Laryngeal cancer in acquired immunodeficiency syndrome

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Summary: With improved survival, more AIDS patients, especially heavy smokers and alcohol abusers, may be confronted with laryngeal squamous cell carcinoma. Since curative treatment may require aggressive combined therapy, these patients, often suffering from immunosupression and poor general condition, present unique therapeutic challenges. The objective of the study was to describe treatment dilemmas. This case report presents a detailed description of an AIDS patient with carcinoma of the larynx. A patient with T3N0M0 laryngeal carcinoma and AIDS underwent tracheotomy and biopsy, followed by severe neck and pulmonary infection. After convalescence, radiotherapy was administered, with no evidence of a disease during a 3.5-year follow-up. During his remaining life, the patient developed severe psychoaffective disorder, his immune state deteriorated until he demised from sepsis. In conclusion, patients with HIV infection, especially having a history of tobacco or alcohol abuse, should be carefully examined for head and neck carcinoma that is likely to be more aggressive. Following surgery, AIDS patients may have worse wound healing and a greater tendency to contract infections. Radiotherapy and especially chemotherapy may cause life-threatening complications. Although early detection may increase survival, curative treatment should involve many disciplines and extra caution.

Keywords: larynx, squamous cell carcinoma, AIDS

INTRODUCTION

Most head and neck malignancies among AIDS patients are non-Hodgkin’s lymphoma and Kaposi’s sarcoma. Squamous cell carcinoma is rare, it is probably non-HIV related; however, it may be more aggressive, with a worse prognosis compared with non-HIV patients.

New antiviral drugs, better supportive care and increased awareness improved survival among the patients and may bring more having squamous cell carcinoma to medical attention. Specifically, the introduction of highly active antiretroviral therapy (HAART) has been associated with reduction in the incidence of Kaposi’s sarcoma and non-Hodgkin’s lymphoma in HIV-infected people, while the rates of other cancers increased. Some cancers, such as laryngeal carcinoma, have been associated with the human papillomavirus. The rates of oral HPV infection may have increased since the initiation of HAART, hence increased head and neck oncology cases are reasonably expected.

Since curative treatment for head and neck squamous cell carcinoma is aggressive and often combines surgery, radiotherapy and chemotherapy, unique therapeutic dilemmas may be encountered.

CASE REPORT

A 58-years-old male was admitted with progressive dyspnea, sore throat, low fever and worsening hoarseness for few days. AIDS was diagnosed 10 years ago, following acute Pneumocystis jirovecii pneumonia. His infection was probably related to a sex adventure tour in Southeast Asia. He has been on different treatment regimens of antiretroviral medications under regular supervision of the AIDS clinic, and was very compliant with his medications, based on information from the clinic and his family. Still his CD4 count on admission was only 50 cell/mm³.

The patient smoked two packs of cigarettes per day for 40 years and denied alcohol or drug abuse. A year before current admittance, a left vocal cord polyp was diagnosed; however, he did not attend either biopsy or follow-up.

Endoscopy revealed supraglottic erythema and irregular, red and oedematous true vocal cords, having full mobility. There was central neck tenderness without lymphadenopathy. Supraglottitis was treated with antibiotics and steroid inhalations. On day 3, panendoscopy was done showing a necrotic mass involving the anterior commisure, the subglottis and the transglottic mass with paraglottic involvement, without neck lymphadenopathy. There were diffuse patches in both lungs that could possibly be interpreted as either an infectious or a neoplastic process. Tissue diagnosis was impossible because of the severity of his general condition; however, the lung lesions responded to the antibiotic treatment and became

smaller along with the improvement in the patient’s general condition.

Laryngeal samples were negative for fungi, tuberculosis, *P. jirovecii* or viruses, as were bronchoalveolar lavage samples. The histological examination of the laryngeal tumour showed invasive squamous cell carcinoma. At this time his right true vocal fold was found fixated. No lymph node enlargement was found clinically or per CT. The tumour was graded as a T3N0M0 glottic carcinoma. T3 was determined due to paraglottic involvement. Lung lesions were considered infectious since no malignant cells were seen on bronchoalveolar lavage and as during the follow-up period their size has not increased.

The treatment options considered were irradiation, chemotherapy, combined approach or surgery, namely total laryngectomy and tracheoesophageal puncture. Several disciplines were consulted, including Oncology, Infectious Diseases, AIDS Clinic and Psychiatry. The patient and his family were actively involved in all consultations. A decision was made to provide curative radiotherapy for both the larynx and the neck. A gastrostomy was made prior to the treatment.

The patient received radiotherapy to the larynx and the neck (overall 66 Gy over 12 weeks). The treatment was discontinued for one month due to decreased CD4 count, and was renewed following treatment with Enfuvirtide (Fuzeon, Roche Laboratories, Basel, Switzerland, a new antiretroviral drug, HIV-T helper cell binding inhibitor). This appeared to be effective, as the CD4 count rose to 100 cell/mm³.

At 1.5 years after completion of the radiotherapy, the patient regained oral feeding and his gastrostomy was closed. During the entire 3.5 years follow-up, there was a laryngeal, mostly supraglottic oedema, however, without any apparent mass, and the vocal folds mobility was normal. He remained tracheotomy-dependent because of this supraglottic oedema, and had limited speech. The neck examination was always normal. CT studies of the neck and the chest show glottic oedema and two small lesions in the left lung that have not changed.

During the last year of his life, the patient developed severe depressive disorder that required numerous admissions, several psychiatric medications and electroconvulsive treatments. Obviously, his limited speech was a salient obstacle. During the last three months of his life, he suffered from severe chest infection, parallel with very low CD4 counts, until he passed away from sepsis at the age of 62.

**DISCUSSION**

An AIDS patient with laryngeal mass presents diagnostic and therapeutic dilemmas to the otolaryngologist.

The differential diagnosis should include infectious diseases, i.e. tuberculosis, histoplasmosis or candidiasis, in addition to lymphoma, Kaposi’s sarcoma and squamous cell carcinoma. Patients with HIV and squamous cell carcinoma appear to be younger and present with more advanced disease than non-HIV patients. Patients with HIV and squamous cell carcinoma appear to be younger and present with more advanced disease than non-HIV patients. Cervical lymphadenopathy, however, can be related to the HIV infection and not to metastatic cancer, hence clinical staging of neck disease might be found in as many as 36% of the patients.

AIDS should be differentiated from HIV infection. Patients with AIDS usually have low CD4 count and poor general condition. Low CD4 count may prevent chemotherapy treatment, influence radiotherapy and surgery complication rate and overall survival. Therefore, treatment planning for laryngeal cancer should be based not only on the usual TNM staging, but also on the CD4 count. In this respect, cooperation with Infectious Diseases and AIDS units should be most helpful.

A handful of laryngeal carcinoma cases in AIDS were reported in the literature. Most patients appear to be HIV carriers, and only a few had AIDS.

Singh et al. presented large series of upper aerodigestive tract squamous cell carcinoma in 24 HIV-positive patients. He compared the course of the disease between patients with HIV and non-HIV-infected patients. Patients infected with HIV were found to be younger, had larger tumours and presented with more advanced stages. Tumour-related survival was significantly poorer in patients with HIV (57% at one year and 32% at two years) compared with 74% and 59% for non-HIV-infected patients. There was no distinction between HIV and AIDS. The treatment was based on accepted guidelines for the location and stage of the lesion; no special considerations were given to the HIV status. The patients had an increased incidence of surgical complications, most commonly infection, and increased radiation complication rate, mainly mucositis.

Munoz et al. described a 29-year-old patient with AIDS and squamous cell carcinoma of the larynx, who was treated with palliative radiotherapy and died six months later due to lung infection. Roland et al. reported eight HIV-positive patients with squamous cell carcinoma of the head and neck. Five of them suffered from laryngeal squamous cell carcinoma and one had manifestation of AIDS. The four HIV-positive patients were treated with combined therapy (surgery, radiotherapy and chemotherapy), and the AIDS patient was treated with radiotherapy alone. Only one HIV-positive patient succumbed to the oncological disease after 15 months, while the rest were without evidence of cancer at the time of the report. Harris et al. described a case of laryngeal squamous cell carcinoma in an HIV-positive patient, whose CD4 count was 350, which was treated successfully with radiotherapy. This may accentuate the importance of regular antiretroviral therapy.

Other series include laryngeal cancer as one of the afflictions of HIV patients, without many details. It appears that while the nature of the carcinomas may be aggressive, they are rare, and not part of the spectrum of AIDS. There is no similar case ever recorded in the Israeli National Cancer Registry.

Faced with an advanced laryngeal cancer, such as T3N0M0 in the present case, one should decide if the usual aggressive, combined approach is warranted, or rather a more conservative therapy should be chosen.

Given the aggressive course of squamous cell carcinoma in HIV patients and increasing life span of AIDS patients owing to effective antiretroviral medications, palliative care may be an improper treatment decision, and a curative aim is warranted.

Surgery for advanced head and neck carcinoma may require prolonged anaesthesia, drainage, cauterization, tube feeding, flaps and fair wound healing.

Wound healing may be defective in HIV infections. When there was preoperative contamination, increased incidence of wound infection was found in HIV-positive patients compared with that in HIV-negative patients (42% versus 11%, respectively). CD4 lymphocyte count is one of the key determinants in the healing process. Healing prospects vary also in relation to the nature of the surgical intervention - whether it is elective or emergent. While watchful monitoring is indicated, like in any immunocompromised patient, the risk cannot be predicted in either a carrier or an AIDS patient.
Chemoradiation in such laryngeal cases is often considered as an organ preservation treatment; however, such a treatment may be difficult to tolerate in HIV-positive patients. Chemotherapy may increase infection risk, especially in patients whose immune system is impaired. Patients with CD4 less than 200 cells mm$^{-3}$ experience increased therapy-related acute toxicity.30

Radiotherapy in HIV-positive patients may cause severe mucositis.31 Proper irradiation treatments necessitate good compliance and good physical condition during the treatment period. AIDS patients often do not meet these requirements. The presented patient with a squamous cell carcinoma of the larynx was an AIDS patient, unresponsive to anti-AIDS therapy, and with a low CD4 count. Since he developed severe post-surgery infection, chemotherapy and further surgery were excluded, and therefore radiotherapy was elected as the sole modality. While the regular irradiation course was disrupted due to low CD4 count, it was eventually completed, and the patient seemed to be doing fine. The laryngeal oedema was clinically monitored; however, in a usual patient a biopsy is indicated.

In addition to the direct treatment dilemmas, the surgical and the nursing staff of the Department of Otolaryngology had to be constantly aware of the risks to themselves and take precautions such as double gloving, eye protection and waterproof gowns. Decontamination of the examination tools became an issue, especially with regard to the flexible endoscope. The patient was semi-contained in order to protect him from acquiring hospital-related infections. On the other hand, particular attention was given to provide him with a welcoming atmosphere, he was encouraged to have daily walks and entertain visitors, and along with his family they were escorted by the Psychiatry, Social Work, Nutrition and AIDS units.

Despite our great efforts and apparent success to save his life from cancer, this poor individual was struck by severe affective disorder and later his general condition deteriorated until he demised with great suffering. This has left a great impression on our staff, and partially motivated this publication.

ACKNOWLEDGEMENTS

During the early stages of case management, we consulted with several colleagues (see list below). Their cordial responses and (variable) advice are gratefully acknowledged. (Drs Bedrin, Duek, Feinmesser, Fliss, Freeman, Gullane, Johnson, Leemans, Shah, Urken, van den Brekel, Witterick.)

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