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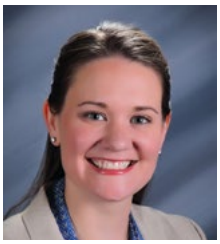
Pathways in Cancer

Clinical insight and analysis in advanced cancer care

Identifying and Treating Oropharyngeal Squamous Cell Cancer



Deanne Roberts, MD

Incidence of squamous cell carcinoma, the most common malignancy of the upper aerodigestive tract, has been steadily decreasing over the past three decades. However, the incidence of oropharyngeal squamous cell (OPSCC) has shown a marked increase due to the association with human papilloma virus (HPV). HPV-related oropharyngeal cancers have increased by 225% since 1988. This has changed the way we consider head and neck cancer patients; they aren't older with significant tobacco and alcohol exposure. They are 50 to 60 year old males with virtually no tobacco or alcohol exposure, but with significant past sexual histories. More than five oral sexual partners and more than 25 vaginal sexual partners increases the risks of HPV-related OPSCC by about 30%.[1,4]

Typically, HPV-related OPSCC presents as either a symptomatic mass in the oropharynx or an asymptomatic neck mass without primary site symptoms; the latter being the most common. 70% of T1 lesions present with metastatic lymphadenopathy.[4] In a patient presenting with a neck mass without significant tobacco or alcohol exposure, HPV-related OPSCC should be high on the differential. Patient should undergo full complete head and neck exam including visualization and palpation of the oropharynx. Next, fine needle aspiration can be performed on the neck mass; this is a safe and effective procedure. Use of p16 staining, which is a surrogate marker for HPV disease, can be helpful in making the diagnosis. Next, pan endoscopy with biopsy is performed. If there are no suspicious lesions on exam under anesthesia, palatine tonsillectomy is done. This results in a 10-fold greater yield of identifying the primary.[7] Some recent research advocates lingual tonsillectomy with identification of the primary in greater than 70% of cases.[5] An excisional biopsy of the neck mass with frozen section can be performed if nothing else has led to a diagnosis. Careful counseling should be given to the patient that, in the event the biopsy is positive for metastatic squamous cell carcinoma, a neck dissection will be completed.

Imaging is critical for staging of all head and neck cancer patients. Imaging modality of choice for head and neck cancer of the oropharynx is CT. It offers several advantages over MRI including reduced cost, reduced time, better visualization of bony or cartilaginous invasion, and less artifact from breathing or swallowing. PET-CT scan can be helpful for evaluation of unknown primaries, however its use is limited by its spatial resolution (>5mm lesions) and the fact that tissue of Waldeyer's ring often has intrinsic FDG-avidity. HPV-related OPSCC are three times as likely to present with cystic metastases on imaging as traditional head and neck squamous cell carcinoma.[2,6]

HPV positive tumors have longer overall and progression-free survival rates as well as lower locoregional recurrence rates.[4] Traditionally, OPSCC was treated with an open procedure, division of the mandible often requiring gastrostomy and tracheostomy. In 2009, transoral surgery using the da Vinci robot (TORS) was approved for use in treatment of OPSCC. Using the robot, the surgeon can excise the primary tumor of the oropharynx through the mouth. The transoral resection is done in conjunction with a neck dissection. In comparison to traditional open approaches, TORS has shorter hospital stays, lower cost, less tracheostomy and gastrostomy use, less bleeding and wound complications, and higher likelihood of negative margins with the primary resection.[3] TORS is a highly specialized procedure and offered at academic tertiary care centers such as UC Davis, UCSF and Stanford.

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[3] Chung, et al. Transoral robotic surgery for oropharyngeal and tongue cancer in the United States.
[4] Laryngoscope 2015; 125 (1):140-145.
[5] D-Souza G, Kreimer AR, Viscidi R, et al. Case- controlled study of human papilloma virus and oropharyngeal cancer. N Engl J Med. 2010; 33:1683-1694
[6] Durmas K, et al. Transoral robotic approach to the carcinoma of unknown primary. Head Neck 2014;36(6): 848-852
[7] Lindberg R, Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer 1972; 29: 1446-1449.
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Systemic Therapy of Head and Neck Cancer

Ram Lalchandani, MD

Head and neck cancer affects about 59,000 persons and causes 12,000 deaths in the United States annually.

Risk factors for head and neck cancer include tobacco and alcohol use, and infection by human papilloma virus. Interestingly, cancers associated with human papilloma virus infection have improved outcomes with treatment.

About 40% of the head and neck cancers present with localized disease and are treated primarily with surgery or definitive radiation therapy. Systemic therapy is used for more advanced disease.

Local-regionally advanced disease is associated with a high risk of local recurrence and metastatic disease. Combined modality approach is required in such cases with surgery, radiation therapy, and chemotherapy or targeted therapy. Chemotherapy has been integrated into treatments to try to improve cure rates, improve organ preservation and to maintain function.

Concurrent chemotherapy and radiotherapy has shown improved survival over radiotherapy alone in a large meta-analysis of 93 trials. Survival was improved also with induction chemotherapy with Cisplatinum and 5-fluorouracil over surgery or radiation therapy alone. Concurrent chemoradiotherapy versus induction chemotherapy followed by radiotherapy showed similar effectiveness, although there was better local control with concurrent chemoradiation therapy, and better systemic control with induction chemotherapy. Adjuvant chemotherapy after definitive treatment has not shown improved survival.

Cisplatin had generally been used concomitantly with radiation therapy, but Carboplatin combined with paclitaxel is often used instead as it is comparable in efficacy but is better tolerated. Standard cisplatin at 100 mg/m2 days 1, 22, 43 is generally associated with more severe side effects, and is used primarily in patients with good performance status and minimal comorbidities.

The addition of Taxanes to induction regimens showed improved effectiveness, however side effects are increased with grade 3-4 neutropenia and neutropenic fever, which occurs in 12% of patients. G-CSF is used cautiously during radiation therapy as it may have a protective effect on tumors. Prophylactic antibiotics with fluoroquinolones are recommended during such induction chemotherapy.

Induction chemotherapy with Docetaxel, Cisplatin, 5-fluorouracil for three cycles followed by chemoradiation therapy improved survival significantly compared to chemoradiotherapy according to a certain Italian trial by Ghi, MG et al, but conflicting results were reported in two other trials and this approach is used on an individual basis taking into consideration the patient's age, performance status, comorbidities, psychosocial support network, and the risk of systemic recurrence versus local failure. Patients over the age of 70 with multiple comorbidities are less likely to benefit from the addition of chemotherapy.

Epidermal growth factor is overexpressed in head and neck cancer and is associated with poor prognosis. Cetuximab is an EGFR inhibitor, a "targeted therapy." Cetuximab plus radiation therapy has shown improved survival compared to radiation therapy alone. Cetuximab was associated with greater incidence of grade 3-4 radiation dermatitis. 3% of patients had severe infusion related reactions. Comparative trials of Cetuximab with radiation therapy versus chemoradiation therapy have not been completed, but are in process. Cetuximab with Cisplatin plus radiation therapy did not offer any advantage over cetuximab and radiation therapy alone.

In case of recurrent or metastatic disease, consideration is given to the options of repeat surgery, radiation therapy and systemic therapies. In addition to the above agents, other options include methotrexate, Capecitabine, Vinorelbine, and various clinical trials. Programmed death-1 ligand and its receptors are involved in suppressing the immune response to tumors, and agents targeting them and stimulating the immune response are yielding promising results in various tumor types including head and neck cancer, and clinical trials are underway exploring their role. With advances in genomics, multiple genetic mutations have been identified in head and neck cancers, some of which are "driver mutations" that cause the cancer to grow and spread, and agents to block their action are under investigation.

Primary Radiation Therapy for Non-Melanoma Skin Cancer of the Head and Neck

Ellen Wiegner, MD

Non-melanoma skin cancers are the most common cancer in the United States with an estimated 1.3 million cases diagnosed annually. Basal cell skin cancers comprise the majority (80%) of non-melanoma skin cancers while 20% are squamous cell carcinomas. The most significant risk factor for development of skin cancer is sun exposure, particularly significant burns experienced during childhood and total cumulative lifetime sun exposure. Other risk factors include fair complexion that easily burns, blonde/red hair, immunosuppression, rare genetic syndromes, and prior history of ionizing radiation therapy at a young age. The majority (>70%) of non-melanoma skin cancers occur in the head and neck region. Skin cancers occurring in the head and neck region, particularly those arising in the "mask areas" of the face (Figure 1), have higher rates of recurrence. Additional risk factors for recurrence include large tumor size, poorly defined tumor borders, squamous cell histology, recurrent tumors, deeply invasive tumors and adverse pathologic features including perineural invasion, vascular invasion, and poorly differentiated tumors. Locally advanced high risk non-melanoma skin cancers (primarily squamous cell carcinomas) can uncommonly metastasize to regional lymph nodes or distant sites.

The goal of local therapy for non-melanoma skin cancer is to eradicate the tumor while optimizing cosmetic outcome. Local treatment options include surgery, cryosurgery, curettage and electrodesiccation, radiation therapy and topical therapies. The majority of skin cancers in the head and neck region are treated with either Mohs micrographic surgery or surgical excision. Mohs micrographic surgery is typically reserved for cancers at high risk of local recurrence and those cancers located near the nose, lips and eyelids. Five-year local recurrence rates are 5 to 8% with standard surgical excision and 1 to 3% with Mohs micrographic dissection.[1]

While surgery remains the most common treatment approach for non-melanoma skin cancers, primary radiation therapy is an alternative treatment option. Radiation therapy is a preferable treatment option for larger skin cancers involving the face for which surgical excision and reconstruction would result in sub-optimal cosmetic outcome. Radiation therapy may also be a preferable treatment for elderly patients or patient's whose health status precludes an operation. Radiation therapy delivers superficial X-rays or electron beam therapy 3 to 5 times per week during 15-minute treatment sessions.

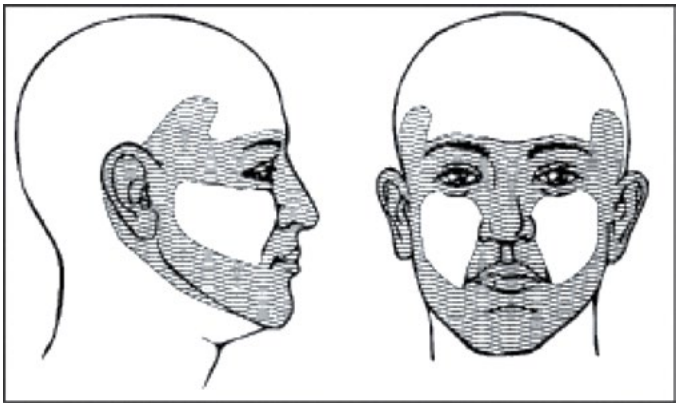

Figure 1. Skin cancers occurring in the highlighted "mask" regions of face have higher rates of local recurrence. 2010 J Natl Compr Canc Network 2010; 8: 836-864.

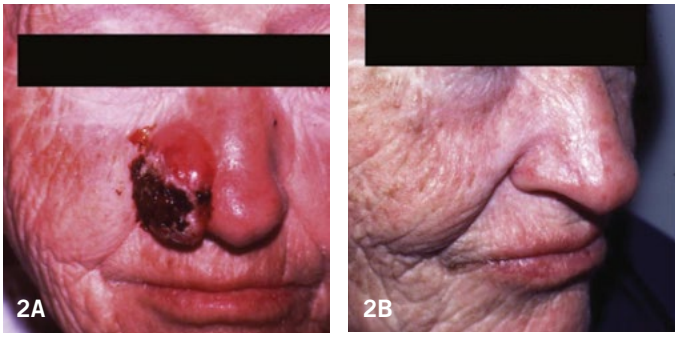

Figure 2A. A basal cell carcinoma involving the nasal ala prior to treatment. *Image courtesy of Leibel and Philips Textbook of Radiation Oncology 3rd edition.*
Figure 2B. Complete regression of basal cell carcinoma after radiation therapy. *Image courtesy of Leibel and Philips Textbook of Radiation Oncology 3rd edition.*

Depending on the size and location of the skin cancer, treatment courses can consist of as few as 10 sessions to as many as 35 sessions. The 5-year local-recurrence rate of skin cancers treated with primary radiation is 8 to 10%.[2,3] Radiation therapy is generally well tolerated and temporary side effects include a temporary skin burn in the treated area and temporary eye irritation for lesions involving or adjacent to the eyelid. Figure 2A shows a patient with a basal cell carcinoma involving the nasal ala prior to radiation treatment. Figure 2B shows complete tumor regression after therapy with excellent cosmesis. Long term sequelae of radiation can include hypopigmentation in the treated area, telangiectasia formation, and rarely secondary malignancy in treated area decades after therapy. Because of these uncommon but potential risks, radiation therapy is best suited for patients over the age of 60. In conclusion, radiation therapy is one of several local treatment options for non-melanoma skin cancers. Selection of therapy should be based on size and location of tumor, recurrence risk, and patient's age and general health status.

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CANCER CONFERENCES

For each of our Cancer Conferences, physicians are eligible for 1 CME credit.

To present a case at an upcoming Cancer Conference, please email, fax, or call contacts noted below. To present a case, please provide:

- **Patient's name**
- **Date of birth and/or medical record number**
- **Disease site**
- **Diagnosis**
- **Where path and imaging can be found**

Hospital Cancer Conferences

Mercy General Hospital
Wednesdays at 12:30 p.m.
Location: Greenhouse Conference Room
Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Mercy Hospital of Folsom
4th Wednesday of every other month at Noon
(January, March, May, July, September, November)
Location: CC1 and 2 or PCU conference room
Contact: Mansoor Javeed, MD
mansoor.javeed@dignityhealth.org
916.984.6230 (phone)

Mercy San Juan Medical Center
Thursdays at 12:30 p.m.
Location: Conference Room 2
Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Methodist Hospital of Sacramento
3rd Friday of each month at Noon
Location: Bistro Conference Room
Contact: Starr Fesler
sfesler@uscmc.com
916.683.9616 (phone)

Sierra Nevada Memorial Hospital
Thursdays at 12:30 p.m.
Location: OPC 110-120
Contact: Debby Kirk
debby.kirk@dignityhealth.org
530.274.6872 (phone)

Woodland Healthcare
Tuesdays at 12:15 p.m.
Location: DCR 5
Contact: Michelle Ing, PA
michelle.ing@dignityhealth.org
530.662.3961 (phone)

TUMOR-SPECIFIC CANCER CONFERENCES

Breast Cancer Conference
3rd Tuesday of each month at 12:30 p.m.
Location: Mercy Cancer Center
3301 C Street, Suite 550
Large Conference Room
Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

GU Cancer Conference
4th Tuesday of each month at 7:30 a.m.
Location: Mercy San Juan, CC3
Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Cases may be brought directly to the conference. Pathology and imaging will not be routinely ordered unless there is a question regarding the results.

Neuro-Oncology Cancer Conference
3rd Thursday of each month at 7:30 a.m.
Location: Mercy Cancer Center
3301 C Street, Suite 550
Large Conference Room
Contact: Mark Cruz
mark.cruz@dignityhealth.org
916.537.5069 (phone)
916.536.3044 (fax)

Thoracic Cancer Conference
2nd Wednesday of each month at 4 p.m.
Location: Mercy San Juan, CC3
Contact: Renae Huwes
renae.huwes@dignityhealth.org
916.536.3157 (phone)
916.536.3044 (fax)

Cases may also be brought directly to this conference.