

Human papillomavirus-associated cancers as acquired immunodeficiency syndrome defining illnesses

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Abstract

The Centers for Disease Control currently report cervical, vulvar, vaginal, anal and some head and neck cancers as human papillomavirus (HPV)-associated cancers. Only cervical cancer is listed amongst acquired immunodeficiency syndrome (AIDS) defining illnesses. All of these cancers may represent progression of the immunocompromised state with the inability to eradicate viral infection. This study reports the case of a 27-year old HIV positive female presenting with a persistent right vulvar exophytic lesion. High-risk HPV analysis and immunostaining for P16 were both positive. A biopsy of the lesion revealed invasive squamous cell carcinoma. The patient underwent neoadjuvant radiation and chemotherapy followed by a radical vulvectomy. During treatment, her CD4 T-lymphocyte count decreased to 120 advancing her condition from HIV to AIDS. This case suggests that all HPV-associated cancers should be included as AIDS defining illnesses.

Introduction

In January 2003, the Centers for Disease Control and Prevention (CDC) expanded the definition of AIDS to include invasive cervical cancer based upon preliminary data showing a high incidence of cervical intraepithelial neoplasia (CIN) amongst women infected with HIV. Currently, it is accepted that HIV-positive women have higher incidences of high-risk HPV infections and CIN than the general population.¹ Due to the compromised immune system, CIN is more likely to progress to an intra-epithelial neoplasia or invasive carcinoma.

Case Report

We report the case of a 27-year-old G5 P2 HIV positive female with a long history of a right vulvar mass. She presented with a 15x10x7 cm right vulvar lesion extending to the perianal region (Figure 1). Multiple lymph nodes were palpable bilaterally in the groin. A biopsy of the lesion was performed and revealed invasive squamous cell carcinoma with spindle sarcomatoid feature and no lympho-vascular invasion. High risk HPV analysis and immunostaining for P16 were both positive.

She was on highly active anti-retroviral therapy (HAART) including Norvir, Reyataz and Truvada for 10 years. Her CD4 T lymphocytes count at the time of presentation was 675 cells per cubic mm/blood with a viral load of 85 copies/mL.

A pre-operative PET/CT scan revealed a large vulvar mass with extension to the medial aspect of the right thigh with intense uptake of all reported areas. Bilateral inguinal lymph nodes showed moderate to intense uptake, suspicious of metastases.

Based on the extent of her disease she underwent neoadjuvant chemotherapy and radiation as per the Gynecologic Oncology Group (GOG) protocol 101.² The patient tolerated concurrent cisplatin and 5-fluorouracil (5-FU) chemotherapy and radiation. Based on persistent superficial vulvar lesions and palpable bilateral inguinal nodes, the patient underwent a radical vulvectomy with bilateral superficial inguinal and deep femoral lymph node dissection.

Final pathology revealed carcinoma-*in-situ*, with no invasive carcinoma. All lymph nodes were negative for malignancy. Patient tolerated surgery well with no complications. During her treatment course her CD4 count decreased to 120 cells per cubic mm/blood advancing her condition from HIV to AIDS.

Discussion

Current diagnostic criteria for AIDS includes infection with HIV and a CD4 count <200 cells per cubic mm/blood or a CD4 percentage <14 regardless of symptoms or opportunistic diseases or the presence of a specified opportunistic disease, regardless of CD4 count.³

According to the CDC, HPV-associated cancers include: cervical, vulvar, vaginal, penile, anal and some head and neck cancers. Only cervical cancer may be used as an AIDS defining illness today.

Intraepithelial neoplasias of the cervix and vulva have strong associations with HPV subtypes 16, 18, 31, 33, 35 and 51. Current litera-

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Key words: HIV, HPV associated cancer, AIDS.

Contributions: KF, MF, DL, RS, SS, conception and design, manuscript writing, final approval of the manuscript.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 16 August 2012.

Revision received: 4 March 2013.

Accepted for publication: 12 April 2013.

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Rare Tumors 2013; 5:e25
doi:10.4081/rt.2013.e25

ture shows a relationship between HPV subtype 16 and vulvar cancer.⁴ It's currently estimated that 60% of vulvar cancer can be linked to HPV, and of these cancers 56% are caused by HPV subtypes 16 and 18. HPV subtype 16 is also the most common subtype associated with cervical cancer.⁴

Recurrence of CIN, after surgical treatment, has been associated with elevated viral loads and low CD4 counts, but was not affected by the degree of CIN;⁵ leading to the theory that the degree of immunocompromise has a greater effect on the recurrence of the neoplasia than the original severity of the cervical disease.

Earlier literature has shown that the immunocompromised state following renal transplants resulted in a 100-fold increase in the incidence of vulvar and anal carcinomas.⁶

A recent retrospective study by Gray *et al.* determined that a low CD4 count was associated with a statistically significant increase in vulvar and vaginal carcinoma *in situ* and invasive cancer 28-60 months after the diagnosis of AIDS.⁴ Therefore, we propose that AIDS defining illnesses should include all HPV associated cancers in addition to cervical cancer.

Conclusions

The patient that we described here developed invasive vulvar cancer with a CD4 count



Figure 1. Persistent right vulvar exophytic lesion.

greater than 200. Changing the current definition of AIDS defining illnesses would have given her the diagnosis of AIDS at the time of

biopsy. As her CD4 count eventually decreased to 120 her disease progressed to AIDS. Despite the progression of her immunocompromised state, she responded well to her treatment course.

Taken together these observations suggest that despite the challenges of immunocompromised and impaired wound healing in this population, treatments based on chemotherapy, radiation and surgery may be successful.

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