Case Presentation

A patient who is a 49 year old female who presented to an outside clinic with complaints of hoarseness. At the time of initial presentation, she denied any dysphagia, odynophagia, dyspnea, or shortness of breath. She also denied any fevers, chills, or weight loss. She underwent fiberoptic laryngoscopy which revealed a pigmented lesion. The lesion was noted on the right arytenoid and secondary lesion on the right base of tongue. With these findings, she was counseled to undergo a biopsy of these lesions. She underwent a microsuspension direct laryngoscopy with biopsy of the lesions which revealed melanoma. She was given a diagnosis of mucosal melanoma. She was then asked regarding any dermatological issues – moles, lesions, current or prior skin cancers – which she did not have. She also was referred to see a dermatologist for a full exam which also did not reveal any skin lesions.

After all of this work-up, she was referred to see our service. Her main history was unchanged with only progressive hoarseness. Further history of the patient included a review of systems which was positive for anxiety but nothing else. Her family history was negative for any cutaneous malignancies or head and neck cancers. Her past medical history was significant for ulcerative colitis, hay fever, asthma, and migraines. Her past surgical history was significant for tubal ligation. With regards to her social history, she smoked for 9 years but had quit 12 years prior. She also noted 2 alcoholic beverages per week and denied any illicit drug use.

Our physical exam revealed her to be afebrile with stable vital signs. She appeared in no acute distress. Her skin exam revealed no visible lesions or prior scars showing signs of surgical excision. Her head and neck exam was negative for any gross lesions and no pertinent findings were noted. She had no cervical lymphadenopathy. Fiberoptic laryngoscopy was performed which revealed the following pictures.
Further work-up included several radiological studies. A CT Neck with contrast demonstrated two foci of enhancement (measuring 1.5 cm) in the right base of tongue with no cervical adenopathy noted. A CT Thorax with contrast revealed no metastatic disease. A CT Abdomen and Pelvis with contrast showed no evidence of metastatic disease in the abdomen or pelvis. She also underwent a PET/CT at an outside institution which was negative for metastasis. Outside pathology demonstrated ulcerated melanoma which was involving the submucosa of the right arytenoid as well as melanoma in the right tongue base.

**Mucosal Melanoma Background**

Mucosal melanoma is a rare disease, accounting for less than 1% of all melanoma cases in the United States. It accounts for 0.8 – 1.8% of all melanomas and 6.3 – 8% of all head and neck melanomas. Typical characteristics of a patient with mucosal melanoma include a mean age of 60-69 years and equal male/female preponderance. Greater than 50% of mucosal melanomas are located in the head and neck with sinonasal being the most common site.

Mucosal melanoma is a rare cancer with a very poor prognosis. Oral mucosal melanoma typically presents earlier than sinonasal mucosal melanoma. There is typically decreased nodal metastasis in comparison to cutaneous melanoma. Despite decreased regional spread, there is a high rate of distant metastasis.

When mucosal melanoma presents in the head and neck, 60% typically present in the nasal and paranasal sinus region. Common sites in order include the nasal septum, lateral nasal wall, turbinates, and nasal vestibule. Of the sinuses, the maxillary sinus is the most common accounting for 6% of all mucosal melanoma – followed by the ethmoid, frontal, and sphenoid sinus cavities. Oral mucosa is the second most common site of head and neck mucosal melanoma, with nearly 70% arising in the upper alveolus and hard palate. Oropharyngeal and laryngeal mucosal melanomas are exceedingly rare and only mentioned in case reports.
Sinonasal mucosal melanoma has typical presentations of epistaxis, nasal obstruction, facial deformity, facial pain, and proptosis with diplopia. The lesions are typically bulky or polypoid in appearance and more than likely not pigmented. Oral lesions are often flat and pigmented. These patients are often asymptomatic at time of presentation.

Ballantyne devised an initial staging system for mucosal melanoma. Stage I is limited to localized disease. Stage II indicates the presence of nodal involvement, while stage III indicates the presence of distant metastasis. Due to the advanced and aggressive nature of mucosal melanoma, a new staging system was created to better reflect this nature.

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Description</th>
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<tbody>
<tr>
<td>T3</td>
<td>Epithelium/submucosa (mucosal disease)</td>
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<tr>
<td>T4a</td>
<td>Deep soft tissue, cartilage, bone, or overlying skin</td>
</tr>
<tr>
<td>T4b</td>
<td>Brain, dura, skull base, lower cranial nerves, masticator space, carotid artery, prevertebral space, mediastinal structures, cartilage, skeletal muscle, or bone</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Staging group</th>
<th>Tumor</th>
<th>Node</th>
<th>Metastases</th>
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<tbody>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td></td>
</tr>
<tr>
<td>IVA</td>
<td>T4a</td>
<td>N0</td>
<td></td>
</tr>
<tr>
<td>IVB</td>
<td>T3-T4a</td>
<td>N1</td>
<td></td>
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<tr>
<td></td>
<td>T4b</td>
<td>Any N</td>
<td></td>
</tr>
<tr>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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**Mucosal Melanoma Treatment Guidelines**

With a mucosal melanoma patient, the work up begins after a positive biopsy. The concern with this disease is always metastatic disease. Radiological work-up of the patient should include a CT Chest and likely a PET/CT to assess for distant metastasis. Unlike a cutaneous melanoma, mucosal melanoma must always be considered for multimodality therapy – surgical excision, medical oncology, and radiation therapy.

The NCCN provides several guidelines regarding work-up of mucosal melanoma. The slides below are taken from their guidelines.
Mucosal Melanoma Treatment

Management of a head and neck mucosal melanoma begins with surgical resection with clear margins. Then, treatment of the neck must be considered. The options include sentinel lymph node biopsy and prophylactic neck dissection. Further considerations include the role of radiation therapy and chemotherapy.

Some considerations include assessing typical neck involvement. 25% of patients with oral mucosal melanoma present with neck metastasis while only 6% of sinonasal melanoma patient present initially with neck involvement. Initially, it was considered that sentinel lymph node biopsy may be beneficial much as is the case with cutaneous melanoma. However, studies show that it is not as efficacious due to a low reported rate of nodal metastasis as well as delayed neck metastasis. Several studies evaluate sentinel lymph nodes biopsies and demonstrated no clear benefit. It did not show improvement in preventing locoregional recurrence or distant metastasis.

With regards to sinonasal mucosal melanoma, prophylactic neck dissections are not advocated. This belief is in conjunction with the rarity of cervical involvement on initial presentation. In sinonasal cases, recurrence tends to be either local or distant. The regional control of a neck dissection does not provide much benefit. Of several case series, the greatest percentage of regional site of recurrence was only 25%. This thought process is reflected in the NCCN guidelines.
For oral mucosal melanoma, the topic of prophylactic neck dissections has been debated more due to the greater frequency of regional metastasis upon initial presentation. The rate of regional recurrence in oral mucosal melanomas is much greater – estimated around 70%. This increased rate of recurrence has led to more frequent prophylactic neck dissections in treatment of oral mucosal melanoma.
The role of radiation therapy following surgical intervention has typically been advocated. However, the topic of primary radiation therapy has been debated. Currently, there are only a small number of cases discussing patient receiving primary radiation therapy. One specific paper – Gaze et al – demonstrated complete clinical response in 8/13 patients with primary radiation therapy alone. Despite this one study’s promising findings, the other papers do not seem to show similar findings. Therefore, primary radiation therapy is best reserved for patients unable to undergo surgery or those with primary tumors in locations which prevent surgical resection.

Post-operative radiation therapy has shown significant benefits – highlighted by two studies. Temam et al demonstrated greater improved local control (62% vs 26%) in patients treated surgery and radiation therapy versus those with surgery alone. Similarly, Owens et al found similar benefit with 83% vs 55% in comparing those patient receiving surgery with post-operative radiation therapy and those receiving surgery alone.
The final area of treatment lies with chemotherapy. This may be the greatest area for the future. Currently, 4 different classes of drugs have been used as adjuvant chemotherapy for treatment of mucosal melanomas – IL-2, IFN alpha, Dacarbazine, and Imatinib along with other KIT inhibitors. Dacarbazine had been considered the standard of care; however, the initial testing and results of the KIT inhibitors has shown greater success.

There are two major genes which are targeted by chemotherapy. The first is the B-Raf gene which is targeted in chemotherapy for cutaneous melanoma. Unfortunately, the frequency of this mutation in mucosal melanoma is greatly decreased in comparison to its cutaneous counterpart. KIT gene has been identified in nearly 15 – 30% of mucosal melanoma cases. Some preliminary studies have even suggested that treatment with a KIT inhibitor may lead one further year of survival.

**Conclusion**

In summary, mucosal melanoma remains a devastating disease that while rare carries a very poor prognosis. Early diagnosis followed by surgical excision remains the mainstay. Post-operative radiation therapy is also recommended. The domain of medical oncology and genetic research may provide further clues – especially in light of preliminary benefits noted of KIT inhibitors. We look to the future as a chance where surgical technology (TORS) will allow greater resection of these cancers with a negative margin so that these patient can be treated by cutting edge chemotherapy agents targeted at specific genetic mutations.
Bibliography