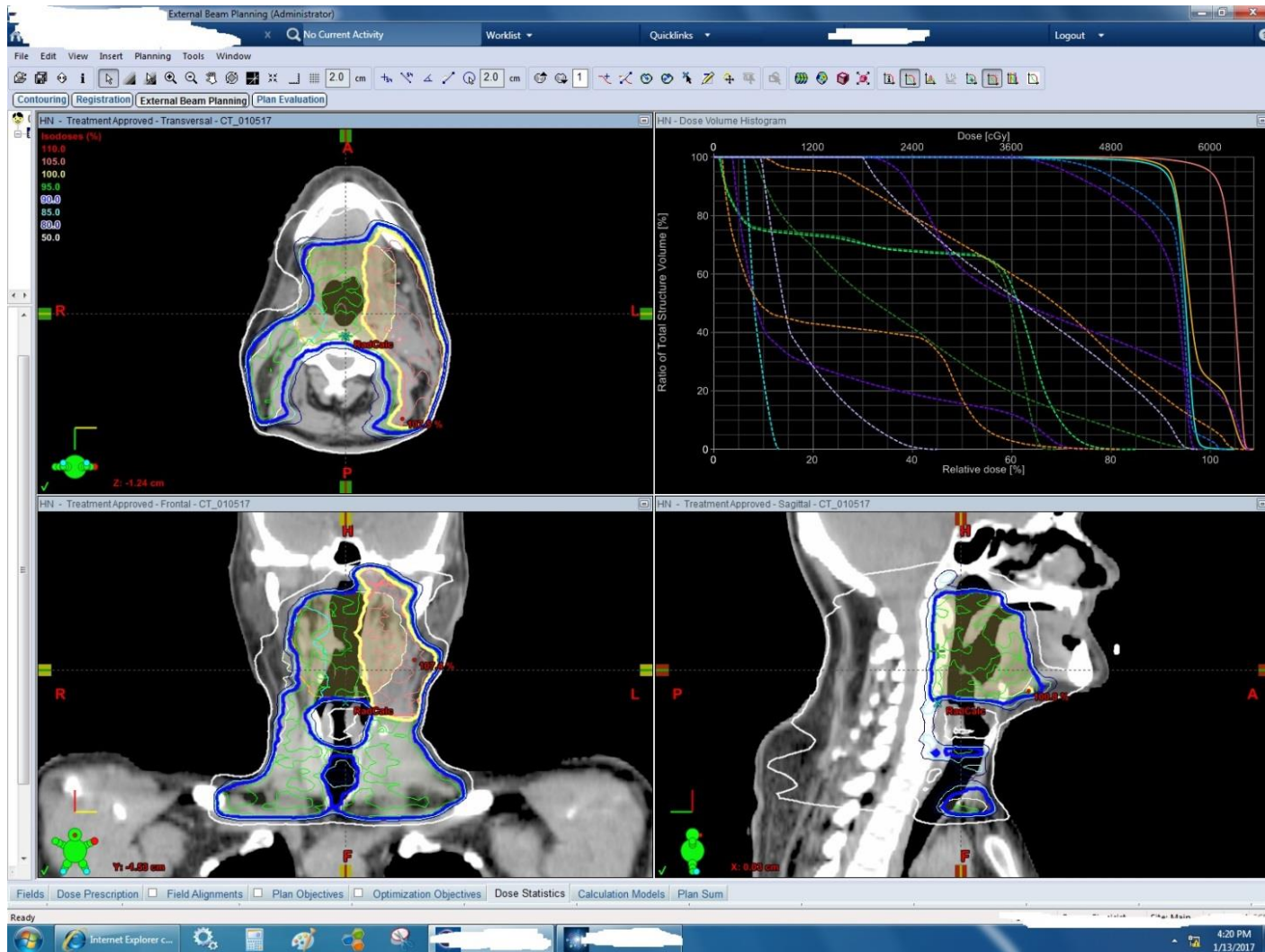
Treatment Algorithm

Stage	Treatment options
T0, cN1	<ul style="list-style-type: none">• Neck dissection (preferred)• Definitive RT• Definitive chemoradiation
T0, cN2-3	<ul style="list-style-type: none">• Neck dissection• Definitive chemoradiation
Postop T0, pN1, no ECE	<ul style="list-style-type: none">• Adjuvant RT• Observation
Postop T0, pN2-3, no ECE	<ul style="list-style-type: none">• Adjuvant RT (preferred)• Adjuvant chemoradiation
Postop with ECE	<ul style="list-style-type: none">• Adjuvant chemoradiation (preferred)• Adjuvant RT
M1	<ul style="list-style-type: none">• Platinum-based combination chemo (preferred)• Clinical trial• Palliation with RT or surgery• Supportive care

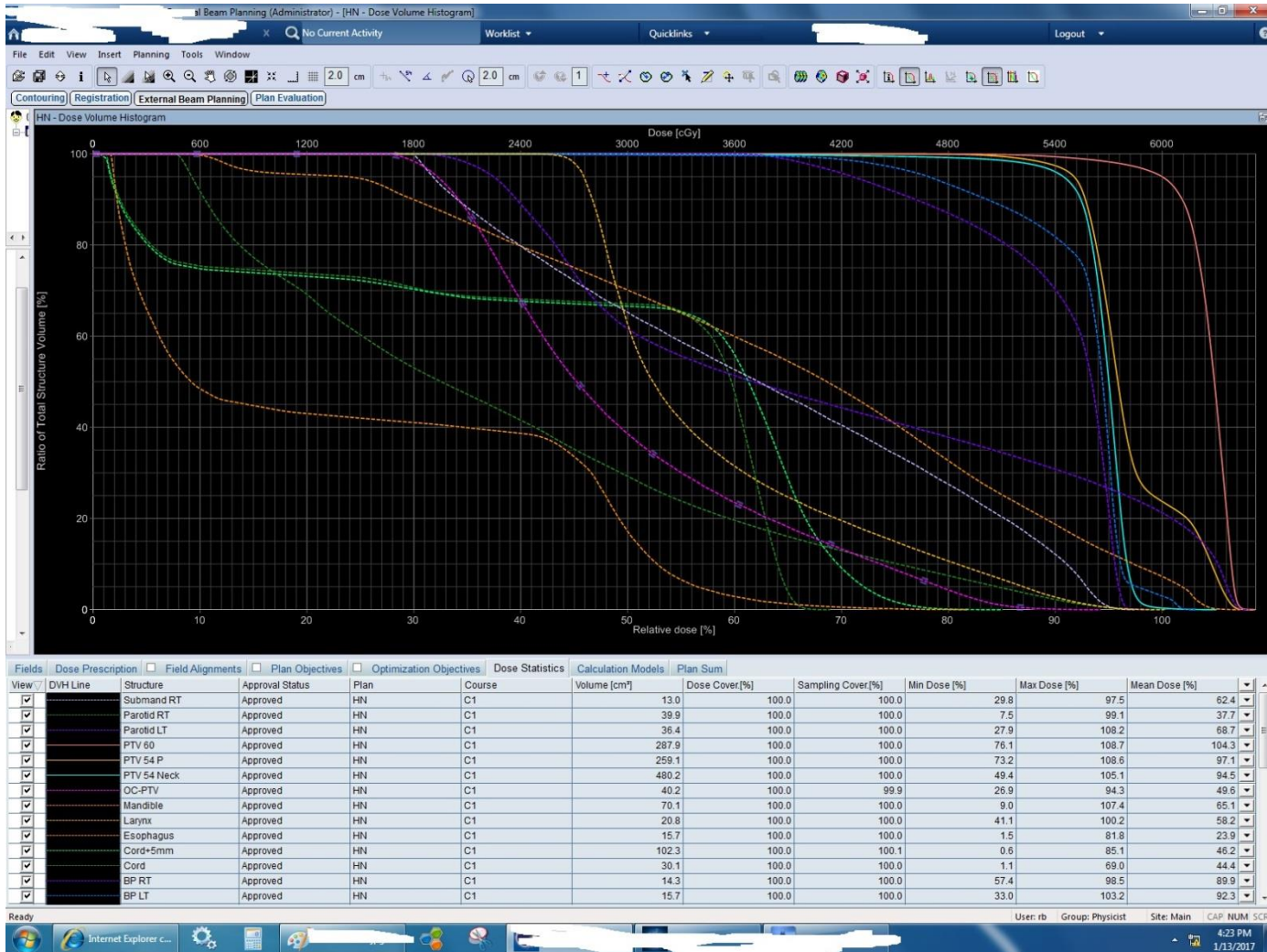
Dose Constraints

Structure	Type	Volume/Dose
Brainstem	Tolerance dose	Entire brainstem <54Gy
Chiasm	Max dose	<60Gy
Ears: Cochlea	Mean dose	<45Gy (<35Gy if pt treated with cisplatinium)
Eyes: Lens	Max dose	<7Gy
Eyes: Optic nerve	Max dose	<55Gy
Larynx	Max dose	<66Gy
Oral cavity	Mean dose	<30Gy
Parotid gland	Mean dose	≤26Gy in at least one gland, or at least 50% of one gland to receive <30Gy
Submandibular gland	Mean dose	<39Gy
Mandible	Max dose	<70Gy

Case: Isodose Distribution



Case: Dose Volume Histogram



Follow Up for Occult Primary H&N

- PET-CT every 3 months after definitive RT/CRT
- If suspicion for residual neck disease, consider neck dissection
- After adjuvant RT, posttx baseline imaging of head and neck within 6 months
- If asymptomatic, H&P and NPL
 - every 1-3 mo for yr 1
 - every 2-6 mo for yr 2
 - every 4-8 mo for yr 3-5, then annually
- TSH every 6-12 mo
- Low threshold for biopsy if suspect emergence of primary
- Nutrition, dental, speech, swallow, hearing and smoking cessation

Selected Studies

- Indications for withholding RT (Coster, Red J 1992)
 - 24 patients with occult primary, unilateral neck disease underwent curative resection
 - 25% had recurrence in dissected neck; 5/6 of recurrences were in those with ECE+
 - For pN1 and no ECE, surgery alone is sufficient; if pN2+ or ECE, consider adjuvant RT

Selected Studies

- Occult Primary Site Detection (Cianchetti, Laryngoscope 2009)
 - 236 patients with occult primary underwent CT, MRI, panendoscopy with directed biopsies, PET, and/or tonsillectomies
 - Occult primary was detected in 53% with majority of these found in the tonsil (45%) and BOT (44%)
- Bilateral Tonsillectomy (Koch, Otolaryngol Head Neck Surg 2001)
 - Oncologic rationale for bilateral tonsillectomy in head and neck SCC of unknown primary
 - Rate of contralateral tonsil primary approaches 10%

Selected Studies

- EORTC 22931 and RTOG 9501 (Bernier, Head Neck 2005)
 - CRT improved DFS and LRC in patients with ECE or positive margins, but provided only trend for improvements in stage III-IV, PNI, LVSI, and/or enlarged level IV to V nodes
 - Patients with ≥ 2 involved nodes without ECE as their only risk factor did not benefit from chemo
- Cancer of Unknown Primary Treated with IMRT (Shoushtari, Red J 2001)
 - Definitive IMRT and neck dissection results in excellent nodal control and OS, DFS with acceptable toxicity for patients with T0N1 or T0N2a disease without ECE

References

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