Original Articles

Surveillance report

Rectal lymphogranuloma venereum surveillance in France 2004-2005

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Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* strains belonging to the L1, L2 or L3 genotype.

An alert about an outbreak of LGV among MSM in the Netherlands was published in January 2004. The first cases of rectal LGV in France were retrospectively diagnosed in March 2004 and sentinel surveillance for LGV was implemented in April 2004.

Most of the participating centres were located in the cities of Paris and Bordeaux. Only confirmed rectal LGV cases were included in the surveillance. Rectal specimens from men that were found to be positive for *C. trachomatis* by PCR were sent to the National Reference Centre for Chlamydia infection for genotyping. Simple epidemiological data provided by clinicians and genotyping results were sent to the Institut de Veille Sanitaire (InVS) where data were anonymously recorded.

A total of 328 *C. trachomatis* rectal strains isolated in men were genotyped by the end of December 2005. Of these, 244 (74%) were LGV strains belonging to the L2 genotype. No L1 or L3 *C. trachomatis* genotype was found.

Diagnosis was made retrospectively for 46 cases. The median age of patients with LGV was 39 years. HIV status was known for 96 patients: 82/96 (85%) were HIV-infected. Most LGV cases were diagnosed in the Paris area (92%). Among the remaining 26% C. trachomatis strains, genotypes Da and G were the most frequent.

As with syphilis in recent years, the emergence of LGV in Europe is mainly affecting HIV-infected MSM. The screening and treatment of STIs should be included in the clinical follow-up of all HIV-infected MSM.

Euro Surveill. 2006;11(9): 155-6 Published online September 2006

Key words: Lymphogranuloma venereum, MSM, France

Introduction

An outbreak of rectal lymphogranuloma venereum (LGV) was detected among men who have sex with men (MSM) in Rotterdam during the summer of 2003 [1]. LGV, a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* genotype L1, L2 or L3 is endemic in tropical countries but remains rare in industrialized countries. The classical clinical presentation of the infection is a genital ulcer with buboes. Rectal presentations have also been described, especially in MSM [2].

After the Dutch alert, a retrospective investigation was conducted in France which identified 21 cases of rectal LGV. Epidemiological information obtained for 14 of these 21 cases showed that all the patients were MSM, 8 were infected with HIV and 9 had also another sexually transmitted infection (STI). The mean duration of symptoms before diagnosis was lengthy (50 days), suggesting that clinicians were not aware of this STI [3].

In April 2004, as a public health response to these findings, a large-scale information campaign aimed at microbiologists, clinicians and groups focusing on MSM was begun, and a voluntary-based sentinel LGV surveillance system was launched in France. The results of this surveillance are presented in this paper.

Methods

Sentinel Surveillance design

In April 2004, six centres were recruited on a volunteer basis. They included two STI clinics, a laboratory, an outpatient proctology clinic and two microbiology laboratories, and all were located in Paris. The national reference centre, which is located in Bordeaux, also participated. In 2005, six additional laboratories located in other large cities were recruited

All rectal swabs positive for *C. trachomatis* by PCR were sent to the national reference centre, where genotyping was performed. Participating clinicians and microbiologists were also asked to provide basic epidemiological data such as age, HIV status, date of symptom onset, and date of sampling. Anonymised microbiological and clinical data were sent to InVS for analysis.

Case definition

Only confirmed rectal cases were included in the LGV surveillance. A confirmed rectal case was defined as a male patient with symptomatic proctitis due to *C. trachomatis* diagnosed using polymerase chain reaction (PCR) [Cobas Amplicor Roche Diagnostic System, Meylan, France] with the *C. trachomatis* strain belonging to L1, L2 or L3 genotype.

C. trachomatis strain genotyping was performed at the national reference centre for *Chlamydia* infection using a nested *omp1* PCR-restriction fragment length polymorphism assay [4].

Since a new LGV *C. trachomatis* variant characterised by a single mutation in the *omp1* gene of the major outer membrane protein (MOMP) and named L2b had recently been identified [5], the *omp1* gene of a random sample of L2 strains isolated in France during 2004-2005 was sequenced.

Results

From March 2004 to December 2005, 328 rectal *C. trachomatis* strains were genotpyed.

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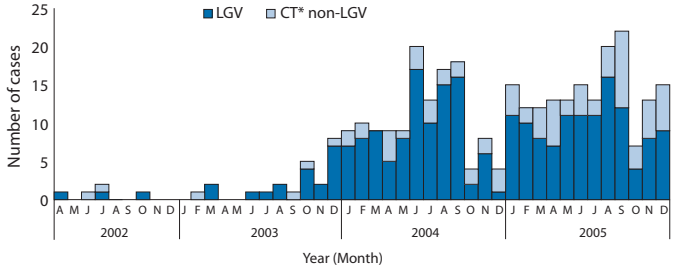
Of these, 244 (74%) belonged to the L2 genotype, which confirmed the diagnosis of rectal LGV. No *C. trachomatis* strain belonging to the L1 or L3 genotype was found.

For 22 rectal LGV cases which occurred between April 2002 and December 2003, the diagnosis was made retrospectively in March 2004. For 2004, 104 rectal LGV cases (24 cases retrospectively from January to March and 80 prospectively from April onwards) were reported to the LGV surveillance system. For 2005, 118 rectal cases were recorded [FIGURE].

FIGURE

Monthly rectal LGV and rectal CT non-LGV cases, France 2002-2005



* *Chlamydia trachomatis*

Of the 244 identified rectal LGV, 174 (72%) were sequenced, and all these exhibited the *omp1* gene mutation of the MOMP that characterises the newly described L2b variant. The median age of patients with a rectal LGV infection was 39 years (range: 34-44). HIV status was available for 96 patients, and 82 (85%) were known to be infected with HIV. Most of the patients with rectal LGV lived in the Paris area (92%). Of the remaining patients, 5% lived in Bordeaux and 3% were diagnosed in other cities, includingTourcoing, Lille and Marseille.

Eighty five of the genotyped *C. trachomatis* rectal strains (26%) did not belong to the LGV genotypes. For these 85 strains, the genotypes were found to be mainly Da (10%) and G (9%). In 2004, the proportion of non-LGV genotypes was 20%, in 2005 this proportion increased significantly from 20% to 30% (c2= 4.4, P=0.03). Patients with *C. trachomatis* proctitis were younger than patients with LGV proctitis, with a median age of 34 years (range: 21-58), and were less likely to have an HIV infection (60%) (c2=8.1, P=0.004) than those with LGV proctitis.

Discussion

Since the French surveillance system includes only confirmed cases which require strain genotyping, and there are only a small number of participating centres, mainly located in Paris, the number of reported rectal LGV cases is certainly underestimated for France. However, the number of reported rectal LGV cases in 2004-2005 higher than in previous years. A study in the late 1980s at a STI clinic in Paris found two rectal forms diagnosed in MSM among a total of 27 LGV cases [6], and no further cases were reported in France until the current epidemic.

The genotyping of *C. trachomatis* strains appears to be necessary to confirm the diagnosis of LGV, because a quarter of *C. trachomatis* strains isolated in men were not LGV strains.

The number of LGV cases in 2004 and 2005 are similar, but reports of non-LGV *C. trachomatis* proctitis increased during this period, almost certainly due to a surveillance bias (more participating centres).

LGV cases have been diagnosed in several Europeans countries [7] and in some cities in the United States [8]. In all these countries, LGV proctitis has only been seen in MSM, most of whom were HIV-infected. A recent case-control study (LGV proctitis versus non-LGV *C. trachomatis* proctitis) showed that HIV infection was strongly associated with LGV [9]. This result is consistent with the French data in which patients with LGV are more frequently HIV-infected than those with a non-LGV proctitis (82% versus 60%). The new variant L2b recently described in the Netherlands was found in all the sequenced L2 *C. trachomatis* stains in France suggesting that this specific LGV strain has spread in the two countries.

The LGV emergence is a serious concern for gay men and in Europe. LGV diagnosis should be prompt and appropriated treatment administered to avoid serious sequels as rectal stricture (2) and to interrupt transmission. Furthermore, rectal LGV characterised by deep mucosal lesions could facilitate HIV transmission. Patients with rectal LGV are often infected with several others pathogens such as herpes simplex virus or human papillomavirus. Screening and treating STIs should be included in the clinical follow–up of all HIV-infected MSM.

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