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

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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/m\(^2\) 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 3), 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.

![FIGURE 1](image1.png)

**FIGURE 1** The patient’s enlarging orbital mass in the region of the right nasal lacrimal system.

![FIGURE 2](image2.png)

**FIGURE 2** Computed tomography imaging revealed a mass in the right medial canthus.

![FIGURE 3](image3.png)

**FIGURE 3** Positron-emission tomography imaging revealed avidity for fluorodeoxyglucose in the right orbital area.
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 in cases of head-and-neck SCC metas- tasizing 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.

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