Orbital mass as first presentation of metastatic p16-positive oropharyngeal squamous cell carcinoma

J. Corbett MD,* D. Wilke MD MSc,† J. Trites MD,‡ and N. Lamond MD*

ABSTRACT

We describe a case in which a 67-year-old man was diagnosed with a metastatic recurrence of p16-positive oropharyngeal squamous cell carcinoma after presenting with a medial orbital mass in the region of the nasolacrimal apparatus. A review of the literature revealed that metastasis to the orbit from any malignancy is an uncommon occurrence, and no cases of p16-positive oropharyngeal squamous cell carcinoma have previously been reported. Our case highlights the importance of maintaining a high index of suspicion during surveillance visits with such patients.

Key Words  Human papillomavirus, oropharyngeal squamous cell carcinoma, p16-positive disease, distant metastases, orbital metastases

INTRODUCTION

Rates of oropharyngeal squamous cell carcinoma (OPSCC) are increasing because of the recent rise in diagnoses related to the human papillomavirus (HPV). Clinical recognition of the association with HPV is commonly based on biopsied tumour tissue staining positive for p16 (p16+) on immunohistochemistry. Although p16+ OPSCC generally carries a more favourable prognosis and an improved rate of locoregional control than are seen in OPSCC that is unassociated with HPV, the rate of distant metastasis is similar. In the setting of p16+ OPSCC, distant metastasis often involves more than one organ and has been described in rare sites.

CASE DESCRIPTION

A 67-year-old male patient was diagnosed with squamous cell carcinoma (SCC) of the right oropharynx after presenting to his family physician with odynophagia and a right neck mass. This patient had a 15 pack–year cumulative history of tobacco exposure, and he continued to smoke 3–4 marijuana cigarettes daily, mixed with tobacco. He had consumed alcohol heavily in the past, but had stopped drinking before the time of presentation.

At the patient’s initial consultation in the head-and-neck surgery clinic, physical examination revealed a right-sided exophytic lesion of the oropharyngeal mucosa with its epicenter in the glosstonsillar sulcus. The lesion extended onto the ipsilateral palatine tonsil, the base of the tongue, and the lateral pharyngeal wall. Accompanying firm cervical adenopathy was noted bilaterally. In the right neck, a fixed 7 cm mass centred on the sternocleidomastoid muscle involved levels II, III, VA, and VB. Inferior to the latter mass, a separate mass measuring 2 cm was found in the suprACLavicular space (level VB). In the contralateral neck, a single mass measuring 2 cm was palpable in level IIA. The remainder of the physical examination was unremarkable.

Biopsies taken at that time confirmed a poorly-differentiated non-keratinizing SCC of the right oropharynx, with multifocal lymphovascular invasion and diffuse strong nuclear and cytoplasmic staining for p16 on immunohistochemistry.

Enhanced computed tomography imaging of the neck and chest revealed the primary in the right oropharynx together with the clinically apparent bilateral cervical adenopathy, including the large right-sided nodal conglomerate measuring up to 9 cm in its maximal diameter. Subsequently, combined positron-emission tomography–computed tomography imaging of the body showed the known areas of involvement to be intensely avid for fluorodeoxyglucose. Neither exam revealed evidence of distant metastatic disease.

The patient was subsequently discussed at multidisciplinary rounds, where the clinical findings were felt to be consistent with a p16+ C3N3M0 SCC of the right...
oropharynx, which was considered high risk because of the bilateral neck adenopathy, N3 nodal disease, and smoking history. The recommended curative-intent treatment was definitive chemoradiotherapy.

After a discussion of the relevant risks and benefits of the recommended treatment, the patient underwent concurrent chemoradiotherapy consisting of 70 Gy in 35 fractions to the gross tumour volume and 56 Gy in 35 fractions to the elective lymph node volume, with 3 cycles of concurrent high-dose intravenous cisplatin (100 mg/m² every 21 days). The patient completed all treatments on schedule, with the expected toxicities of moderate fatigue, mucositis, dermatitis, and associated weight loss.

At the patient’s 3-month post treatment follow-up appointment, a favourable response to treatment within the radiation field was evident. No contralateral adenopathy or abnormality remained within the oropharynx. At the site of the prior nodal conglomerate in the right neck, a residual 1.5 cm mobile lesion was observed. The patient did, however, note a new swelling at the medial aspect of his right eye.

On examination, the swelling at the eye consisted of a superficial non-tender nodule located medial to the right epicanthus in the region of the nasolacrimal apparatus. The lesion was neither erythematous nor fluctuant and measured 4 mm in maximal diameter. The feeling at the time was that, given its highly atypical location, the lesion was not concerning for metastasis, and therefore no specific management was undertaken. Post-therapy follow-up imaging was arranged for further response assessment.

During the subsequent 2 weeks and before the scheduled imaging, the aforementioned nodule in the region of the nasolacrimal apparatus rapidly enlarged. Repeat clinical assessment revealed a large non-mobile mass involving the medial right orbit (Figure 1). Irrigation of both nasal lacrimal systems revealed no evidence of nasolacrimal duct obstruction. The anterior segment of the eye was unremarkable, and the posterior pole revealed a normal disc, macula, and vessels. Eye movements were normal.

A fine-needle aspirate of the orbital mass demonstrated a population of diffusely p16+ scc cells, consistent with metastasis from the patient’s oropharyngeal primary. Computed tomography imaging showed a mass at the medial canthus of the right orbit, abutting the right globe, the medial rectus muscle, and the nasal bone (Figure 2). Repeat positron-emission tomography imaging revealed intense uptake in the orbital mass (Figure 2), together with multiple new sites of uptake in the mediastinal, right hilar, and axillary lymph nodes. Within the treatment field, the residual 1.5 cm lesion in the right neck remained fluorodeoxyglucose-avid, but no other areas of persistent fluorodeoxyglucose uptake were observed.
The patient was diagnosed with incurable distant metastases from his p16+ OPSCC.

Based on a borderline performance status and the short interval to recurrence, the patient was then treated with single-agent palliative-intent docetaxel chemotherapy. After 2 cycles, the orbital mass was observed to have grown, which was considered to be objective disease progression. The patient then proceeded to receive palliative radiotherapy at 30 Gy in 10 fractions, which led to a significant reduction in the size of the orbital mass.

DISCUSSION

Historically, OPSCC has been considered a malignancy of the head and neck that is related to tobacco and alcohol exposure. Today, despite declining smoking rates, OPSCC rates have risen because of the increased incidence of HPV-related oropharyngeal cancers. Currently, more than 80% of OPSCC diagnoses are HPV-related. Clinically, the relationship is commonly identified by an immunohistochemical analysis of biopsied tumour tissue for p16 expression, with positivity serving as a surrogate marker for HPV infection. Evidence to date suggests that HPV status is a strong and independent biomarker for prognosis. Compared with patients having disease unrelated to HPV, patients with HPV-related cancers respond more favourably to treatment and subsequently experience lower rates of local recurrence and improved survival. However, both groups experience similar rates of distant metastasis, and the pattern of recurrence is proportionally more common in patients with HPV-related disease.

The most common site of distant metastasis in OPSCC is the lung, followed by bone and liver. Recently, a number of articles have outlined atypical cases of metastasis in HPV-related OPSCCs, including solitary dural metastasis, solitary osseous metastasis 11 years after initial treatment, multiple brain metastases, and infiltrative bone marrow carcinomatosis. Retrospective reviews have similarly suggested that metastases in patients with HPV-related disease are more likely to include unusual sites or to involve multiple organs, which is rarely seen in HPV-unrelated disease. To the best of our knowledge, the present report describes the first case of an orbital mass as the first sign of distant recurrence in p16+ OPSCC.

Cancer recurrences within the medial orbit in the region of the nasolacrimal apparatus occur infrequently and are usually caused by locoregional extension of neighbouring primary malignancies such as conjunctival melanoma. Orbital metastases in the lacrimal sac region, while very rare, have previously been described as arising from hepatocellular carcinoma and renal cell carcinoma primaries. Orbital metastases originating from other primary cancers—including breast, prostate, lung, skin, parotid, colon, kidney, thyroid, and neuroblastoma—have been described. No cases of head-and-neck SCC metastasizing to this region have been reported.

Our case, and the evidence review documenting unusual sites of recurrence in patients previously treated for HPV-related OPSCC, underscore the need for health care practitioners to maintain a high level of clinical suspicion during follow-up so as to promptly recognize a potential metastasis despite a favourable prognosis.

SUMMARY

Our case highlights an early metastatic recurrence of p16+ OPSCC after definitive chemoradiotherapy in which the presenting metastasis was in an unusual site, the medial orbit. The subsequent discussion of the relevant literature documents the occurrence of distant metastases from p16+ OPSCC at rare anatomic sites. Our case suggests that a high level of suspicion is necessary to correctly recognize potential metastases during surveillance visits after treatment for p16+ OPSCC.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

AUTHOR AFFILIATIONS

*Division of Medical Oncology, Department of Medicine, 1Department of Radiation Oncology, and 2Division of Otolaryngology—Head and Neck Surgery, Department of Surgery, Dalhousie University, Halifax, NS.

REFERENCES


