Primary malignant melanoma of the epiglottis: A rare presentation

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Abstract
Primary malignant melanoma of the epiglottis is extremely rare. Until now, only 4 cases have been reported in the world literature. We describe a new case of epiglottic primary malignant melanoma in a 74-year-old man who presented with hoarseness and a foreign-body sensation. Clinical examination revealed the presence of a small, whitish, polypoid tumor on the laryngeal surface of the epiglottis; no other primary melanoma was detected. Wide excision of the lesion was performed, and microscopy revealed that it contained melanin-pigmented tumor cells in both the mucosa and submucosa. Immunostaining was positive for S-100 protein. The patient was treated with radiotherapy, and he remained well 1 year after the diagnosis with no evidence of recurrence.

Introduction
Malignant melanoma is a neoplasm that arises from melanocytes. Melanocytes are derived from the neural crest and are widely distributed throughout all cutaneous and mucosal surfaces. They are found in the basal layer of the epidermis near the dermal-epidermal junction; they have been reported in the larynx, nasal cavity, and mouth. Although melanoma usually arises from the skin, in rare cases it can affect the eye, meninges, and the mucous membranes of the digestive and upper respiratory tract.

Several varieties of epiglottic neoplasms have been described in the literature. Of these, malignant melanoma is rare. When malignant melanoma of the epiglottis does occur, it can be either primary or secondary. Until now, only 4 cases of primary malignant melanoma of the epiglottis have been reported in the world literature. None of them were associated with basal cell carcinoma. A case of secondary amelanotic melanoma of the epiglottis was reported by Ikeda et al in 1991. In this article, we report a new case of primary malignant melanoma of the epiglottis, and we briefly review the relevant literature.

Case report
A 74-year-old man presented to the Department of Laryngology and Otology at James Paget Hospital with a 3-month history of hoarseness and an unusual sensation in his throat. His medical history was significant for several recurrent basal cell carcinomas of the head and neck (which had been treated with cryotherapy and excision) and for tuberculous cervical lymphadenitis (for which he had received a full course of standard antituberculosis chemotherapy). He was a smoker and had been so for more than 40 years.

Clinical examination did not reveal any cutaneous melanomas or palpable cervical lymph nodes. Fiberoptic laryngoscopy detected a small, white, polypoid lesion on the posterior aspect of the epiglottis (figure 1). Under general anesthesia, the patient underwent direct laryngoscopy, and the lesion was excised and submitted for histopathologic examination. A paraffin section stained with hematoxylin and eosin (H&E) showed tumor cells with clear nuclei exhibiting pleomorphism and melanin pigmentation in the cytoplasm (figure 2). These cells had hyperchromatic nuclei, and they invaded both the mucosa and submucosa. On immunohistochemistry for S-100 protein, the tumor cells demonstrated a strong positive staining in both the nuclei and cytoplasm (figure 3). The lesion was diagnosed as a primary malignant melanoma because all clinical, panendoscopic, and ophthalmologic examinations conducted to identify a possible primary lesion elsewhere were negative. Following surgical excision, the patient opted to undergo radiotherapy. One year after his diagnosis, he was well and showed no evidence of recurrence.

Discussion
No case of malignant melanoma of the epiglottis has been published since 1991. Only 0.6 to 9.3% of patients with cutaneous malignant melanoma will experience metastasis to the mucosa of the upper aerodigestive tract. Mucosal melanomas are usually of the acral lentiginous type, and they occur most often in the nasal cavity and sinuses.
Among laryngeal melanomas, the supraglottic region is the most common site of involvement. Cases of metastatic melanoma from an unknown primary may be attributable to (1) spontaneous regression of the primary, (2) the location of a primary in a visceral organ, or (3) an inability to detect a primary in the skin. The clinical features of laryngeal melanomas include hoarseness, hemoptysis, dysphagia, airway obstruction, and stridor. Enlarged cervical lymph nodes may be present. The tumor can spread to the brain, lungs, and spine. Our patient presented with hoarseness and a foreign-body sensation. His hoarseness may have been attributable to chronic laryngitis secondary to his smoking. The foreign-body sensation disappeared after the tumor was excised.

A diagnosis of melanoma must be confirmed by histologic examination of an excisional biopsy specimen; obtaining a specimen might require direct laryngoscopy under anesthesia. Under light microscopy, the tumor will exhibit a pleomorphic epithelioid cell population of malignant cells. Malignant spindle-shaped cells may also be identified. Cells often contain dark-brown cytoplasmic and nuclear melanin. The presence of melanin is identifiable on H&E staining, Fontana staining, and immunohistochemistry, which will show immunoreactivity with S-100 protein and HMB-45. Electron microscopy may identify the presence of melanosomes or premelanosomes. Although the tumor in our patient appeared to be amelanotic on clinical examination, melanin pigmentation was seen in the cytoplasm on microscopy, and immunohistology was positive for S-100 protein.

Three conditions usually exist that help identify a tumor as a primary malignant melanoma: (1) the tumor should be the dominant lesion, (2) there may be local and regional metastasis, and (3) the patient should have no history of a primary cutaneous or ocular melanoma or nevus that regressed spontaneously. The hallmark of a primary malignant melanoma is the presence of junctional activity in the overlying or adjacent mucosa. Malignant cells must be identified in the surface epithelium to establish a diagnosis of a primary malignant melanoma. In our patient, malignant cells were clearly seen in the surface epithelium (figure 2). Our patient had no other identifiable malignant lesion, and histology of his previous basal cell carcinomas did not provide any evidence of pigmentation. Therefore, his tumor was diagnosed as a primary.

Positron-emission tomography (PET) and magnetic resonance imaging (MRI) may be used for staging malignant melanomas. In a retrospective study of fluorodeoxyglucose (FDG) PET in 18 patients with mucosal melanoma, Goerres et al reported that all tumors were visible at staging, but the FDG uptake was dependent on the size and anatomic site of the lesion. Big nodular lesions were more visible than the more superficial spreading lesions. Lesions in the anterior part of the nose were more difficult to detect than those located elsewhere.
Yoshioka et al analyzed MRI findings in 6 patients with mucosal melanoma and found that on T1-weighted imaging, 5 melanomas were hyperintense and 1 was isointense. On T2-weighted imaging, 5 were of mixed intensity and 1 was isointense. The mean signal intensity ratios for the primary melanoma to muscle on T1-weighted imaging were 1.51 with gadolinium contrast and 1.39 without it; the difference was not statistically significant. This finding suggests that hyperintensity on T1-weighted imaging is a common characteristic of mucosal melanoma but not a universal finding.

The only curative treatment is radical local excision (total laryngectomy and neck dissection for laryngeal melanoma). Local recurrences are common, even when surgical margins are wide. A simple local excision is occasionally used. There is 1 report in the literature of a case of melanoma of the right vocal fold that was managed with a right cordectomy and adjuvant radiotherapy. That patient remained well without any evidence of local recurrence or metastasis for more than 3 years. In the case described by Ikeda et al, a patient with cutaneous amelanotic melanoma developed a metastatic tumor that involved the epiglottis; the tumor was successfully excised via an intraoral approach and KTP/532 laser surgery.

Nonsurgical treatments include radiotherapy, chemotherapy, immunotherapy, and CO₂ laser ablation. Several reports published during the past decade on radiotherapy alone have documented complete response rates of 50 to 75% and enduring long-term control in one-half to two-thirds of the complete responders. These data, taken in conjunction with the high rate of local failure after surgery alone, suggest that radiotherapy would have a useful role as a surgical adjuvant in a combined-modality approach, as well as being of value in the primary management of unresectable disease. Currently, chemotherapy is principally used for the treatment of disseminated disease and for palliation. Immunotherapeutic options include OK-432, interleukin 2, lymphokine-activated killer cells, and cyclophosphamide. The American Joint Committee on Cancer conducted a large cohort study of 734 patients with stage I to III melanoma and found that bacille Calmette-Guérin (BCG) vaccine as an adjuvant to dacarbazine delayed the progression of disease and improved survival. BCG vaccination usually lowers the risk of developing melanoma.

Several reasons explain the poor prognosis associated with mucosal melanoma: (1) the nonspecific nature of its symptoms leads to delays in diagnosis, (2) the tumor affects many older people whose immune function is inefficient, (3) the rich vascular and lymphatic efferents of the mucosa favor early metastasis, and (4) mucosal melanoma is histologically aggressive. Even so, overall mortality for early head and neck melanoma has actually declined because a higher percentage of patients are seeking treatment when the tumor is at an early stage (table 2).

Acknowledgment
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Table 1. Location of mucosal melanomas of the head and neck in 259 patients in Merseyside, U.K.

<table>
<thead>
<tr>
<th>Site</th>
<th>%</th>
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<tbody>
<tr>
<td>Nasal cavities and sinuses</td>
<td>69</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>22</td>
</tr>
<tr>
<td>Pharynx, larynx, and upper esophagus</td>
<td>9</td>
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Table 2. Prognosis of stage I primary mucosal melanomas of the head and neck

<table>
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<tr>
<th>Level</th>
<th>Invasion</th>
<th>Survival</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>In situ</td>
<td>11 yr 6 mo</td>
</tr>
<tr>
<td>II</td>
<td>Lamina propria only</td>
<td>5 yr 9 mo</td>
</tr>
<tr>
<td>III</td>
<td>Deep tissue</td>
<td>1 yr 5 mo</td>
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References