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HIV-Associated Anorectal Lymphogranuloma Venereum: An Emerging Epidemic

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summary

Anorectal Lymphogranuloma Venereum (AR-LGV) has recently been recognized as an emerging problem among HIV-infected men who have sex with men (MSM). AR-LGV may resemble other conditions such as Crohn's disease, resulting in misdiagnosis and the potential for the development of disabling and irreversible long-term complications. Prompt, appropriate antibiotic therapy is essential. We review the epidemiology, pathology, clinical presentation, diagnosis, treatment and public health concerns of AR-LGV.

key words

Anus, Chlamydia, Crohn's, HIV, Lymphogranuloma Venereum, Rectum

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Introduction

Lymphogranuloma venereum (LGV) is a sexually transmitted disease (STD) caused by the invasive serovars L_{1-3}, of Chlamydia trachomatis. Until recently, LGV was considered a rare disease in developed countries. Following the outbreak of anorectal LGV (AR-LGV or LGV proctitis) in 2003 in the Netherlands[1-3], and the subsequent report of additional cases in other countries, LGV has emerged as a significant problem among men who have sex with men (MSM). The majority of these patients were co-infected with HIV. These recent outbreaks have brought renewed attention to LGV. As a result, there has been a recent increase in the number of publications on AR-LGV. However, there has been no comprehensive review dealing with this subject. Therefore, we set out to review the literature regarding the current epidemiology, pathology, clinical presentation, diagnosis, treatment and public health concerns of AR-LGV.

Epidemiology

The more well known sexually transmitted Chlamydia trachomatis infections (serovars D-K) occur worldwide, while LGV infections (Chlamydia trachomatis serovars L_{1-3}) are endemic in Africa, India, South and Central America, Asia and the Caribbean.[4] Only in the pre-antibiotic era was LGV also endemic in Europe, the USA and Australia. In recent times, LGV in these latter industrialized countries was rare. Kornblith (1936) provided one of the earliest accounts of rectal involvement in LGV.[5] Very little was published on AR-LGV since then, until the 1980's when there were sporadic reports of LGV proctitis occurring in MSM in non-endemic countries.[6-9] In 2003 there was a disquieting outbreak of AR-LGV reported in the Netherlands among gay men.[1-3] Shortly thereafter, following warnings launched by national and international health authorities such as the European Union and to the European Surveillance of Sexually Transmitted Infections Network (ESSTI), there were accounts of AR-LGV affecting hundreds of MSM across several European countries (Belgium, France, Germany, Sweden, Italy and Switzerland), the United States, Canada and Australia.[10-20]

Many of the European cases were found to be caused by a newly discovered Chlamydia variant L2b (the Amsterdam variant). Interestingly, this L2b variant was traced back and isolated from anal swabs of MSM who visited a STD clinic in San Francisco in 1981.[13,21-22] New cases of this slowly evolving epidemic continue to be reported. However, the true extent and actual number of persons with AR-LGV is likely to be considerably larger than has been reported thus far. This is because AR-LGV is difficult to diagnose and/or mimics other conditions, and physicians may not even be aware of its existence. Risk factors for acquiring AR-LGV include unprotected anal intercourse in MSM, HIV seropositivity, multiple sexual partners, concurrent STDs, and particular sexual activities such as fisting or sharing of sex toys.[1-3,16,23-25] So far, neither young age nor ethnicity has been identified as risk factors.[26]

Microbiology

Chlamydia trachomatis is a small Gram negative, obligate intracellular bacterium that replicates within membrane-bound inclusions (**Figure 1**). They cannot grow outside living cells because they are unable to synthesize their own ATP. Within these inclusions elementary bodies become reticulate bodies. After having multiplied, up to 1000 elementary bodies may burst out of the host cell in order to infect more host cells. Chlamydia can enter their human host via breaks in the skin or mucosa. The non-LGV serovars (designated A to K) cause genital tract infections, trachoma, and pneumonia. LGV, on the other hand, is the result of infection with the more virulent Chlamydia serovars L1, L2 and L3. So far, most of the reported cases of AR-LGV in MSM have been caused by the L2 serovar[26-28], which is clinically more severe than L1 infections.[29] All LGV serovars tend to cause severe inflammation and invasive infection, pass through the epithelial surface to regional lymph nodes, and may cause disseminated infection often with systemic symptoms.[30] Tissue damage is immune mediated. While host immunity ultimately limits chlamydia multiplication, it does not entirely eliminate these microorganisms. Therefore, it is not surprising that in some patients infection may persistent for even up to 20 years.[31] Immunity to infection is also not long-lived. As a result, reinfection is possible. Bacterial superinfection of AR-LGV may occur and further complicate the disease course.

Clinical Findings

The clinical manifestations of LGV depend on the site of chlamydia entry (i.e. the sexual contact as a site of microtrauma) and the clinical course[32-34], which can be conveniently divided into three stages: (i) a primary stage that involves the site of inoculation; (ii) a secondary stage that occurs 2-6 weeks later, in which the inguinal lymph nodes and/or anorectum are affected; and (iii) a tertiary stage in which there may be late sequelae of the genitals and/or rectum. In rare cases, LGV may remain asymptomatic but detectable.[21]

Following exposure, the incubation period is 3-30 days.[34] Primary infection is characterized by a self-limited, painless mucosal inflammatory reaction (papule) or ulcer at the site of inoculation, i.e. genital, anal, or adjacent skin. Hence, such lesions often go unnoticed. This stage is similar in the HIV-positive and HIV–negative. In one study comparing 45 HIV-infected patients to 8 non-HIV-infected patients the clinical presentations of LGV and non-LGV ulcers were similar.[32]

Two to six weeks later, inoculation of the penis, vulva, or vagina leads to an inguinal syndrome, whereas infection of the rectal mucosa (through anal sex or migration from the cervical lymphatics or posterior vaginal wall) causes an anorectal syndrome. A pharyngeal syndrome with enlarged nodes in the neck is rare, and is due to infection of pharyngeal tissue following inoculation during oral sex. The inguinal syndrome is caused by inguinal bubos (painful, enlarged, and fluctuant nodes that may rupture to form discharging sinuses). The presence of lymphadenopathy above and below the inguinal ligament gives rise to a characteris-