

Clinical Problem Solving | PATHOLOGY

Subglottic Presentation of a Rare Tumor: Primary or Metastatic?

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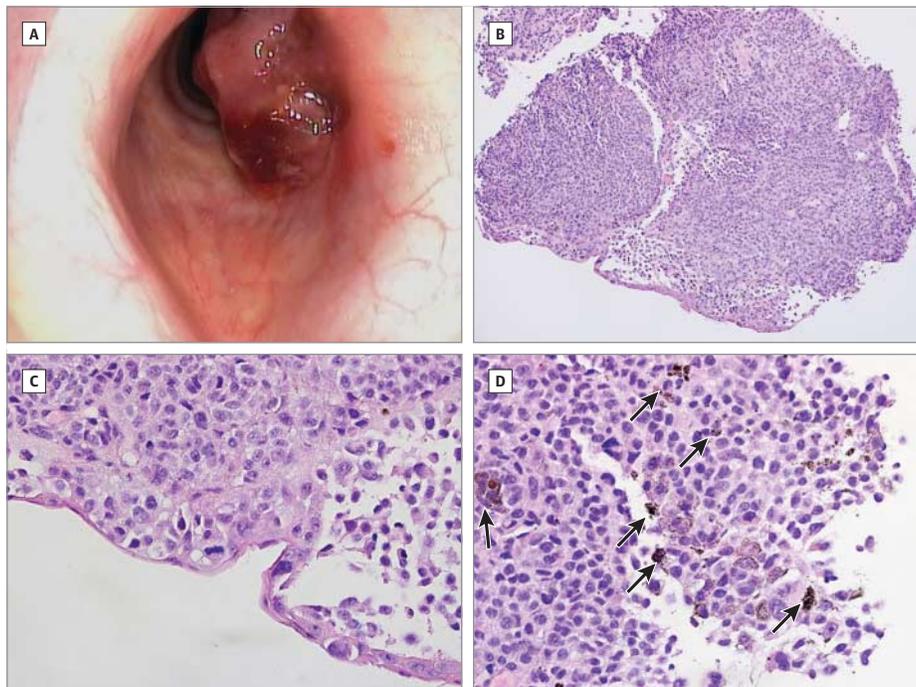


Figure.

A 66-year-old white female ex-smoker presented for evaluation of worsening shortness of breath and dysphagia over the course of 1 week. Her medical history was notable for osteoarthritis, hyperlipidemia, and gastroesophageal reflux disease. She had a 30-pack-year history of smoking cigarettes but had quit smoking 20 years prior. Her social history was notable for occasionally drinking wine.

On office endoscopic examination, there was a large, left-sided exophytic subglottic mass at the level of the cricoid with approximately 50% to 70% obstruction of the subglottic airway (Figure, A). There were no other masses in the oral cavity, oropharynx, or nasal cavity, or distal trachea. There was no cervical neck lymphadenopathy. She was admitted for airway monitoring and then taken to the operating room for direct laryngoscopy, biopsy, and carbon dioxide laser debulking of the mass. Examination at direct

laryngoscopy revealed a large, left-sided subglottic mass at the level of the cricoid with approximately 70% obstruction of the subglottic trachea. The mass extended from the left anterior cricoid to the posterior cricoid just inferior to the left arytenoid cartilage.

The hematoxylin-eosin photomicrographs from the biopsy specimen (Figure, B and C) revealed diffuse sheets and nests of epithelioid cells involving the overlying markedly attenuated, nonkeratinizing squamous mucosa and extending into the lamina propria. The nuclei were significantly pleomorphic with prominent macronucleoli and mitotic figures present. Nests of tumor cells were present within the squamous mucosa (Figure, C). Focal areas contained finely granular, brown granules (Figure, D). Immunohistochemical staining was positive for the protein S-100 and markers HMB-45 and MART-1.

What is your diagnosis?

Diagnosis

Primary mucosal melanoma of the subglottic larynx.

Microscopic Findings and Clinical Course

The patient underwent total laryngectomy with primary closure and bilateral neck dissection. Pathologic analysis of the resected specimen revealed subglottic mucosal malignant melanoma, ulcerated, and 1.8 × 1.4 × 1.1 cm in dimension. The macroscopic extent of the tumor was located just inferior to the left arytenoid and abutting the cricoid cartilage; there was a distance of 1.7 cm in the resected specimen from the closest margin at the distal trachea. The tumor was confined to the submucosal tissue without invasion of the underlying cartilage. There was no regional lymph node metastasis or perineural invasion; however, lymphovascular invasion was present. The *BRAF*^{V600E} activating oncogene mutation was identified. The patient declined postoperative radiation and chemotherapy. On postoperative follow-up 4 months later, the patient was found to have developed local recurrence as well as evidence of distal metastasis to the spine and lungs.

Discussion

Melanoma is an increasingly prevalent neoplasm that stems from malignant transformation of melanocytes (melanin-producing, dendritic-like cells derived from the neuroectoderm). It is subdivided according to the site of origin into cutaneous, ocular, and mucosal melanoma. Although most melanomas are cutaneous in origin, primary malignant melanomas do occasionally arise from noncutaneous tissues that contain melanocytes, such as the uvea, leptomeninges, gastrointestinal, respiratory, and genitourinary tracts. Mucosal melanoma is the most rare form of the tumor entity, accounting for 1.3% to 1.4% of all.¹

The most common sites of mucosal melanoma in the upper respiratory tract are the nasal septum, turbinates, lateral wall of the nasal cavities, and maxillary and ethmoid sinuses; the hard palate and alveolus are the most frequent locations in the oral cavity. However, primary malignant melanoma of the larynx is extremely rare.^{2,3} A review of literature by our group identified 68 total cases of primary laryngeal melanoma that had been reported. Our literature review also revealed 8 cases of tracheal melanoma. To our knowledge, no case of subglottic melanoma has previously been described, underscoring the rarity of this case. Indeed, primary cancer of the subglottic region is in and of itself uncommon, constituting only 1% to 3.6% of the cases of laryngeal cancers reported in the literature.⁴

It can be challenging to differentiate a primary mucosal melanoma from a metastasis of an unknown or regressed cutaneous tumor. Histopathologically, primary melanoma tumors show junctional activity in the overlying or adjacent lateral mucosa (or both), but metastatic melanoma has both intact overlying mucosa and adjacent mucosa devoid of junctional changes.³ The diagnosis of melanoma depends on histopathologic appearance as well as immunoreactivity with S-100 protein and melanocytic markers, including HMB-45, melan-A, or PNL2. The presence of S-100 protein and reactivity for any one of the foregoing melanocytic markers in a pleomorphic epithelioid or spindle cell neoplasm is almost exclusively diagnostic of melanoma.²

The treatment of choice for mucosal melanomas of head and neck, including laryngeal lesions, is complete surgical excision. Of the 8 presented cases of tracheal melanoma, 4 patients were disease free at 1, 3, 4, and 8 years of follow-up; 1 died immediately after surgery from tracheal resection; and the other died after 13 months. Melanoma has traditionally been considered as a radioresistant tumor, but preliminary results suggests that locoregional control can potentially be improved by using postoperative high-linear energy transfer radiation.⁵ Elective neck dissection is not considered routine practice for mucosal melanoma of the head and neck in general because of the relatively low incidence of regional lymph node metastases. Among patients with primary mucosal melanoma of the larynx, however, cervical metastasis to regional lymph nodes at presentation is in fact quite high—cervical metastasis was observed in 19 of 29 cases (65.5%) in the series compiled by Terada et al⁶; 23 of 29 cases (79.3%) had metastasis either to regional lymph nodes or distant sites. Despite treatment with complete surgical excision or radiation therapy, for either primary mucosal or metastatic melanoma of the larynx, prognosis has been uniformly poor. Unfortunately, local control is limited by distant spread. Among 60 cases of primary laryngeal melanoma described by Terada et al,⁶ overall 3- and 5-year survival rates were 28.6% and 7.1%, respectively.

Most patients with mucosal melanoma already have micrometastases present at the time of diagnosis of the primary tumor. Although there is no role for adjuvant systemic therapy at this time, developments in understanding the biology of melanoma growth pathways hold promise for the future.⁷ Until then, quality of life and palliative considerations should remain at the forefront in the management of this lethal disease.

ARTICLE INFORMATION

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REFERENCES

1. Chang AE, Karnell LH, Menck HR; American College of Surgeons Commission on Cancer and American Cancer Society. The National Cancer Data Base report on cutaneous and noncutaneous melanoma. *Cancer*. 1998;83(8):1664-1678.
2. Wenig BM. Laryngeal mucosal malignant melanoma. *Cancer*. 1995;75(7):1568-1577.
3. Amin HH, Petruzzelli GJ, Husain AN, Nickoloff BJ. Primary malignant melanoma of the larynx. *Arch Pathol Lab Med*. 2001;125(2):271-273.
4. Santoro R, Turelli M, Polli G. Primary carcinoma of the subglottic larynx. *Eur Arch Otorhinolaryngol*. 2000;257(10):548-551.
5. Krenkli M, Jereczek-Fossa BA, Kaanders JH, Masini L, Beldi D, Orecchia R. What is the role of radiotherapy in the treatment of mucosal melanoma of the head and neck? *Crit Rev Oncol Hematol*. 2008;65(2):121-128.
6. Terada T, Saeki N, Toh K, et al. Primary malignant melanoma of the larynx. *Auris Nasus Larynx*. 2007;34(1):105-110.
7. Singhal SS, Figarola J, Singhal J, et al. 1,3-Bis(3,5-dichlorophenyl) urea compound "COH-SR4" inhibits proliferation and activates apoptosis in melanoma. *Biochem Pharmacol*. 2012;84(11):1419-1429.