Squamous Cell Carcinoma of the Anal Canal

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The estimated time to complete this activity is 1 hour.

GOAL

To understand squamous cell carcinoma of the anal canal (SCCAC) to better manage patients with the condition

LEARNING OBJECTIVES

Upon completion of this activity, you will be able to:

1. Discuss the incidence of SCCAC in immunocompromised individuals.
2. Identify risk factors for SCCAC.
3. Evaluate treatment options in patients with and without human immunodeficiency virus infection.

INTENDED AUDIENCE

This CME activity is designed for dermatologists and general practitioners.

CME Test and Instructions on page 132.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: February 2010.

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Squamous cell carcinoma of the anal canal (SCCAC) is an increasing concern in the human immunodeficiency virus (HIV)–positive population in the highly active antiretroviral therapy (HAART) era. A discussion of the epidemiology, risk factors, clinical presentation, diagnosis, and treatment of SCCAC is presented.

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Epidemiology

The incidence of squamous cell carcinoma of the anal canal (SCCAC) has increased from 0.6 per 100,000 individuals in the pre–human immunodeficiency virus (HIV) era (1973-1981) to 0.8 in the HIV era (1982-1995) to 1.0 in the highly active

antiretroviral therapy (HAART) era (1996-2001). With improved HAART for patients with HIV and consequently a longer lifespan, the prevalence rates of SCCAC are an increasing concern.[1] Squamous cell carcinoma of the anal canal associated with human papillomavirus (HPV) in HIV-infected homosexual males appears to be increasing in high-risk populations. Once a relatively uncommon condition, SCCAC is now recognized as a sexually transmitted disease seen more commonly in immunocompromised individuals.[2]

Risk Factors

Squamous cell carcinoma of the anal canal is associated with chronic HIV infection, anal intercourse, anal condylomata, and high-risk HPV-16 and HPV-18.[3] Piketty et al[4] reported the following risk factors for abnormal anal cytology: a CD4 lymphocyte count less than 250×10^6 cells/L, a nadir CD4 lymphocyte count less than 100×10^6 cells/L, plasma HIV RNA level greater than 1.7 log copies/mL, a prior AIDS-defining event, and a test result positive for HPV on polymerase chain reaction. Human papillomavirus is believed to transform anal epithelia into low-grade squamous intraepithelial lesions (SILs), high-grade SIL, and eventually squamous cell carcinoma.[3]

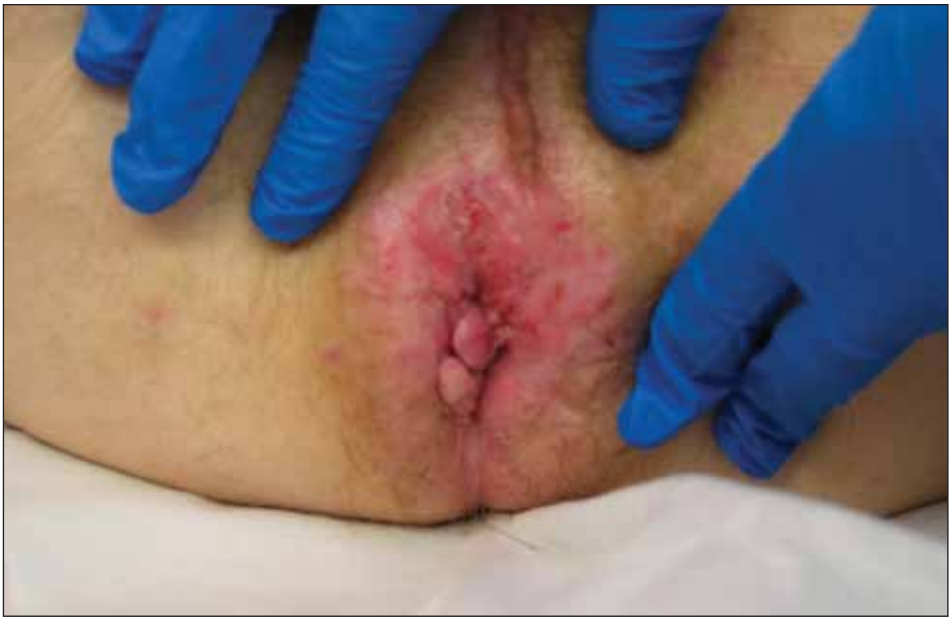
Human immunodeficiency virus–immunocompromised hosts have a reduced ability to combat HPV infections, resulting in high-grade SIL being 3 times more common in HIV-positive males than in HIV-negative males. In a study of 257,605 HIV-positive males over 5 years, the relative risks for developing in situ anal cancer and invasive anal cancer were 60.1 (95% CI, 49.2-72.7) and 37.9 (95% CI, 33.0-43.4), respectively.[5] The increased incidence of anogenital SIL associated with declining CD4 lymphocyte counts may be associated with altered HPV-16 and HPV-18 E6 and E7 gene expression or an accumulation of additional genetic damage from unknown cofactors. The risk is highest with a CD4 lymphocyte count of 500 cells/μL or less, with no further increased risk for CD4 lymphocyte counts less than 100 cells/μL.[5]

Clinical Presentation and Diagnosis

The clinical presentation of SCCAC typically includes a mass in the anal area with bleeding and pain (Figure). Patients with SCCAC often have symptoms similar to common anal conditions such as fissures or hemorrhoids. The disease can become symptomatic with anal bleeding, pain, presence of a mass, pruritus, anal discharge, tenesmus, or fecal incontinence.[2] Screening with anal cytology for HPV has been recommended for HIV-positive patients practicing receptive anal intercourse. The diagnosis of SCCAC is established by histopathologic examination of lesional tissue.[6]

Treatment

Standard therapy for HIV-negative patients with SCCAC is a combination of radiation therapy and chemotherapy with intravenous 5-fluorouracil and mitomycin C.[7,8] There is no consensus on the optimal treatment of HIV-positive individuals receiving HAART because of limited available data. Human immunodeficiency virus–infected individuals experience an increase in side effects from standard chemoradiotherapy for SCCAC as compared to HIV-negative individuals. These side effects include radiotherapy-induced severe cutaneous toxicity



Nodules and ulceration representing invasive squamous cell carcinoma of the anal canal in a human immunodeficiency virus–negative patient. The surrounding erythema represents Bowen disease. Photograph courtesy of Paul A. Lucha Jr, DO, Department of Surgery, Naval Medical Center, Portsmouth, Virginia.

and chemotherapy-induced hematologic toxicity in patients receiving mitomycin.[9] Treatment protocols can be modified to decrease toxicity, including longer treatment breaks, continuous 5-fluorouracil with a lower mitomycin C dosage, and a smaller radiation field size with the use of intensity-modulated radiation therapy.[10]

Treatment with radiotherapy or chemoradiotherapy with intravenous fluorouracil and mitomycin or cisplatin was evaluated in a retrospective study of 40 HIV-positive patients taking HAART and 81 HIV-negative patients primarily with SCCAC (1 HIV-positive patient had anal neuroendrocrine carcinoma and 1 HIV-negative patient had anal adenocarcinoma).[9] A complete response was noted in 92% of HIV-positive patients and 96% of HIV-negative patients. The 5-year overall survival was 61% in HIV-positive patients and 65% in HIV-negative patients. The 5-year local disease control was 38% in HIV-positive patients and 87% in HIV-negative patients. The 5-year overall survival was similar for HIV-positive and HIV-negative patients, but the local relapse rate was higher in HIV-positive patients.[9] Disease stage and completion of radiotherapy are the most remarkable predictors of relapse-free survival in both HIV-positive and HIV-negative individuals.[11]

Patients who failed initial chemoradiotherapy for SCCAC may be candidates for salvage surgery. A 39% calculated (actuarial) 5-year overall survival has been reported in 40 patients who have undergone salvage surgery (multivisceral resection, abdominoperineal resection, or local excision) after failing initial combined chemoradiation or radiation alone for SCCAC.[12]

Conclusion

Squamous cell carcinoma of the anal canal is an increasing concern in the HIV-positive population with improved HAART.[1] Additional studies are needed to delineate the most appropriate therapy for SCCAC in HIV-positive patients.

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