



## Herpes Simplex Viral Cytopathic Effect in Anorectal Cytology of a HIV Positive Homosexual Man Presented with Acute Proctitis

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### Abstract

**Objective:** Herpes Simplex Virus (HSV) cytopathic effects in anorectal cytology specimens have rarely been described. Presence of HSV viral cytopathic effect in anorectal pap cytology can confirm the diagnosis in symptomatic patients. Awareness of herpetic proctitis in HIV positive and/or homosexual men may initiate prompt diagnosis and treatment. An anorectal cytology is cost effective, and provides a time efficient diagnosis.

**Design:** We encountered an anorectal pap smear of a young homosexual man who was newly diagnosed with HIV and presented with symptomatic acute anal proctitis.

**Results:** The anorectal pap smear cytology demonstrated the classic cytopathic effect of herpes-simplex in infected squamous cells and columnar cells of the anal canal. This was also confirmed with positive viral culture of the anal canal for HSV-2.

**Conclusion:** In symptomatic patients the identification of HSV viral cytopathic effect on anorectal cytology will confirm the diagnosis of herpetic proctitis. Although not commonly seen, the anorectal cytology in this case demonstrates the classic cytopathic effects of herpes-simplex infection.

**Keywords:** HIV/AIDS; Anorectal region; Antiviral therapy; Immunodeficiency; Mucosal infection

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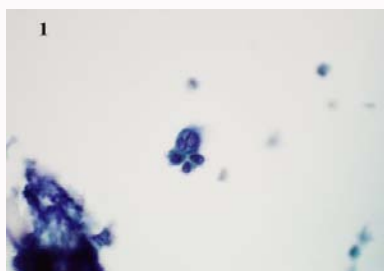
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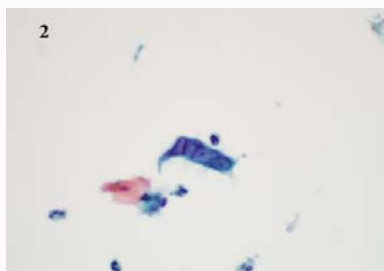
### Introduction

The characteristic viral cytopathic effects of herpes simplex virus (HSV) in anorectal cytology specimens are rarely encountered. When present, if clinically asymptomatic, this could represent subclinical shedding of the HSV. Men who have sex with men (MSM) have especially higher rates of shedding HSV than the general population [1,2]. HSV-2-seropositive MSM has more frequent subclinical HSV-2 shedding predominantly from the perianal area and more frequent prodromal HSV-2 shedding [1]. The frequency of viral shedding is comparable in men and women [2]. In symptomatic patients the identification of HSV viral cytopathic effect on anorectal cytology will confirm the diagnosis of herpes proctitis.

HSV-2 is one of the most common sexually transmitted infections (STIs) in the United States particularly among young people ages 15-24. In February of 2013, the Center of Disease Control (CDC) estimated that there are approximately 20 million new cases of STIs diagnosed every year of which 766,000 are caused by HSV-2 [3]. It is worth noting that the routine screening for HSV-2 infection is not recommended for the general population. However the CDC does recommend routine screening for herpetic proctitis in high risk populations for instance MSM and in individuals who are positive for the human immunodeficiency virus (HIV) as the HIV can be transmitted through the herpetic vesicles [3]. In immunocompetent individuals HSV can be transmitted through herpetic vesicles. The viral cytopathic effect can appear as early as four hours after infection with herpes virus [4]. Reising and Melnick [5] studied the herpes virus and its effect on the cells in vitro thoroughly early in the 1950's using electron microscopy. They described the changes occurring in infected cells and noted that the earliest sign within four hours of incubation was coarsening of the nuclear chromatin and margination of the chromatin toward the periphery of the infected nucleus leaving a central halo. In the late stage 24 to 36 hours there is a marked decrease or near absence of chromatin material giving rise to a membrane-bound clear glassy vesicle which



**Figure 1:** A cell infected with HSV displaying multinucleation; chromatin margination and nuclear molding Papanicolaou Stain x400).



**Figure 2:** HSV viral cytopathic effect including a ground glass chromatin; multinucleation; chromatin margination and nuclear molding in a columnar cell (Papanicolaou Stain x400).

is now known as the viral inclusion body [5]. It is hypothesized that the virus disseminates the host nuclear structures and intranuclear framework thereby remodeling the infected cell nucleus and providing a structural basis for efficient viral DNA replication and ultimately enhancing the replication process [6,7]. In 1974 Enlander et al. [8] further characterized the nuclear features of molding and multinucleation by the decrease in number of micro-villi in between infected cells as well as diminished intracellular filaments. Adjacent infected cells are thought to merge forming a larger multinucleated cell [9]. Reviewing the literature the authors did not find any reports describing the histopathologic differences between asymptomatic viral shedding vs. symptomatic disease. According to CDC all patients with acute proctitis should be evaluated for HSV *N. gonorrhoeae*, *Chlamydia trachomatis* and *T. pallidum*. Interestingly the 2015 sexually transmitted disease treatment guidelines by CDC do not recognize cytology as a sensitive and specific means to detect HSV infection of genital lesions [10]. As discussed above the cytomorphologic features of epithelial cells infected with HSV are well established and HSV infection is routinely diagnosed on cytology material by cytopathologists. We have reported HSV viral cytopathic effects in urine cytology previously [11]. Herein we report HSV viral cytopathic effects in anal cytology.

## Case Presentation

A 20-year-old homosexual male who was diagnosed with HIV six months prior to his current symptoms presented to the emergency department complaining of severe rectal pain and a sore throat that developed 3 days after having repetitive unprotected anal and oral intercourse with a new male partner. He also described a white creamy foul smelling rectal discharge as well as difficulty speaking and dysphagia. On examination scant white mucoid discharge was present around the anus but no anal or penile lesions were identified. His oropharynx showed unilateral tonsillar erythema and exudate with a tender enlarged cervical lymph node. The differential diagnosis at the time was gonorrhea/chlamydia (GC/CT) infection

lymphogranulovenereum (LGV) HSV proctitis and anal trauma with foreign material. Anal trauma was excluded based on history and physical examination. A rectal culture was obtained and confirmed HSV-2 rectal proctitis. Rectal and urine cultures were negative for GC/CT. Cytological evaluation of the anorectal specimen was expedited. A cytospin slide was prepared and stained with Papanicolaou stain. It revealed scattered squamous cells and columnar cells exhibiting large ground-glass nuclei with chromatin marginating towards the membrane (Figure 1 and 2). Mono and multinucleated cells contained nuclei with ground glass appearance and margination of chromatin on the nuclear membrane. These changes are due to accumulation of viral particles in the center of the nuclei which causes margination of chromatin to the periphery. In addition multinucleated cells displayed nuclear molding. Multinucleation margination of chromatin and molding which are known as “three M’s of herpes” were present in our examined anal cytology material.

These changes were classic for viral cytopathic effect consistent with Herpes virus. Additional findings were rare atypical squamous cells of undetermined significance (ASC-US) and scattered acute inflammatory cells in the background.

## Conclusion

Herpetic proctitis is common in MSM with a typical acute presentation. Although not commonly seen the anorectal cytology in this case demonstrates the classic cytopathic effects of herpes-simplex in infected squamous cells and columnar cells of the anal canal.

## Author Contributions

Zahra Maleki has contributed in design and acquisition of clinical data for the case report and providing the images and GazalAlsaati has contributed in writing the case and literature research. Both authors have worked equally.

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