

## LYMPHOGRANULOMA VENEREUM IN SLOVENIA - A FORGOTTEN DISEASE?

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### ABSTRACT

In Slovenia, lymphogranuloma venereum is a rare disease. After the Second World War, we registered only 6 patients, and all of them became infected in tropic and subtropic countries of Africa and Asia. Since the disease appears only rarely, it can easily be overlooked or misdiagnosed.

We present a case of a sailor who was presumably infected in the South of Africa. The clinical investigations and laboratory diagnosis were conducted in the Primary Health Centre in Celje, and in the Institute of Microbiology, Medical Faculty, Ljubljana.

### KEY WORDS

*lymphogranuloma venereum (LGV), clinical investigations, laboratory diagnosis, therapy, Slovenia*

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### INTRODUCTION

Lymphogranuloma venereum (LGV) is a widespread sexually transmitted disease. It is rather rare in Europe and is mostly found in patients, who have spent some time in tropical countries of Africa and Asia or elsewhere (1).

After the Second World War, there were few cases of LGV in Slovenia (2,3). The last recorded case was in 1984 in a patient who had spent some time in Iraq, where he got infected. He was treated at the Department of Dermatology, Clinical Centre, Ljubljana. Previously we registered two cases in 1975, two cases in 1976, one more case in 1982. The former two patients got infected in Central Africa and Nepal, and the latter two through sexual

contacts in Istanbul and Lusaka (4). The LGV patient registered in 1982 spent some time in Bamako. We present a case of LGV detected in 1995.

### PATIENT AND METHODS

#### **Venerologic anamnesis**

The 31-year-old sailor was seeking medical assistance in the Primary Health Centre in Celje on 29.5.1995. In February, he had had sexual intercourse without protection in Bangkok. In the beginning of April, he had sex with protection in South Africa. Approximately one month later (2.5.1995), a painful swelling appeared in the left groin. His body

temperature was elevated (37,5 to 37,6°C). The patient did not notice any ulcer on his genitals nor any urethral discharge. His elevated body temperature started one week after the second risky sexual intercourse when he had boarded the ship. He was treated on the ship with Achromycin (tetracycline hydrochloride) for 10 days (the doses are not known). His fever disappeared, but the swelling of the inguinal lymph node remained unchanged until 29.5.1995, when he consulted a doctor.

### Status

The general somatic status was within normal limits. There were no pathologic changes noticeable on his external genitalia (penis, testicles, epididymis). In the left groin there was a hard, palpable, movable bubo, the skin covering it, was unchanged. The right-side inguinal lymph nodes were not enlarged. Rectally, we could not identify any changes.

### Diagnostic procedures

The organs in the abdominal cavity of the diseased were checked by ultrasound, a needle biopsy of the left inguinal bubo was performed to do the necessary laboratory tests. The patient's urethral swab and blood were submitted to biochemical, haematological and microbiological investigations.

## RESULTS

No pathological changes were shown by the ultrasound of the abdominal cavity. Along the abdominal aorta and near both iliacal arteries no enlarged lymph nodes could be seen. The spleen

showed no abnormalities.

The cytologic investigation indicated suppurative granulomatous lymphadenitis (lymphocytes, polymorphocytes, some plasma cells, macrophages with fagocytosed particles, clusters of epitheloid cells and the massive fibrinous material).

The biochemical and haematological tests showed no divergences from the normal. The patient's sedimentation rate was normal, as well as his haemogramme, bilirubin, transaminases, proteinogramme and cryoglobulines. The differential blood-cell-count indicated an increased number of monocytes ( $1,0 \times 10^9/l$ ) compared to the normal value ( $0,1-0,6 \times 10^9/l$ ).

The assays for the rheumatoid factor (AST, latex test, CRP) were negative. The possibility of a gonococcal infection was excluded by staining of the urethral discharge with methylen blue and Gram (the patient stated that he had gonorrhoea the year before). The HIV test was negative, nevertheless the patient's blood was tested for HIV in October again. In the differential diagnosis we excluded the infection with *Treponema pallidum* by testing his serum for nonspecific and specific treponemal antibodies (VDRL, Wassermann test, FTR-ABS, TPHA). All the tests were negative.

Because of the one-sided swelling of the inguinal lymph node and the anamnestic data we concentrated on proving the chlamydial etiology of the disease. First we examined the urethral material. The direct immunofluorescence assay (DFA) with monoclonal antibodies for chlamydial antigens was negative for two subsequent times (Micro Trak Syva) (13. 06. and 10. 07. 1995). Since there was a strong suspicion of LGV, we tried to isolate *Chlamydia trachomatis* from the suppurative lymph node. The isolation of chlamydia in He La 229 cells by standard procedure

Table 1. Microbiological assays for the confirmation of LGV

Specimens	Isolation/HeLa 229	DFA	PCR	IIF	IPA
Urethral swab material	NT	NEG	NT		
Lymph node aspirate	NEG	POS	POS		
Serum				IgG/256*	IgG/4096 IgA/1024

\* tested at Institute of Public Health Celje

NT - not tested

POS - positive

NEG - negative

was unsuccessful, because the punctured material was toxic for the tissue culture. Further examinations made on the aspirated lymph node material included DFA test with monoclonals and the polymerase chain reaction (PCR, Amplicor La Roche). Numerous elementary bodies of chlamydia were found in the aspirate and the presence of chlamydial DNA was also confirmed by PCR (more than 10 times higher values than cut-off in all parallels and in all repetitions of the test).

LGV was also confirmed serologically. The patient had high titres of specific chlamydial IgG antibodies (1:256) proven by indirect immunofluorescence test (IIF) (Chlamydia trachomatis-Spot IF, Biomerieux) and by immunoperoxidase (IPA) assay (1:4096) as well as a significant quantity of specific IgA (IPAZyme Chlamydia, Savyon Diagnostics LTD) (Table 1).

The therapy was applied according to the Guidelines of STD Study Group of the Austrian Society of Dermatology and Center for Disease Control (CDC) recommendations (5,6). The patient was given doxycycline (Vibramycin) in a dose of 100 mg bid per os for 21 days. During the therapy, the suppurative bubo turned to normal and at the time of the second check-up the patient was without clinical signs and symptoms.

## DISCUSSION

LGV is a sexually transmitted disease caused by intracellular bacteria *Chlamydia trachomatis* (serotypes L1, L2 and L3). After genital inoculation and a relatively long incubation period of 10 to 21 days, a tiny papula with erosion or epidermal ulceration appears on the genitalia or rectum. The papula disappears in a short time. The microbe spreads from the side of the inoculation through the lymph vessels. As a consequence, the regional lymph nodes become enlarged 2 to 4 weeks later. Primarily, the inguinal lymph nodes are affected, but the infection may spread to the lymph nodes of the anus, rectum and pelvis as well. The infection of the lymph nodes is an invasive process. The induration of the lymph nodes, multifocal suppuration and numerous fistula formations with scarring are typical signs of it. The inflammation spreads to the femoral and inguinal lymph node group and can produce swelling of both sides of the inguinal ligament (7).

The disease affects more frequently men than women. The resulting "groove sign" has been thought to be pathognomonic of LGV, but occurs only in 10

to 15% of the affected persons. LGV can produce chronic scarring and lymphoedema, particularly if the rectum is involved. The cicatricial scarring in lower rectum can produce long fibrotic narrowings of the colonic lumen (8). Histologically a chronic inflammation and fibrotic changes with granulations can be detected.

Stating literature sources, the hiperglobulinaemia is quite frequent early in the infective process. It is sometimes connected with the rheumatoid factor, elevated cryoglobulins and total IgA. These parameters were not obvious in our patient.

LGV can be confirmed either by isolating the agent from the lymph node or by serologic testing. We tried to isolate chlamydia but were unsuccessful. A similar experience was made by others, because the punctured material contained a large number of inflammatory cells, fibrin and other material. That is why isolation is not always successful. The chlamydial etiology of the disease was proven by DFA and PCR but it is the detection of chlamydial genome that has a specific importance in such cases.

In the past (9) and in some laboratories nowadays, the clinical suspicion of LGV was confirmed only by serologic tests. The classic complement fixation test (CF) has been used in the LGV diagnosis since 1940 and is now acceptable only for the laboratory confirmation of psittacosis. The 4-fold rise in CF antibody titres is significant but a negative test does not exclude LGV. Better results can be obtained by IIF with L1 or L2 as antigen (10). The IPA test applied in our diagnostic procedure is equally useful for the confirmation of the immune response to LGV infection. In the described case, an extraordinary strong immune response was expected because of the length of the infection.

The described case of LGV is the seventh case of the disease in Slovenia after the Second World War. In the former six cases, all patients were infected during their stay in the tropical parts of Africa and Asia where LGV is endemic. Only one affected person claimed to have had sex in Nepal. All patients were treated in Slovenia, and none of them had late manifestations like elephantiasis of the anogenital tissues, although the disease lasted for a long time. LGV is a rare disease in Slovenia, but it shouldn't be ignored when the differential diagnosis of malignancy and other diseases is made.

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