

Squamous Cell Carcinoma of the Anus and HIV Infection

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We retrospectively reviewed six patients with squamous cell carcinoma of the anus (SCCA) and human immunodeficiency virus (HIV) infection treated between 1985 and 1988. All six patients were homosexual men. Five patients had AIDS and one was HIV-positive. The most common symptoms and signs were pain ($n = 5$), mass ($n = 5$), and bleeding ($n = 5$). The average tumor size was 3.2 cm with a range of 1-10 cm. Five tumors were located in the anal canal and one at the anodermal junction. One patient was treated with biopsy alone, one with local excision, one with wide local excision and radiation therapy, and two with diverting colostomy. The average follow-up was 8 months. Of the five AIDS patients, two died, one was transferred to a hospice facility, one was lost to follow-up, and one remains alive 1 year following treatment. The HIV-positive patient died secondary to metastatic SCCA. This group of patients raises the question of a possible association between HIV and SCCA. [Key words: Squamous cell carcinoma; Anus; HIV; AIDS]

We retrospectively reviewed our experience with squamous cell carcinoma of the anus (SCCA) in patients with human immunodeficiency virus (HIV) infection at the University of California, San Francisco, because of a perceived increase in frequency of patients presenting with both diagnoses.

MATERIALS AND METHODS

Tumor registry and pathology records were scanned, and hospital charts were reviewed for all patients with both SCCA and HIV infection between 1980 and 1988. Six patients were identified with a diagnosis of HIV infection and SCCA. Five patients had AIDS and one patient was HIV-positive without a history of AIDS. All of the patients with a diagnosis of AIDS had either a history of *Pneumocystis carinii* pneumonia or Kaposi's sarcoma. All six patients were gay men with biopsy-proven SCCA diagnosed between 1985 and 1988. Data were coded for risk factors, symptoms, signs, lab-

complications, and survival. Tumors were staged retrospectively according to the method of Richards *et al.* (Table 1).¹

RESULTS

The average age was 37 with a range of 31-57 years. The clinical history of each patient is summarized in Table 2. The patients had a variety of common anorectal disorders in addition to the anal cancer. There were three patients who had hemorrhoids. One patient with hemorrhoids had an associated fistula-in-ano. The most common presenting symptoms and signs were anal mass, pain, and bleeding. The mean hematocrit was 25.6 with a range of 16-41. All of the gay men with AIDS had hematocrits less than or equal to 30. The alkaline phosphatase was normal in all six patients. The mean tumor size was 3.3 cm at diagnosis, with a range of 1-10 cm. Three tumors were stage A, and two stage C. One patient could not be staged retrospectively because of insufficient data recorded in the medical record.

One of the tumors was located at the anodermal junction and five tumors were located in the anal canal. One of the two patients with AIDS and SCCA who had a diagnostic biopsy but no further therapy was considered to be too ill to tolerate chemotherapy or radiation therapy (XRT). The other patient initially refused treatment and presented 18 months later with obstruction requiring an emergency diverting colostomy (Patient 4). One patient was treated with local excision and XRT initially, but required diverting colostomy 8 months later (Patient 3).

Follow-up ranged from 3 months to 1 year, with an average follow-up of 8 months. Two patients died; one of these patients died as a result of AIDS (Patient 4). The HIV-positive patient died as a result of metastatic SCCA 9 months after diagnosis (Patient 3). Two additional patients with advanced AIDS were lost to follow-up (Patients 1 and 6). Two of the AIDS patients treated with local exci-

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sion of the tumor were alive 3 and 12 months after diagnosis (Patients 2 and 5). Both of the surviving patients with AIDS and SCCA had Stage A tumors. One of these Stage A tumors was located at the anodermal junction (Patient 2).

DISCUSSION

The incidence of SCCA has increased in the past decade²⁻⁵ and the disease is now more common in men than women in San Francisco. Homosexual behavior and anoreceptive sexual intercourse are associated with an increased incidence of SCCA.⁶⁻⁸ Anal condylomata and human papillomavirus (HPV) have been associated with SCCA, raising the possibility of a viral etiology of the tumor.⁸⁻¹¹ Recently, HPV DNA has been localized in SCCA cells.¹² Surprisingly, none of the six patients we treated with HIV infection and SCCA in the past 3 years had associated anal condylomata. All of our patients were at high risk for both human immunodeficiency virus (HIV) infection and SCCA. An

association of anorectal epithelial dysplasia with HIV seropositivity in homosexual men was noted prospectively by Frazer *et al.*⁸ In their study, HIV did not appear to initiate anal dysplasia but acted as a promoter. HIV may be a cofactor that HPV requires to induced anorectal dysplasia.⁸

Specific treatment recommendations for this unique group of patients are difficult based on the small number of patients in this study. Although case reports exist,¹³ to date, no published series of HIV-infected patients with SCCA exist. Most authors currently recommend preoperative XRT and/or CTX with local resection of residual tumor or definitive CTX and XRT without surgery in the treatment of SCCA in non-HIV-infected patients.¹⁴⁻²⁰ Small tumors and areas of carcinoma *in situ* or dysplasia are amenable to local excision. Radical resection is reserved for those patients with residual or recurrent disease.

We recommend radiotherapy or wide local excision for the control and possible cure of patients with Stage A disease. No chemotherapy was administered to any of our patients for fear of worsening their immunocompromised state. For Stage B or C patients, we recommend primary radiotherapy with later excision of local tumor, if necessary.

Although follow-up information on this group of patients is incomplete, the outcome was poor. Five

Table 1.
Staging of SCCA

Stage	Depth of Tumor Invasion
A	Tumor invasion into anal sphincter muscle
B	Tumor invasion through anal sphincter muscle
C	Tumor metastatic tumor to regional lymph

Table 2.
Clinical Summary

Patient	Associated Anorectal Disorders	Findings	Treatment	Complications	Location	Size (cm)	Stage	Survival
1	None	Bleeding, pain	Biopsy	None	Canal	1	?	Lost to F/U Referred for XRT
2	Fistula PRA	Mass, drainage	Biopsy, I & D PRA	None	Anoderm	1	A	F/U 1 year Alive
3*	None	Bleeding, pain, mass, CBH	Local excision, XRT colostomy	Radiation proctitis	Canal	3	C	F/U 9 months Died
4	Hemorrhoid	Bleeding, pain, mass, CBH	Biopsy, colostomy	Prolapsed mucous fistula	Canal	10	C	F/U 11 months Died
5	Fistula Hemorrhoid	Bleeding, pain, mass, drainage, CBH	Local excision	None	Canal	1	A	F/U 3 months Alive
6	Hemorrhoid Anal herpes	Bleeding, pain, mass, drainage	Biopsy	None	Canal	2	A	Lost to F/U after 4 months Referred for hospice care

PRA = perirectal abscess; I & D = incision and drainage; CBH = change of bowel habits; F/U = follow-up.

* HIV+ without AIDS.

patients had AIDS. The HIV-positive patient without AIDS had an aggressive tumor that caused his death. Therapy should be directed at local control of the tumor. As the AIDS epidemic progresses, we may be faced with an increasing number of patients with SCCA. The solution to this clinical problem awaits improved understanding and treatment of HIV infection.

CONCLUSION

Six patients with a diagnosis of HIV infection and SCCA have been treated at the University of California, San Francisco, in the past 3 years. The most common complaints were pain, bleeding, and a mass. The tumors were aggressive and the outcome poor. The question of a possible relation between HIV infection and SCCA is unresolved.

REFERENCES

- Richards JC, Beahrs OH, Woolner LB. Squamous cell carcinoma of the anus, anal canal, and rectum in 109 patients. *Surg Gynecol Obstet* 1962;114:475-82.
- Crombleholme T, Schecter WP, Wilson W. Anal carcinoma: changes in incidence, natural history, and treatment: a 26-year review of the UCSF-SFGH experience (abstr). *Pro Am Soc Clin Oncol* 1989;8:4.
- Peters RK, Mack TM. Patterns of anal carcinoma by gender and marital status in Los Angeles County. *Br J Cancer* 1983;48:629-36.
- Wexner SD, Milsom JW, Dailey TH. The demographics of anal cancers are changing: identification of a high-risk population. *Dis Colon Rectum* 187;30:942-6.
- Daling JR, Weiss NS, Hislop TG, *et al.* Sexual practices, sexually transmitted diseases, and the incidence of anal cancer. *N Engl J Med* 1987;317:973-7.
- Daling JR, Weiss NS, Klopfenstein LL, *et al.* Correlates of homosexual behavior and the incidence of anal cancer. *JAMA* 1982;247:1988-90.
- Holmes F, Borek D, Owen-Kummer M, *et al.* Anal cancer in women. *Gastroenterology* 1988;95:107-11.
- Frazer IH, Medley G, Crapper RM, *et al.* Association between anorectal dysplasia, HPV, and human immunodeficiency virus infection in homosexual men. *Lancet* 1986;2:657-60.
- Howley PM. On human papillomaviruses (editorial). *N Engl J Med* 1986;315:1089-90.
- Macnab JC, Walkinshaw SA, Cordiner JW, Clements JB. Human papillomavirus in clinically and histologically normal tissue of patients with genital cancer. *N Engl J Med* 1986;315:1052-8.
- Palmar JG, Scholefield JH, Coates PJ, *et al.* Anal cancer and human papilloma viruses. *Dis Colon Rectum* 1989;32:1016-22.
- Gal AA, Saul SH, Stoler MH. *In situ* hybridization analysis of human papillomavirus in anal squamous cell carcinoma. *Mod Pathol* 1989;2:439-43.
- Rudlinger R, Buchmann P. HPV 16-positive Bowenoid papulosis and squamous-cell carcinoma of the anus in an HIV-positive man. *Dis Colon Rectum* 1989;32:1042-5.
- Boman BM, Moertel CG, O'Connell MJ, *et al.* Carcinoma of the anal canal: a clinical and pathological study of 188 cases. *Cancer* 1984;54:114-25.
- Cummings B, Keane T, Thomas G, *et al.* Results and toxicity of the treatment of anal canal carcinoma by radiation therapy or radiation therapy and chemotherapy. *Cancer* 1984;54:2062-8.
- Flam MS, Madhu JJ, Mowry PA, Loralvo LJ, Ramalho LD, Wade J. Definitive combined modality therapy of carcinoma of the anus: a report of 30 cases including results of salvage therapy in patients with residual disease. *Dis Colon Rectum* 1987;30:495-502.
- Gerard A, Buyse M, Nordlinger B, *et al.* Preoperative radiotherapy as adjuvant treatment in rectal cancer: final results of a randomized study of the European organization for research and treatment of cancer (EORTC). *Ann Surg* 1988;208:606-14.
- Greenhall MJ, Quan SH, Stearns MW, *et al.* Epidermoid cancer of the anal margins: pathological features, treatment, and clinical results. *Am J Surg* 1985;149:95-101.
- Papillon J, Montbarbon JF. Epidermoid carcinoma of the anal canal: a series of 276 cases. *Dis Colon Rectum* 1987;30:324-33.
- Talbot RW. Changing nature of anal cancer: radical operations can often be avoided. *Br Med J* 1988;297:239-40.