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CLINICAL VIGNETTE

An Important Cause of Rectal Bleeding in a Young Male

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A 36-year-old male presented with intermittent rectal bleeding for one month. He initially tried over the counter topical steroid creams, without improvement. He denied any significant past medical or surgical history and he had no family history of gastrointestinal diseases. His social history was significant for polysubstance abuse and unprotected sex with men. On exam, the patient appeared underweight, his rectal examination showed external hemorrhoids and poor sphincter tone. Laboratory evaluation demonstrated a mild normocytic anemia and a new positive HIV test. Colonoscopic examination revealed an 8cm circumferential, fungating rectal mass abutting the dentate line and extending proximally into the rectum. Pathology showed dense lymphoplasmacytic infiltrate, and p16 and high-risk HPV stain positivity confirming diagnosis of high-grade dysplasia. The spirochete stain was negative. The final pathologic diagnosis was anal intraepithelial neoplasia further classified as a high-grade squamous intra-epithelial lesion. The patient was evaluated by Infectious Diseases and Colorectal surgery and started on bicitgravir-emtricitabine-tenofovir for HIV.

Discussion

Patients with HIV are at risk for various types of anorectal disease. HPV associated anal intraepithelial neoplasia (AIN) or squamous intraepithelial lesions (SIL) are important pathways to invasive squamous anal carcinoma with portends significant morbidity and mortality. This discussion will briefly review the epidemiology, diagnosis, screening, and prevention methods and treatment of AIN.

Critical to this discussion is that the anal canal and cervix share embryologic, histologic and pathologic characteristics. During embryonic development, both the anal canal and cervix, endodermal and ectodermal tissue fuse to form a squamocolumnar epithelial junction. This junctional tissue can display abnormal changes due to HPV infection. Anal SIL shares cytological features with cervical SIL.

The terminology describing AIN now includes the Bethesda classification system in the cytological and pathological evaluation. These are 5 different categories of abnormality, in order of increasing severity: Anal cytology is described as negative for SIL, Atypical squamous cells of undetermined significance, Low grade SIL, Atypical squamous cells cannot exclude high-grade SIL and High-Grade SIL.¹

The overall incidence of anal cancer is low, approximately 1.8 cases per 100,000 patients, which makes the determination of the incidence of AIN difficult. Patients with HIV, HPV or with history of organ transplantation are at significantly higher risk for AIN and anal cancer.² The rate of conversion of AIN to anal cancer is undefined. Studies suggest the rate is similar to cervical cancer, with about 9-13% conversion for high risk lesions.³ There are also reports of spontaneous disease regression. One study showed that high grade AIN can regress to low grade at a rate of 17% and to no disease at a rate of 7%.⁴

Retrospective analyses have shown HPV to have a clear association with AIN and anal cancer with the prevalence of HPV among patients with AIN estimated at over 90%.⁵

In addition to HPV, HIV infection also is a significant public health concern and plays an important role in AIN and anal cancer. Patients with HIV, particularly men who have sex with men (MSM) have an increased risk of AIN and anal cancer. Rates of anal cancer are 30-100 times higher in patients with HIV compared to the general population.⁶

Finally, patients with immunocompromising conditions such as organ transplant or inflammatory bowel disease may have increased risk of AIN, although more studies are needed to further understand this connection.^{7,8}

Currently, there is no standardized screening protocol for AIN. Similar to screening in cervical cancer, it is thought that screening for AIN could reduce the incidence of anal cancer. In regards to screening, patients can be categorized as low or high risk. There is no current recommendation for screening patients thought to be at low risk for AIN or anal cancer. The low risk group includes patients who are immunocompetent, HIV negative, men who have sex with women without IBD and with no history of cervical cancer. High risk patients are those who are HIV-positive, MSM, or immunocompromised. Various infectious disease societies have recommended annual cytology for HIV-positive patients, especially MSM, or have a history of cervical cancer.⁹ However, the optimal screening tool for high risk patients has not been established. While anal cytology can be easily performed in a primary care setting, similar to screening for cervical cancer, it has a high rate of false negatives in high risk patients. High resolution anoscopy has better sensitivity and specificity compared to cytology, but is more difficult to perform with higher cost.

Although no consensus regarding surveillance intervals exist, most societies recommend yearly surveillance for HIV positive males, and every 3-6 months for those with low-or high-grade AIN.

Along with screening, HPV vaccination may help prevent AIN and anal cancer. Studies report AIN patients who had received the HPV vaccine have reduced rates of progression of AIN to anal cancer.^{8,10}

No consensus guidelines on the treatment of AIN exist. Management is separated into watchful waiting or interventional therapies. There are no randomized studies comparing therapeutic modalities. Most of the supporting data is derived from case reports, case control series or single institution studies. Treatment options include surgical excision, ablation with either fulguration or laser coagulation and topical therapies. One large single center study suggests combination therapy with topical and invasive therapy may offer the best benefit.¹¹

Following initiation of HAART, the patient returned to the colorectal surgery. Examination showed the anal lesion to appear smaller and improved compared to before HAART was begun. Continued surveillance was recommended with no immediate therapy for the AIN. This case highlights several important points. First, the evaluation of a young patient with new onset rectal bleeding should prompt a referral for thorough examination with either sigmoidoscopy or colonoscopy. Even if the underlying cause is benign, it is critical to make the correct diagnosis and exclude more dangerous alternatives. Lastly, this exemplifies a condition for which standardized screening and treatment protocols do not exist. It is important to remember that some conditions require a nuanced patient specific treatment approach that is best accomplished in a multi-disciplinary, collaborative manner.

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