HIV-Positive Patients with Anal Carcinoma Have Poorer Treatment Tolerance and Outcome than HIV-Negative Patients

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PURPOSE: Anal carcinoma is being found in HIV-positive patients with increasing frequency. Most patients are treated with combined chemotherapy and radiation. It was our impression that HIV-positive patients do not fare as well as HIV-negative patients in terms of both response to and tolerance of therapy. METHODS: To test this hypothesis, we reviewed our experience with anal carcinoma and compared HIV-positive to HIV-negative patients by age, gender, sexual orientation, stage at diagnosis, treatment rendered, response to treatment, tolerance, and survival. From 1985 to 1998, 98 patients with anal neoplasms were treated. Seventy-three patients had invasive squamous-cell carcinoma (including cloacogenic carcinoma), and this cohort was analyzed. Thirteen patients were HIV positive and 60 were HIV negative. RESULTS: The HIV-positive and HIV-negative groups differed significantly by age (42 vs. 62 years, \( P < 0.001 \)), male gender (92 vs. 42 percent, \( P < 0.001 \)), and homosexuality (46 vs. 15 percent, \( P < 0.05 \)). There were no differences by stage at diagnosis or radiation dose received. Acute treatment major toxicity differed significantly (HIV positive 80 percent vs. HIV negative 30 percent; \( P < 0.005 \)). Only 62 percent of HIV-positive patients were rendered disease free after initial therapy vs. 85 percent of HIV-negative patients (\( P = 0.11 \)). Median time to cancer-related death was 1.4 vs. 5.3 years (\( P < 0.05 \)). A survival model did not show age, gender, stage, or treatment to be independent predictors. CONCLUSION: We found that HIV-positive patients with anal carcinoma seem to be a different population from HIV-negative patients by age, gender, and sexual orientation. They have a poorer tolerance for combined therapy and a shorter time to cancer-related death. A strong trend to poorer initial response rate was also seen. These results suggest that the treatment of HIV-positive patients with anal carcinoma needs to be reassessed. [Key words: Anal cancer; Anal carcinoma; Cloacogenic carcinoma; Squamous-cell carcinoma; HIV; AIDS; Radiation therapy; Chemotherapy]

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adenocarcinomas, 4 lymphomas, and 1 malignant melanoma) were treated at The George Washington University Medical Center and the Veterans Administration Medical Center, Washington, D.C., between May of 1985 and October of 1998. Among them, 23 patients were HIV positive (13 epidermoid cancers, 7 Bowen's disease, 2 lymphomas, and 1 adenocarcinoma). Seventy-three patients had invasive anal epidermoid (squamous or cloacogenic) carcinoma and formed the study group. This cohort was analyzed retrospectively by review of their medical records, phone calls to the patients, and contact with their other physicians.

Of the 73 patients, 13 were HIV+ and 60 were HIV−. Biopsies were performed on all primary tumors. Preoperative staging was performed using examination, anal ultrasound, chest x-rays, and CT scanning. After completion of primary therapy, patients were seen every two to three months for three years, every six months until the end of the fifth year, and then annually. Posttreatment evaluation included a careful clinical examination with digital palpation and anoscopy at each visit. Posttreatment biopsies were only performed when a suspicious area was identified. Most patients were followed with regular anal ultrasounds, and all had annual chest x-rays and CT scans. Patients were staged according to the system adopted by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) before primary treatment (Table 1).

Most patients were treated with combined chemotherapy and radiation (Table 2). Twenty percent of the HIV− patients had limited, small lesions and underwent surgery only for treatment of their disease. Among the HIV+ patients, three did not receive combined therapy (one each because of a severe anal fissure, a small lesion excised from the anal verge, and a large ulcerating cancer invading into the coccyx). Combined chemoradiotherapy was performed in a standard fashion. Radiotherapy was administered over a six-week period to a planned dose of 5000 to 5400 cGy. The mean radiation doses completed did not vary between the two groups (HIV+ 5117 ± 243 cGy, HIV− 5146 ± 118 cGy; P = 0.46). Chemotherapy was administered in two cycles. 5-Fluorouracil at a dosage of 1000 mg/m² was given as a continuous infusion during the first four days of radiation therapy and again at its completion. Mitomycin C (10 mg/m²) was given as a bolus injection on the first day of chemotherapy. The Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) scoring criteria was used in assessing acute and late treatment toxicity. Follow-up records addressing toxicity of combined chemoradiation therapy were available for 33 of the 42 HIV− patients.

Survival curves for the two groups were modeled using the Kaplan-Meier method. Differences in survival across the groups were tested using the Wilcoxon test. Cox’s proportional hazards regression was used to evaluate the effects of potential covariates. Differences between groups on continuous variables were tested using the Student’s t-test. The Fisher’s exact test was used to test for differences between groups on categorical variables.

**RESULTS**

There were significant differences between the HIV+ and HIV− populations. The HIV+ patients were younger (42 vs. 62 years, P < 0.001), mostly male (92 vs. 42 percent, P < 0.001), and more likely to be homosexual (46 vs. 15 percent, P < 0.05) (Table 3).

Nine of the 13 HIV+ patients were categorized as having AIDS by Centers for Disease Control and Prevention criteria. The CD4 cell count in these patients averaged 146 cells per microliter at the time of diagnosis (range, 30–290).

Therapy was much more poorly tolerated in the HIV+ group, with higher rates of acute and late toxicity (Tables 4 and 5). Major acute toxicity (Grades 3 and 4) was seen in 8 of 10 HIV+ patients (80 percent).