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### Recommended Citation

Vogel, Andrew D.; Asta, Anthony; and Ammar, Hussam () "Oropharyngeal Lymphogranuloma Venereum: A clinical reasoning challenge and literature review," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 15: Iss. 1, Article 17.

DOI: 10.55729/2000-9666.1439

Available at: <https://scholarlycommons.gbmc.org/jchimp/vol15/iss1/17>

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# Oropharyngeal Lymphogranuloma Venereum: A Clinical Reasoning Challenge and Literature Review

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## Abstract

Lymphogranuloma venereum (LGV) is a sexually transmitted infection typically caused by serovars L1-L3 of *Chlamydia trachomatis*. These serovars are tissue-invasive with a preponderance for lymphatic spread and can be acquired via unprotected oral, anal, or vaginal sex. We present the case of a 23-year-old with a prior history of syphilis admitted with four weeks of progressively enlarging painful right cervical lymphadenopathy. Extensive testing, including oropharyngeal swabs and microbiological testing, did not yield a diagnosis, nor did extensive pathological and microbial testing of the lymph node biopsy tissue. Serological test of lymphogranuloma venereum revealed positive *Chlamydia trachomatis* L1 serovar antibodies. The patient had a complete resolution of his symptoms after three weeks of doxycycline therapy.

**Keywords:** Oropharyngeal lymphogranuloma venereum, Granulomatous lymphadenitis, Cervical adenopathy

## 1. Introduction

Lymphogranuloma venereum (LGV) is a sexually transmitted infection caused by L1, L2, and L3 biovars of *Chlamydia trachomatis*. LGV is characterized in its primary stage by the development of a short-lived ulcer or papule at the site of entry. If the inoculation occurs at an internal location like the urethra or the anal canal, it is easily missed. The secondary stage is characterized by tender inguinal and femoral lymphadenopathy with a characteristic “groove sign” formed by swollen, matted lymph nodes developing along the course of the inguinal ligament. A typical sign of secondary stage LGV is the occurrence of ‘buboes,’ fluctuating painful swellings of infected lymph nodes that can suppurate spontaneously and cause cutaneous fistula. Over the past decade, LGV has emerged in developed countries as a leading cause of proctitis and proctocolitis in men who have sex with men (MSM). Cases of oropharyngeal LGV associated with large cervical adenopathy have been rarely reported.<sup>1-3</sup>

## 2. Case presentation

A 23-year-old male was admitted for further evaluation after one month of progressively

enlarging right neck swelling, chills, and subjective fevers. His past medical history included syphilis, which was diagnosed and treated three years ago. One week before admission, he sought medical attention at an urgent care facility, where he was prescribed amoxicillin-clavulanate and a five-day course of prednisone without relief. On examination, the temperature was 98.6 F, pulse rate 80/min, and blood pressure 131/90. There was an exquisitely tender right anterior neck mass approximately 4 cm in diameter. The oral mucosa was unremarkable, and he had normal dentition. He had no palpable submandibular, supraclavicular, axillary, or inguinal lymphadenopathy. There were no penile or scrotal lesions, no urethral discharge, and the rectal examination was unremarkable. The patient admitted to unprotected oral, vaginal, and anal sexual intercourse with both men and women. On admission, laboratory tests demonstrated a hemoglobin of 12.6 g/dL, a leukocyte count of 5.90 k/mm<sup>3</sup>, and a platelet count of 314 k/mm<sup>3</sup>. The Comprehensive metabolic panel was unremarkable. A neck computed tomography (CT) demonstrated a right conglomerate cervical cystic lymphadenopathy 4.3 × 2.1 × 2.9 cm (Fig. 1a). We generated a list of potential causes of lymphadenopathy and started

Received 18 August 2024; revised 27 October 2024; accepted 5 November 2024.  
Available online 6 January 2025

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<https://doi.org/10.55729/2000-9666.1439>

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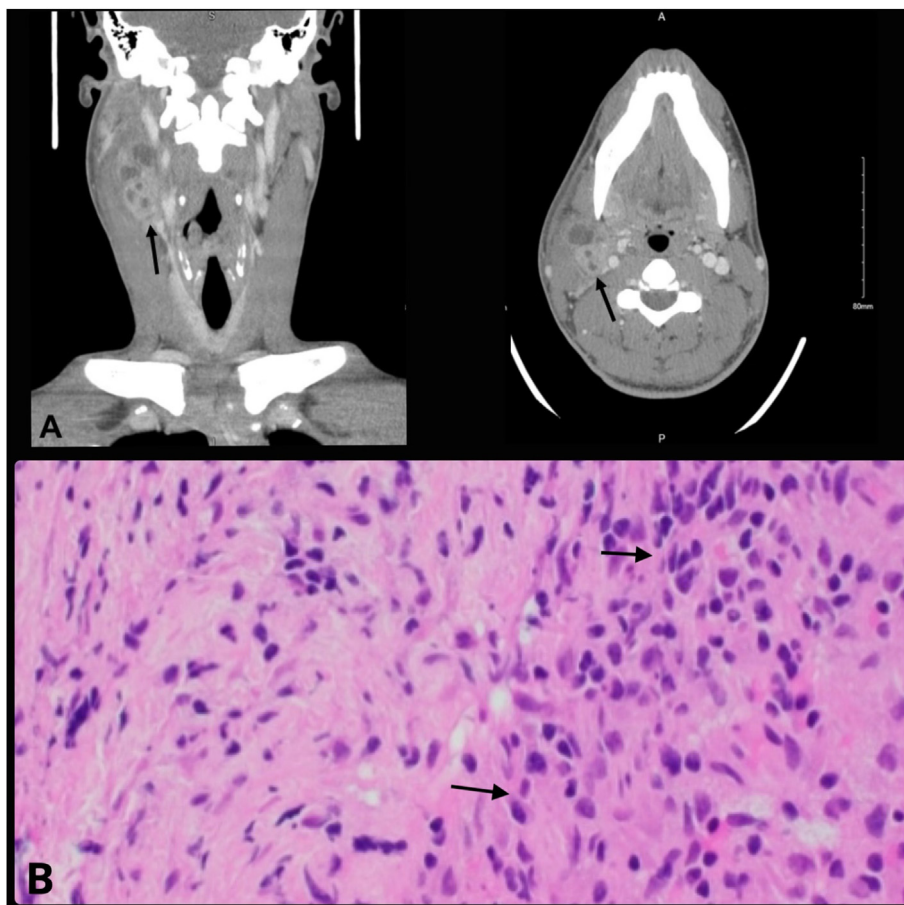


Fig. 1. A Frontal and Axial planes of CT Neck images demonstrate the  $4.3 \times 2.1 \times 2.9$  cm right cervical heterogenous lymph node with areas of necrosis throughout. B Mixed inflammatory cells with a predominance of lymphocytes mixed with neutrophils, plasma cells and macrophages with poorly formed granulation tissue in addition to areas of necrosis, overall suggestive of granulomatous lymphadenitis with necrosis.

ruling out or ruling in each diagnosis based on the clinical history and diagnostic testing (Table 1). On the second night of admission, the patient had a fever of 101.9F, which resolved spontaneously. He

Table 1. Granulomatous lymphadenitis causes.

**Noninfectious granulomatous disorders**

- 1 Sarcoidosis lymphadenitis
- 2 Beryll
- 3 Kikuchi's disease

**Infectious granulomatous disorders**

- 1 Tularemia
- 2 Cat scratch
- 3 Yersenia
- 4 Lymphogranuloma venereum
- 5 Fungal infection
- 6 Tuberculous infection
- 7 Atypical mycobacterial infection
- 8 Toxoplasma
- 9 Mycobacterium leprae
- 10 Syphilis
- 11 Brucella

remained hemodynamically stable throughout his hospitalization. Human immune deficiency virus serology and polymerase chain reaction (PCR) were negative, rapid plasma reagin (RPR) and rapid group A Strep pharyngeal swab were negative. An oropharyngeal swab of C. Trachomatis and N. gonorrhoea nucleic acid amplification test (NAAT) were negative. Epstein-Bar Virus (EBV) IgM and Toxoplasma gondii IgM were also negative. An Ultrasound-Guided core biopsy of his enlarged lymph node subsequently showed granulomatous inflammation with plasma cells but no organisms and no evidence of malignancy. Acid-fast bacillus (AFB) testing of the core biopsy was negative for Mycobacterium tuberculosis. Tissue immunohistochemistry (IHC) returned negative for Treponema Pallidum, EBV, and Herpes simplex1-2 DNA. Three AFB Sputum Cultures were negative. CT Chest, abdomen, and pelvis were unremarkable. An excisional lymph node biopsy was performed. Pathology samples revealed granuloma formation, plasma

cells, and necrosis, with no evidence of malignancy (Fig. 1B). The tissue tested negative for AFB, Gram, and Grocott–Gömöri’s methenamine silver (GMS) stains. IHC for Treponema was again negative. A Brucella serology and tissue PCR were tested negative. The outside laboratory notified us that C. Trachomatis L1 serovar IgA was >1:265, and IgG was >1:1024. IgA correlates with acute LGV infection.<sup>3</sup> The patient was called to our clinic and prescribed 21 days of Doxycycline 100 mg twice daily, and he reported complete resolution of his symptoms in a follow-up visit.

### 3. Discussion

The acute development of isolated large, painful, tender cervical lymphadenopathy associated with subjective fever, chills, and night sweats in a 23-year-old patient with a previous diagnosis of syphilis suggested a likely infectious cause that might be related to his lifestyle. Of the list of potential causes of granulomatous lymphadenopathy in Table 1, those that are sexually transmitted are syphilis and lymphogranuloma venereum. Aggressive cancer was thought to be a distant probability. The patient has no evidence of pharyngeal or odontogenic infection, which are the most common causes of painful cervical lymphadenopathy. Oropharyngeal syphilis can cause painful cervical lymphadenopathy with non-specific symptoms and findings; a negative RPR made this an unlikely diagnosis but not effectively ruled out.<sup>4,5</sup> Specific chlamydia

serotypes L1, L2, and L3 that constitute LGV enter the body through oropharyngeal, rectal, and genital mucosa and migrate through lymphatic to regional lymph nodes, causing large painful lymphadenopathy.<sup>1</sup> The negative NAAT for pharyngeal Chlamydial doesn’t rule out the diagnosis, as it has only a moderate sensitivity of 69%.<sup>5</sup> A specific LGV serology was sent to a lab in a different facility. A Lymph node biopsy was the next most logical step, and it had revealed a granulomatous inflammation. The authors weighed the probabilities of potential causes of granulomatous cervical adenopathy (Table 1).<sup>6</sup>

Direct tissue cultures, stains, PCR, and serological testing ruled out most of the causes listed in (Table 1). The negative tissue syphilis PCR effectively ruled out the diagnosis.

*M. tuberculosis*, toxoplasmosis, syphilis, and cat scratch diseases can specifically cause localized cervical adenopathy, and all of them were effectively ruled out by serological, microbiological, pathological testing, absence of contact with tuberculosis cases, incarceration, and absences of contact with cats and kittens. He has no contact with wild animals and doesn’t eat the raw meat of infected animals, which makes Tularemia unlikely to be a diagnosis.

Kikuchi’s disease, which typically affects patients of asian descent, is also considered an unlikely diagnosis.<sup>6</sup> Two weeks after admission, we were notified of positive LGV serology. Oropharyngeal LGV has been rarely reported in the literature, as seen in (Table 2). The presentation varies from

Table 2. Literature Review of oropharyngeal LGV cases.

Type of publication, Authors, year	Presentation	HIV status	Diagnosis	Course and outcome
Case report Al busaidi et al. 2016. <sup>7</sup>	25 y MSM presented left sided neck pain, swelling and intermittent fever	Negative	Clinical presentation LGV serology	Symptoms resolved on doxycycline
Case report Galeano-valle et al. 2019. <sup>2</sup>	47 y MSM presented with painful cervical mass. CT: Large cervical LN 6.7 × 4.4 x6.2 with central necrosis	Positive	Positive PCR LGV lymph node and serology	Initially treated for TB and pyogenic abscess then treated with doxycycline followed by clarithromycin
Case report Kapoor et al. 2021 <sup>8</sup>	32y MSM presented painful cervical mass and fever.CT: Large cervical LN with central necrosis	Negative	LGV serology and positive oropharyngeal NAAT C.Trachomatis. Positive lymph node IHC for C trachomatis	Initially treated for pyogenic abscess symptoms resolved on doxycycline
Case report Trebing et al. 2004. <sup>9</sup>	36 y MSM presented with vesicle on lower lip follow by painful cervical mass and intermittent fever	Negative	LGV serology Lymph node PCR positive for C.Trachomatis	Symptoms resolved on doxycycline

(continued on next page)

Table 2. (continued)

Type of publication, Authors, year	Presentation	HIV status	Diagnosis	Course and outcome
Case series of 4 oropharyngeal LGV Dosekun et al. 2013. <sup>10</sup>	2 MSM with asymptomatic pharyngeal LGV presented with proctitis symptoms. Third MSM with sore throat and cervical adenopathy, fourth MSM with mouth ulcer, tongue ulcer and cervical adenopathy, He had also proctitis symptoms	2 patients with HIV	Pharyngeal NAAT positive C. Trachomatis AND LGV DNA	Symptoms resolved on doxycycline
Retrospective French cohort of 56 cases of extra rectal LGV infection. Desclaux et al. 2017. <sup>11</sup>	6 patients with oropharyngeal LGV: There were 2 asymptomatic cases. 3 cases with pharyngitis symptoms: Inflamed pharynx and a sore throat in one, tongue ulcer and cervical adenopathy in second and purulent pharyngeal exudate in the third. There were no clinical data on the 6th patient	Not available	Pharyngeal LGV PCR	Symptoms resolved on doxycycline
Case report Albay et al. 2008. <sup>12</sup>	18-year-old woman presented with fever and cervical lymphadenopathy, recent history of recent oro-genital sex	Negative	Clinical presentation and LGV serology	Symptoms resolved on doxycycline
Case report Iliays et al. 2019. <sup>13</sup>	A 25 year old MSM presented with 2 weeks history of 2 lower lip ulcers and painful neck swelling. CT: Large cervical LN with central necrosis	Positive	Pharyngeal and lips ulcers positive NAAT positive for C.Trachomatis. Lips ulcers swab was LGV genotyping positive	Symptoms resolved on doxycycline
Case report Tchernev et al. 2010. <sup>14</sup>	A 36-year-old MSM presented with 3 weeks history of erythematous 1.2 cm nodule on lower lip associated with two smaller lesions on the cheek and zygoma CT has enlarged cervical LN	Negative	Positive LGV serology and positive tissue C. Trachomatis DNA	Symptoms resolution on pentamidine and doxycycline
Case report Riera-Monroig et al. 2018. <sup>15</sup>	A 37 year old MSM presented with one month history of painful tongue ulcer and painful submandibular adenopathy	Positive	Positive LGV NAAT from ulcer tissue	Symptoms resolution on doxycycline
Case report Gjurasin et al. 2014. <sup>16</sup>	A 48 year old MSM presented with perianal pain, painful enlarged cervical adenopathy with no sore throat. He has exudates right tonsils and purulent rectal discharge	Positive	Positive LGV serology, positive C. trachomatis DNA from lymph node aspirate Positive LGV PCR DNA from lymph node biopsy	Symptoms resolution on doxycycline

asymptomatic carriers, pharyngitis symptoms, and signs like sore throat, pharyngeal erythema, and exudate. Tongue and lip ulcers have also been reported. Painful cervical adenopathy was the most common presenting complaint and physical finding in our review. Fever has been frequently reported. Misdiagnosis as pyogenic abscess and tuberculosis lymphadenitis with initiation of tuberculosis treatment has also been reported. Oral and ano-oral sex are potential transmission routes. Most cases were

reported in MSM, and HIV has been frequently diagnosed in our literature review.<sup>2,7-16</sup> The CDC recommended molecular testing (PCR-based genotyping) as the definitive test to diagnose LGV. These tests are available only in certain laboratories, and the results are not available in the time frame that would influence clinical management. The CDC recommends LGV diagnosis be based on clinical suspicion, epidemiological information, and a *C. trachomatis* NAAT that detects both LGV strains and

non-LGV *C. trachomatis* strains at the symptomatic site. In our literature review of 17 patients, LGV serology was used in addition to other testing to make the diagnosis in 40% of the cases and used as the solo diagnostic tool in addition to clinical presentation in 11 of the cases.<sup>2,7-16</sup> The standard therapy is three weeks of oral doxycycline 100 mg twice daily.

#### 4. Conclusion

Good history-taking and appropriate problem representation are key to developing the right diagnosis. The authors put the salient features of this case together and went through hypothetical deductive reasoning, weighing the probabilities of different causes of cervical lymphadenopathy until they reached the diagnosis. Painful cervical lymphadenopathy can be the solo presentation of LGV and should be considered a potential diagnosis within the proper epidemiological context.

#### Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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