Transoral surgery for HIV-infected patient with pharyngeal cancer and supraglottic cancer: A case study and literature review

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ABSTRACT

Background: Pharyngeal cancer is defined as a non-HIV-related malignancy. Although HIV-infected patients are 2.6 times as likely to develop pharyngeal cancer as non-infected patients, the optimal treatment for head and neck cancer in HIV-infected patients remains unclear.

Case presentation: A 63-year-old male with HIV infection was diagnosed with T1N0M0 oropharyngeal cancer and supraglottic carcinoma in situ. He had received highly active anti-retroviral therapy (HAART) for 6 years and had a past history of Hodgkin lymphoma and stomach cancer. Laboratory tests showed a very low CD4⁺ T-cell count of 143 cells/µL. The patient underwent transoral videolaryngoscopic surgery. He needed no additional treatment and has had no postoperative adverse effects, immune decline or swallowing dysfunction.

Conclusions: This HIV-infected patient with head and neck cancer receiving HAART demonstrated that transoral videolaryngoscopic surgery resulted in successful oncological outcomes and functional preservation without radiotherapy or reduced CD4⁺ T-cell counts.

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Introduction

HIV that leads to AIDS infects CD4⁺ T cells, leading to depletion of CD4⁺ T cells. The loss in CD4⁺ T cells was initially thought to be a gradual process as the timing to overt immunodeficiency and AIDS in untreated patients was typically within 10–12 years from primary infection.[1–3] Moreover, HIV-infected patients are prone to develop malignancies. Kaposi’s sarcoma, non-Hodgkin lymphoma, and cervical cancer are classified as AIDS-related malignancies. In addition, the incidence of non-AIDS-related malignancies, including Hodgkin lymphoma, multiple myeloma, leukemia, anal cancer, lung cancer and pharyngeal cancer, increases.

With the development of active antiretroviral therapy, AIDS-related malignancies are decreasing, but because the survival of HIV infected patient is prolonged, non-AIDS-related malignancies have been increasing. In addition, HIV-infected patients are 2.6 times more likely to develop pharyngeal cancer than non-HIV-infected patients.[4]

Pharyngeal cancer has been treated with concurrent chemoradiation, transoral surgery or extended resection. However, the optimal treatment for head and neck cancer in HIV-infected patients remains unclear. Moreover, there have been no reports on the risk of these treatments for HIV-infected patients. The report presented here concerns an HIV-infected patient with a low CD4⁺ T-cell count and pharyngeal cancer, who underwent transoral surgery and the subsequent favorable outcomes for functional preservation. This report has been approved by Tottori University institutional review board (160A154). Informed consent was obtained from the patient for the transoral surgery and the publication of this case report and accompanying images. All the authors declare no competing interests.

Case report

A 63-year-old male was referred to our department for the management of suspected pharyngeal cancer diagnosed by means of endoscopic biopsy at a primary clinic. However, the patient did not present with symptoms related to pharyngeal disease, such as dysphagia or throat discomfort. His performance status...
was 0 according to the Eastern Cooperative Oncology Group system. He was a non-smoker and consumed alcohol on a regular basis (>twice per week).

He was diagnosed with HIV infection 13 years previously. HIV positivity was detected during a blood examination for blood donation. ART therapy with TDF/FTC + EFV was started 6 years ago. Neck lymphnode swellings were found 3 years ago. The patient underwent neck lymphnode biopsy and pathological examination led to a diagnosis of Hodgkin disease and blood antibody test to a diagnosis of EB virus infection. Upper gastrointestinal endoscopy for a screening test detected stomach cancer (poorly differentiated). Total gastrectomy was performed for stomach cancer and the following month ABVD therapy (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine) was initiated for Hodgkin lymphoma. Radiotherapy was not administered. However there was an infusion reaction associated with bleomycin. Two years ago, abdominal lymphadenopathy was found, which was diagnosed as recurrence of Hodgkin lymphoma, and autologous peripheral blood stem cell transplantation (auto-PBSCT) was administered.

Endoscopic examination revealed a tumor at the posterior wall of the oropharynx and left aryepiglottic fold (Figure 1(a) and (b)). There was a sufficient distance between the oropharyngeal tumor and the aryepiglottic fold lesion. Optical enhancement (Ricoh Imaging Company Ltd, Tokyo, Japan) showed dilated, tortuous and irregular intrapapillary capillary loops (Figure 1(c) and (d)), consistent with type V IPCL pattern as described by Inoue et al., and the morphological type was IIa.[5] Contrast-enhanced T1-weighted magnetic resonance imaging (MRI) of the neck showed a hyperintense signal along the posterior wall of the oropharynx and a lateral wall of the hypopharynx but no deep filtration (Figure 2). Contrast enhanced neck and chest computed tomography (CT) scans showed no evidence of lymph node enlargement in the head and neck region or lung metastasis, nor did positron emission tomography-CT scans show any metastasis. Pathological examination in oropharyngeal tumor indicated moderately differentiated squamous cell carcinoma, which was negative for human papillomavirus (HPV) p16.

Figure 1. Endoscopic findings. Preoperative endoscopic findings of the posterior wall of the oropharynx and left aryepiglottic fold. (a) An elevated lesion was observed at the posterior wall of the oropharynx (black arrow). (b) Optical enhancement showed dilated, tortuous and irregular intrapapillary capillary loops (black arrow). (c) A slightly elevated lesion was observed at the left aryepiglottic fold (white arrow). (d) Optical enhancement showed dilated, tortuous and irregular intrapapillary capillary loops (white arrow).
Thus, the final diagnosis was T1N0M0 oropharyngeal cancer and supraglottic carcinoma in situ. Laboratory test reports listed a CD4+ T-cell count of 143 cells/µL (500–1200 cells/µL), and HIV-1 RT-PCR showed no plasma HIV viral load.

Transoral videolaryngoscopic surgery was performed according to the procedure reported by Tomifuji et al under general anesthesia. The patient was operated on in the supine position. He was intubated orotracheally, and a curved laryngoscope (Nagashima Medical Instruments Co., Ltd, Tokyo, Japan) for hypopharyngeal cancer and FK-WO TORS Laryngo-Pharyngoscope Retractor (Olympus Corp., Tokyo, Japan) for oropharyngeal cancer were positioned so as to expose the primary tumor and to provide sufficient working space. The retractor was then suspended with a holder. A flexible endoscope with angulation in 4 directions (Visera LTF-type VP, Olympus Corp., Tokyo, Japan) was inserted through the oral cavity while an assistant held the endoscope and controlled its manipulation for viewing the primary site. The tumor margin was determined with using a narrow band image marked with a 5-mm safety margin. The operator employed a single-use electrosurgical knife with radio frequency (KD-600, Olympus Corp., Tokyo, Japan) to resect the tumor by transoral videolaryngoscopic surgery. This knife has several characteristics as follows: disposable needle, malleable shaft, and adjustable needle length in 2 mm and 4 mm. We used the Swift mode (output power 30, effect 4) of ERVE VIO300D. We cut pharyngeal mucosa and submucosa around and outside the marking and cut the deep margin with part of the constrictor muscle, thus completing the en bloc resection. This procedure could be completed without the need for intraoperative conversion to an open surgical procedure. To confirm adequate resection, frozen sections were examined and no cancer cells were found at the outer edge. The size of the specimens was 28 × 22 mm and 28 × 15 mm (Figure 3). The operation lasted 2 h, there was little blood loss, no blood transfusion was needed, and no tracheostomy was performed either pre- or postoperatively.

In addition, no serious hemorrhage or emergent airway compromise was observed during hospital stay. The patient experienced no serious adverse events that required hospitalization or intervention. He started paste food on postoperative day 7 and a regular diet on postoperative day 10, and the nasogastric tube was removed on postoperative day 7. Actually, wide resection of the posterior pharyngeal wall temporarily weakened pharyngeal constriction, and saliva pooling at the piriform sinus was observed. Thus, postoperative oral intake was delayed. Postoperative swallowing function was normal with a functional outcome swallowing scale (FOSS) of grade 0. Postoperative videofluoroscopy showed a minor penetration and no aspiration (penetration–aspiration score 2).

The oropharyngeal and supraglottic tumors of this case were pathologically diagnosed squamous cell carcinoma and carcinoma in situ, respectively. Both pathological examination revealed negative vertical and horizontal margins, and negative for HPV p16. Pathological data showed that tumor thickness was 2.0 mm with no presence of lymphatic vessel invasion, blood vessel invasion or perineural invasion (Figure 4). No additional treatment was therefore needed.

On post operative 1 month, laboratory test reports listed a CD4 count of 140 cells/µL, and HIV-1 RT-
PCR showed no plasma HIV viral load. We detected no change in the postoperative immunity compared to preoperative.

The patient is alive and has remained disease free 20 months after treatment. He has also not developed AIDS.

**Discussion**

Globally, approximately 34 million people were living with HIV at the end of 2011, the virus that causes AIDS. However, the burden of the epidemic continues to vary considerably between countries and regions. The U.S. HIV/AIDS-related death rate has fallen by more than 80% since the introduction of antiretroviral therapies in 1995.\[7\] Worldwide, the number of people newly infected continues to fall after peaking in 1998: the number of people acquiring HIV infection in 2011 (2.5 million) was 20% lower than in 2001 thanks to the development of the antiretroviral therapies. Japan, however, is the only developed country where the number of newly infected people has increased.\[8\]

It is known that HIV carriers can develop cancer due to eventual immunological deficiency, imbalance between cellular proliferation and differentiation, and disturbances in growth factors and cytokines.\[9\] Pharyngeal cancer is defined as a non-AIDS-defining cancer, a type which comprises anal cancer, Hodgkin lymphoma, liver cancer, lung cancer, melanoma, colorectal cancer, breast cancer, and prostate cancer. The incidence of pharyngeal cancer is significantly higher in the HIV-infected than in the general population (Standardized Rate Ratio: 2.6).\[4\] Thus, along with a drop in the death rate, the number of HIV-infected

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**Figure 3.** Gross findings of the resected lesions. (a) A hyperemic elevated lesion measuring approximately 15 × 13 mm observed in the center of the specimen. (b) A mucosal lesion was observed in the center of the specimen.

**Figure 4.** Microscopic findings of the resected lesion. (a) Squamous cell carcinoma invaded to subepithelial partially. (b) p16 immunostaining was negative. (a: H&E stain; b: p16).
patients with pharyngeal cancer is increasing. Since our patient underwent gastrointestinal endoscopic examination as part of the post-gastrectomy follow-up, the pharyngeal cancer could be detected at an early stage. This indicates that HIV-infected patients need special attention and screening because of the high risk of pharyngeal cancer.

Historically, pharyngeal cancers were treated with extended resection. However, this therapy resulted in significant cosmetic deformity as well as functional deficits in speech and swallowing. Chemoradiotherapy for pharyngeal cancer has been developed and has been confirmed as a major component of treatment to enhance loco-regional disease control, to reduce distant metastasis, and to prolong survival.[10]

However, chemoradiotherapy are not entirely safe, since it is associated with substantial morbidity including tissue fibrosis, mucosal atrophy, xerostomia, bone marrow and renal toxicity.[11] Because of the resultant reduction in morbidity and maintenance of function, transoral minimally invasive surgery has become of growing importance.[12] In the recent literature, the transoral robotic surgery has been described as the first-line therapy for oropharyngeal squamous cell carcinoma with its better 3D visualization of the surgical field and use of miniaturized instruments with tremor filtration.

The optimal treatment for early-stage head and neck cancer has been defined as transoral surgery or radiation. There is ample literature reporting on the identification of molecular biomarkers for head and neck squamous cell carcinoma. It is known that HPV-positive group is radiosensitive. This patient was HPV-negative. Thus, radiotherapy was not selected. However, the therapeutic strategy for HIV-infected patients with head and neck cancer remains uncertain.

There have been no reports on the outcome of transoral surgery for HIV-infected patients with pharyngeal cancer. However, it was reported that an HIV-infected case with T3N2cM0 supraglottic cancer, who was treated with definitive concurrent chemoradiation (70Gy of simultaneous integrated boost intensity-modulated radiotherapy (IMRT) combined with fluorouracil and leucovorin), experienced grade 3 mucositis and dermatitis, although the treatment was completed.[13] Other previous studies reported the rate of acute toxicities for patients with HIV receiving highly active anti-retroviral therapy (HAART) was similar to that for HIV-negative individuals.[14,15] However, one study provided biological evidence that fibroblasts cultured from skin biopsies of patients with AIDS and Kaposi’s sarcoma were more radiosensitive than those from non-HIV-infected sources.[16] It has been suggested that glutathione deficiency and reduced intracellular radioprotective thiol compounds may constitute the mechanism for the enhanced radio sensitivity.[17,18] Chemoradiotherapy may therefore increase the toxicity for HIV-positive patients than for their HIV-negative counterparts. Furthermore, low CD4 counts of <200 cells/µL were associated with increased morbidity during radiation therapy.[19] The reports of HIV-infected patients included patients with various CD4 count. Therefore, the role of CD4 count remains controversial and deserves further investigation. However, a consistent decline in CD4 counts during the course of radiotherapy was reported in patients with HIV-infected prostate, anal, and laryngeal cancer.[13,20–22] Thus, with regard to morbidity as well as viral activity, transoral surgery was considered effective. Since our patient had a low CD4+ T-cell count, HPV-negative tumor and a previous history of interstitial pneumonia, we selected transoral videolaryngoscopic surgery for his treatment and no postoperative functional decline was observed.

According to several report on lung cancer, postoperative complications for 18 patients have been limited to one death due to infection.[23–26] Another report concerning two patients with <200 lymphocytes/mm3 CD4+ T cells counts experienced no postoperative complications and showed satisfactory survival.[24] Surgery should thus be considered for localized or even locally advanced disease in patients with adequate pulmonary function and good general status, regardless of their immune status.[27] Our patient had a low CD4+ T-cell count, but good performance status and good pulmonary and heart function, which account for the absence of postoperative complications and recovery of swallowing function and no depletion of immunity. For this reason, transoral surgery was suitable for our patient.

The additional treatment is required, if the patient has adverse features. In this patient, both pathological examinations revealed negative vertical and horizontal margins. Pathological data showed a tumor thickness of 2.0 mm with no lymphatic vessel, blood vessel, or perineural invasion. In addition, ultrasound examination showed no metastatic lymph nodes. Therefore, we thought that no additional radiotherapy and neck dissection was needed.

This HIV-infected case with head and neck cancer demonstrated that transoral videolaryngoscopic surgery resulted in good oncological outcome, function preservation and no decline of CD4+ T-cell count.
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Disclosure statement

The authors report no conflicts of interest. The authors are responsible for the content and writing of this article.

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