

First case of *Chlamydia trachomatis* L2b proctitis in a woman

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Abstract

Since 2003, outbreaks of lymphogranuloma venereum (LGV) have been reported in European countries, North America, and Australia. Current LGV cases have been caused by *Chlamydia trachomatis* serovar L2. This sexually transmitted infection is predominantly found among men who have sex with men, specifically men who are seropositive for human immunodeficiency virus and have clinical signs of proctitis. The current outbreak has been almost exclusively attributed to a new variant, designated L2b. Although urogenital cases of LGV have been described in the heterosexual population, we report the first case of *C. trachomatis* L2b proctitis in a woman.

Keywords: *Chlamydia trachomatis*, female, first case, L2b, proctitis

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Since 2003, a lymphogranuloma venereum (LGV) *Chlamydia trachomatis* proctitis outbreak caused by the new variant L2b has been reported in industrialized countries in men who have had sex with human immunodeficiency virus (HIV)-positive men [1,2]. We report the first case of *C. trachomatis* L2b proctitis diagnosed in a woman without other sexually transmitted infections (STIs).

In February 2009, a 44-year-old woman presented with gastrointestinal symptoms, such as frequent urge to have a bowel movement, difficulties with continence, and generalized weakness. In April 2009, she arrived for a consultation at the gastroenterology department at Robert Boulin Hospital (Libourne, France) with complaints of anorectal pain, mucopurulent anal discharge, rectal bleeding, and tenesmus. The clinician performed a colonoscopy, which revealed ulcerative proctitis with ulceration of the lower rectum. A rectal biopsy was performed. Taken together, these elements supported a diagnosis of infectious proctitis. Microscopic examination of a Gram-stained rectal biopsy smear specimen revealed a high white blood cell count without diplococci. The rectal biopsy sample was positive for *C. trachomatis* by real-time PCR (Arthus *C. trachomatis* PCR kit; Qiagen, Courtaboeuf, France), and the diagnosis of LGV proctitis was confirmed by the detection of LGV biovar-specific DNA as previously recommended [3]. Genotyping and sequencing of the *ompA* gene conducted at the French National Reference Centre of Chlamydiae (Bordeaux, France) showed that the LGV strain harboured an *ompA* genotype identical to that of the *C. trachomatis* L2b/UCh-1/proctitis reference strain [4]. By use of a multilocus sequence typing (MLST) scheme, targeting five genes, we determined that this LGV strain harboured the MLST sequence type 58, which is specific for the epidemic *C. trachomatis* L2b strain (<http://mlstdb.bmc.uu.se>) [5]. The patient showed positive serology for *C. trachomatis*, with high antibody titres suggestive of LGV (IgG ratio of 5.4 and IgA ratio of >7 for a 1.1 ratio positive threshold (Savyon Diagnostics, Ashdod, Israel)) [6]. No other STI (HIV, hepatitis B virus, hepatitis C virus, syphilis, or gonorrhoea) was diagnosed. The patient has checked for her HIV status every 6 months. She was treated with doxycycline for 3 weeks, which resulted in recovery. The patient reported a sexually promiscuous lifestyle. She had a regular partner, her husband, with whom she had unprotected sex. In addition, she reported having 10–15 anonymous male or female sex partners per month. She reported anal intercourse with an irregular partner 1 week before symptoms appeared.

Until now, LGV has typically presented as severe proctitis in HIV-positive men who have sex with men (MSM), and only proctitis cases with non-LGV serovars or cervicitis with LGV

(non-*C. trachomatis* L2b) serovars [1,3,7,8] have been reported in women. Moreover, other concomitant STIs are often diagnosed in MSM with LGV. In contrast, in the case reported here, the patient had no other STIs or HIV infection.

By sequencing the *ompA* gene, Spaargaren *et al.* [2] demonstrated that *C. trachomatis* L2b was the strain causing the European LGV outbreak. The recent MLST genotyping scheme developed for *C. trachomatis* has been used to investigate genetic variation in LGV strains [5]. In this study, the 22 LGV specimens obtained from MSM in the 1980s were separated into three *ompA* genotypes and five MLST genotypes. In contrast, all 50 specimens obtained from Europe collected between 2004 and 2009, including 15 French isolates, and the five specimens collected from the USA between 2007 and 2009 shared an identical MLST sequence type (ST58). Moreover, all but one of these specimens had an *ompA* genotype identical to that of the *C. trachomatis* L2b/UCH-1/proctitis reference strain. These findings suggest a single source of origin for the LGV outbreak among MSM in Europe. By using the MLST scheme described above, we found that our LGV specimen had an MLST profile and an *ompA* genotype identical to those of the European variant, suggesting that it belongs to the same cluster as the outbreak variant.

Since the beginning of the LGV outbreak, only a few studies have been conducted on *ompA* genotypes of female rectal specimens, especially from high-risk women (women who had receptive anorectal intercourse or anorectal symptoms, or who had contact with gonorrhoea). Recently, Setupathi *et al.* [9] showed that, among 160 rectal swabs obtained from such women, 12.5% (20/160) were positive for *C. trachomatis*, and all of these isolates were of non-LGV serovars. Geisler *et al.* [10] evaluated the distribution and the epidemiology of rectal *ompA* genotypes in women in Birmingham between 2003 and 2007. No LGV genotypes were detected among the 33 *C. trachomatis*-positive rectal specimens found. In a study conducted at Rotterdam between 2001 and 2005, a total of 219 rectal *C. trachomatis* infections were diagnosed [11]. In all, 156 (71.2%) were from male patients and 63 (28.8%) were from females. *C. trachomatis* L2 was identified in 21 rectal specimens, all from men.

Occasional cases of heterosexually transmitted LGV have been seen in Europe, but only cervicitis has been described in women [7,8]. LGV was diagnosed in a heterosexual couple in Spain [7]. The man presented with urethritis and the women with cervicitis. It is important to note that *C. trachomatis* L2, but not *C. trachomatis* L2b, was detected in both partners. Recently, Gomes *et al.* [8] reported LGV cases of urethritis and cervicitis among heterosexual Portuguese patients. Most of these patients were asymptomatic or presented no clear LGV symptoms. All *C. trachomatis*-positive

samples revealed *ompA* sequences that differed from the *C. trachomatis* L2/434 reference strain and from the *C. trachomatis* L2b/14476 strain, which was the most frequently described genotype in the recent LGV outbreak. In a study conducted in France between 2004 and 2009, no LGV strain was found among 2902 female urogenital samples screened by an L serovar-specific real-time PCR assay [12,13].

As recommended by the current guidelines for LGV treatment, our patient received 3 weeks of doxycycline [3]. A complete response was observed to this therapy.

To our knowledge, this is the first case reported of *C. trachomatis* L2B proctitis in a heterosexual woman. Exclusion of extragenital sites (rectal and oropharyngeal), which are not commonly tested for STIs, can leave many infections undiagnosed. These justify clinical awareness and attentive surveillance in all populations that are at risk for sexually acquired *C. trachomatis* infections.

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Transparency Declaration

The authors declare the absence of any relationship or any degree of conflicting or dual interest that may affect professional judgement in relation to the article.

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