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Positron Emission Tomography Scan to Determine the Need for Neck Dissection after Chemoradiation for Head and Neck Cancer: Timing is Everything

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We present a case of a negative positron emission tomography (PET) scan in a patient with pathologic viable cancer at neck dissection. *Study Design:* Case Report. *Methods:* A 69-year-old man presented with clinical stage T2N2c squamous cell cancer of the left tonsil and was treated with definitive chemoradiation. Left-sided adenopathy decreased but remained palpable after therapy. *Results:* PET scan performed 23 days after completion of treatment showed no suspicious uptake in the left neck. Neck dissection performed at 2 months post-therapy revealed viable tumor in left cervical nodes. *Conclusions:* Persistent adenopathy after chemoradiation for head and neck cancer remains a clinical dilemma. A negative PET scan is accurate but only if the scan is performed 3 to 4 months after therapy.

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INTRODUCTION

Concurrent chemotherapy and radiation is standard therapy for locally advanced unresectable cancer of the oropharynx. Many of these patients present with malignant cervical adenopathy. After completing definitive chemoradiation, many patients continue to have palpable adenopathy. Standard practice has been to proceed to neck dissection in these patients 4 to 8 weeks after completing chemoradiation. Unfortunately, clinical response is not accurate in predicting pathologic tumor status in dissected necks. McHam et al.[1] reported 109 patients with N2, N3 necks treated with definitive chemoradiation. Thirty-two of 65 patients with complete clinical response underwent neck dissection, and 8 (25%) had residual viable cancer. Forty-four patients without clinical complete response had neck dissection, but only 17 (39%) had residual viable tumor. Peters et al.[2] reports similar findings on 13 patients with palpable nodes after therapy undergoing neck dissection. Only six (46%) had pathologic evidence of persistent cancer. Therefore, approximately 50% to 60% of patients with palpable nodes after chemoradiation will have no viable tumor found at time of neck dissection.

Recently, positron emission tomography (PET) has been used in an attempt to predict which patients can be spared neck dissection after definitive radiation with or without chemotherapy. We present a case of a patient with locally advanced oropharynx cancer with a negative posttreatment PET but residual viable nodal tumor at neck dissection.

CASE REPORT

The patient is a 69-year-old man presenting with a swollen left neck node, change in speech, dysphagia, and odynophagia. On physical examination, he had lymphadenopathy at left and right level II. A nodal cluster at left level II measured 5 × 5 cm. Computed tomography (CT) scan showed a large left tonsillar mass extending into the left parapharyngeal space. Multiple enlarged lymph nodes were seen in the left retropharyngeal space, levels I, II, and III on the left and level II on the right. Panendoscopy showed a large bulky tumor occupying the entire left tonsillar fossa and extending through both tonsillar pillars into the soft palate. The lateral pharyngeal wall was involved at the level of the left vallecula. Biopsies of the tonsillar fossa and lateral pharyngeal wall revealed invasive moderate to poorly differentiated squamous cell carcinoma. Clinical stage was T2N2c.

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The patient received radiation to his oropharynx and bilateral necks. His oropharynx received 70 Gy in 2 Gy fractions. The right neck received 69.44 Gy and the left neck 70 Gy. He was treated concurrently with chemotherapy consisting of cisplatin and 5-FU. After the first cycle of chemotherapy, he developed neutropenic fever requiring hospitalization. Because of poor tolerance, he received only one of two planned chemotherapy cycles. He developed severe skin reaction with bilateral neck moist desquamation. These side-effects necessitated a 9 day treatment break. A total of 37 treatments were delivered over 65 elapsed calendar days.

At completion of treatment, left-sided adenopathy had decreased but remained palpable. CT performed 2 weeks after treatment showed persistent abnormal soft tissue at left level II (Fig. 1). PET was performed 23 days after completion of treatment to help decide whether neck dissection should be performed at approximately week 8. Abnormal uptake was seen in the pharynx consistent with inflammation or tumor, but no uptake was seen in the cervical lymph nodes (Fig. 2). Left neck dissection was performed2 months after completion of concurrent chemoradiation. Three of three resected nodes from level IIA were positive for viable tumor as were three of six level IIB nodes and a single level IV node (Fig. 3).

DISCUSSION

The role of PET in the management of head and neck cancer has evolved over the last decade. It had been used during initial tumor staging[3] and even to find occult tumors in cervical adenopathy of unknown primary.[4] After radiotherapy, it has proven useful in distinguishing residual or recurrent tumor from inflammation or necrosis.[5] In this case report, we discuss the use of PET in the management of persistent cervical adenopathy after definitive chemoradiation.

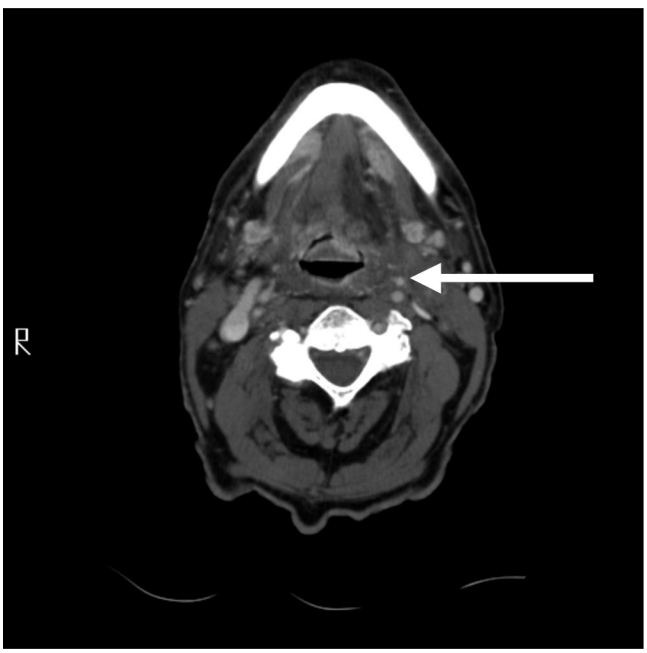

Fig. 1. Arrow points to persistent left-sided cervical adenopathy on computed tomography scan 2 weeks after therapy.

Fig. 2. Posttreatment positron emission tomography scan shows diffuse uptake in the pharynx but no discrete uptake in the cervical lymph nodes.

Calais et al.[6] demonstrated that the addition of concurrent chemotherapy to radiation improved outcome for patients with locally advanced, unresectable oropharynx cancer. Management of the neck after chemoradiation has been controversial. Most have recommended neck dissection for patients with residual adenopathy after therapy. Clayman and colleagues[7] followed 66 patients with oropharynx cancer treated with induction chemotherapy followed by definitive radiation therapy. Patients with no or partial responses of cervical adenopathy who underwent neck dissection had significantly improved survival compared with similar patients who did not undergo dissection. Still, of 18 patients undergoing neck dissection, only 10 (56%) had pathologic evidence of residual cancer. Recently, PET scan has been used to determine which patients have viable tumor remaining in cervical nodes and, therefore, will benefit from neck dissection. This technology is not cheap. The average cost for PET scanning is approximately $1,600 to $2,100.[8] This imaging may be useful to select appropriate patients for neck dissection, but timing of the scan post therapy is critical. Our case report documents that PET scanning performed too early after chemoradiation can not only be expensive but also misleading. A false-negative study can direct therapy

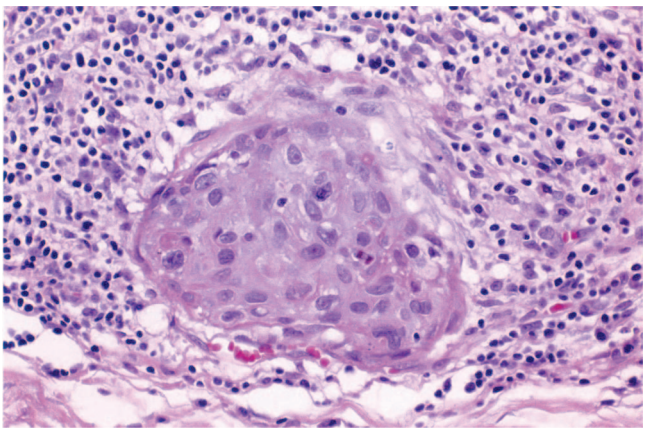

Fig. 3. Residual viable squamous cell carcinoma in nodes at neck dissection 2 months after therapy.

away from curative neck dissection to potentially disastrous observation and disease progression. Greven et al.[9] reported on 36 patients undergoing PET scans at 1 month after definitive radiation. Twenty-five of these scans were interpreted as negative for viable tumor. Unfortunately, seven (28%) of these developed local recurrence at 3 to 12 months after radiation. In a follow-up series, a negative PET at 1 month indicated absence of disease in only 14%.[10] Lowe and colleagues[11] reported a 14% false-negative rate using PET for surveillance at 2 months after therapy for stage III/IV head and neck cancer.

Is there a time after therapy when a negative PET scan becomes useful in predicting for a negative neck dissection? The precise time to wait after definitive radiation to perform PET has never been clearly stated. Still, published reports point to a time interval of 3 to 4 months after radiation to avoid false-negative results. Clearly, the results of Greven et al. show that imaging at 1 month can provide misleading results. Lowe et al.'s 14% false-negative rate at 2 months also indicates a time interval too early for meaningful use. PET scan performed at longer time intervals after radiation have been much more accurate. Yao et al.[12] reported no regional recurrences in 49 patients with negative initial PET scans with "most imaging studies obtained three to five months after treatment completion." Some of these patients with "clinical suspicion for persistent disease" did have imaging "obtained less than three months after treatment," but the specific timing of these scans is not mentioned. Greven[9] herself noted improved accuracy of negative scans at 4 months after therapy. None of the 18 negative scans at 4 months have suffered local recurrence. Finally, in a series perhaps most relevant to our case, Yao et al.[13] reported 12 patients with persistent adenopathy after definitive radiation with or without chemotherapy. Follow-up PET scans were obtained 2.5 to 6 months after treatment "with the majority of them obtained between 3 and 4 months." Using a maximum standardized uptake value of less than 3.0 as the cut-off for a negative PET scan, all seven patients with negative PET scans had negative pathology, resulting in a 100% negative predictive value.

Therefore, it appears that PET can be accurate and, perhaps, useful in limiting unnecessary neck dissections after definitive radiotherapy. Still, PET will only be useful if there is a paradigm shift in therapy. Standard practice has been to perform neck dissection 4 to 8 weeks after completion of radiation therapy. In fact, most decisions to perform neck dissections are made at the initial follow-up 4 to 6 weeks after treatment is completed. A negative PET may be accurate at 3 to 4 months, but will radiation oncologists, surgeons, and patients be comfortable waiting that long? Will a prolonged time interval from radiation lead to more fibrosis and complications of neck dissection? Will a patient with residual viable disease have as good an oncologic outcome if neck dissection is performed at 5 months than at 2 months? Is there increased risk for regional progression or distant spread? In a recent Radiation Therapy Oncology Group study, neck dissection was recommended to "take place within 15 weeks after completion of chemoradiotherapy." Will this be possible or cutting it too close if PET is only useful at 3 to 4 months?

In summary, our case report clearly demonstrates how NOT to use PET after chemoradiation for head and neck cancer. Scanning too early leads to false-negative results, which can be potentially dangerous. A review of the literature suggests that negative PET scans become meaningful at 3 to 4 months. Therefore, PET will only become useful in this setting if radiation oncologists, surgeons, and patients are comfortable waiting at least 3 to 4 months after radiation for neck dissection.

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