



## Case report

# Swollen inguinal lymph nodes with low fever and night sweat: diagnosis and treatment of case of cat-scratch disease lymphadenitis with sinus formation



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## ABSTRACT

A 52-year-old woman complained of inguinal lymph node enlargement, low fever and night sweats for 20 days. After pathological biopsy and metagenomic sequencing, she was diagnosed as having *Bartonella henselae* infection. Her lymph nodes were accompanied by multiple ulcers in the affected area and sinus formation. Azithromycin was administered according to the Sanford Guide to Antimicrobial Therapy 2020, combined with wound repair and partial resection of inguinal lymph nodes. The patient showed good recovery after the operation. In all, lymphadenitis associated with *B. henselae* infection is difficult to diagnose. Lymphadenitis with suppuration and sinus formation needs multidisciplinary consultation. When the causal pathogen is unknown, metagenomic sequencing is recommended for a definite diagnosis.

## 1. Introduction

Lymphadenopathy is body's short-term response to local or systemic inflammatory changes. It is a common clinical presentation, most commonly caused by infection, autoimmune diseases and tumors [1]. *Hemolytic streptococcus* and *Staphylococcus aureus* account for 40–80% of the cases of acute infection-related lymphadenopathy [2]. While, inguinal lymphadenopathy is often associated with sexually-transmitted infections and metastatic tumors. Elucidating the etiology of lymphadenopathy is challenging, and detailed medical history, physical examination and precise sequencing technology are necessary. Additionally, we need to consider *Bartonella spp.* infection in the differential diagnosis of lymphadenopathy, especially granulomatous lymphadenitis.

*Bartonella henselae*, a gram-negative bacillus, is the pathogen causing cat-scratch disease. Its primary host is a cat [3]. Humans are infected by it after being bitten, scratched or licked by cats carrying the pathogen. The

bacteria infects nearby lymph nodes through lymphatic drainage in the trauma area [4]. Lower extremity *Bartonella henselae* infection may lead to enlarged inguinal lymph node. Due to the diversity of clinical manifestations, the misdiagnosis rate of this disease is high [5]. Here, we report a case of cat-scratch disease misdiagnosed as tuberculosis in the early stage. Multiple lymph nodes in the patient's right groin ruptured and produced a sinus. The patient underwent wound repair supplemented with long-term anti-infective treatment after being diagnosed.

## 2. Case report

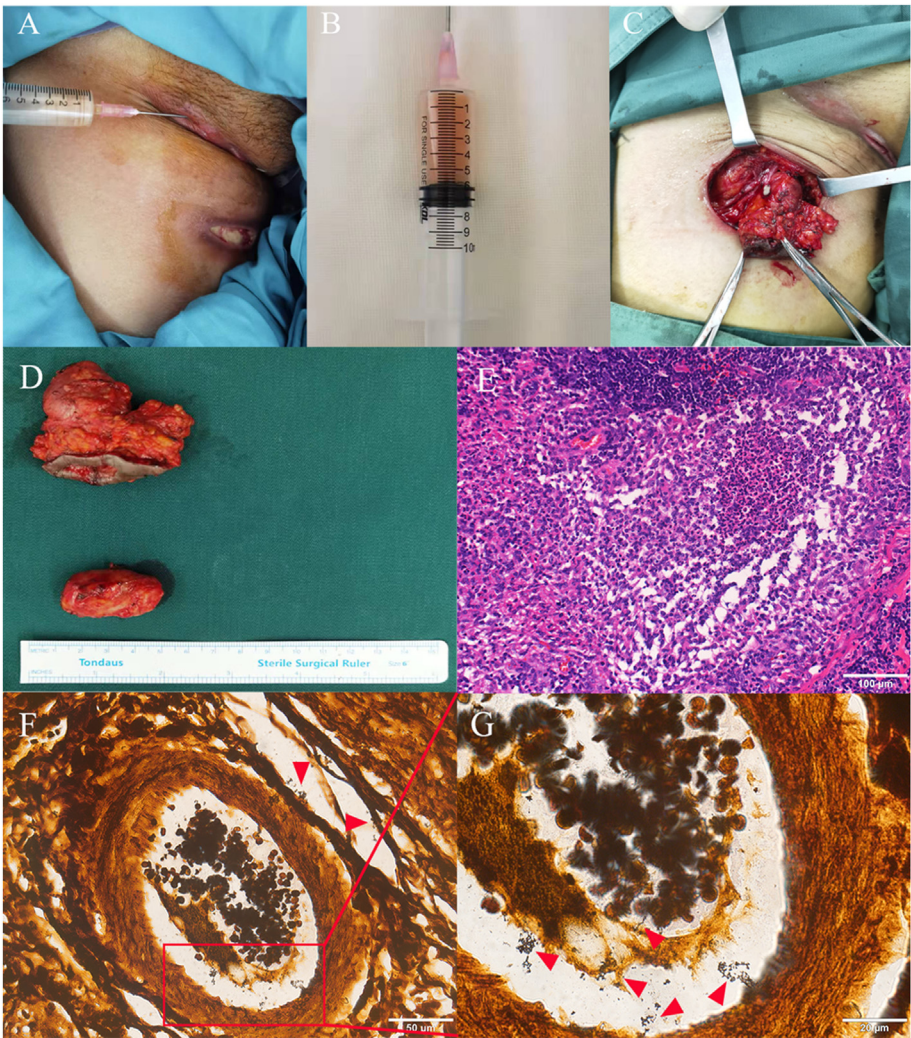
A 52-year-old woman was hospitalized with enlarged inguinal lymph nodes, low fever, and night sweats for more than 20 days (Figure 1A). She had a history of bronchiectasis and cat contact, and denied a history of unclean sexual life. She had kept a cat for about half a year, and her cat had the habit of licking her ankles. Her father and uncle died of gastric

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**Figure 1.** (A) Ulceration of multiple right inguinal lymph nodes with sinus formation. (B) Drainage of clear pus. (C) Wound repair and partial lymphadenectomy. (D) Gross specimens of excised lymph nodes. (E) Results of hematoxylin and eosin staining at 200× magnification. Granuloma with microabscess formation. (F) Results of Warthin-Starry staining at 400× magnification. (G) Results of Warthin-Starry staining at 1000× magnification. Clusters of black rod-shaped pathogens can be seen around blood vessels and necrotic tissues.

cancer. Her routine blood test showed that the levels of her test parameters were in the normal range. The C-reactive protein level was 13.85 mg/L (normal range, 0–10 mg/L) and Erythrocyte Sedimentation Rate was 65 mm/h (normal range, 0–38 mm/h). Results of other tests like liver and kidney function, AIDS, syphilis, tuberculosis antibody, whole blood interferon- $\gamma$  release assay, and other infectious markers were negative. Tuberculin skin test was negative, and Epstein-Barr virus and Cytomegalovirus viral DNA quantification were within normal range. Serum protein electrophoresis, tumor markers, and ANA, dsDNA and other immune disease antibody spectrum were negative (Figure 2). Ultrasound and abdominal CT showed enlarged right inguinal lymph nodes. Chest CT showed bronchiectasis in the middle and lower lobe of the right lung, and no enlarged lymph nodes were found in the axillary mediastinum. After administration of third-generation cephalosporin anti-infective treatment, the patient's body temperature returned to normal level and the patient underwent a lymph node biopsy. The puncture pathology showed granulomatous inflammation and recommended excluding tuberculosis as the diagnosis. Then, moxifloxacin and clarithromycin empirical anti-infective treatment was given for one week. During this period, pain and swelling of lymph nodes became more severe than before, and there were multiple ulcers with pus and a peculiar smell. Needle aspiration was performed on this lymph node to obtain 3 ml of the pus (Figure 1B). The pus samples were sent to Beagle Medical Laboratory (Changzhou, Jiangsu, China). Using third-generation nanopore sequencing technology, the nucleic acid sequence of the sample microorganism was obtained and matched with existing sequences of

microorganisms in the database using bioinformatics methods (Supplementary Material). The number of *B. henselae* was 101 with a relative abundance of 87.07%. Other identified bacteria were considered to be background bacteria. According to the cat contact history and pus gene

laboratory data

blood test parameters	
C-Reactive Protein	13.85mg/L
Erythrocyte Sedimentation Rate	65 mm/h
liver and kidney function	normal
AIDS, syphilis	negative
tuberculosis antibody, interferon- $\gamma$ release assay , Tuberculin skin test	negative
Epstein-Barr and Cytomegalovirus viral DNA quantification	normal
Serum protein electrophoresis, tumor markers	negative
immune disease antibody spectrum were	negative

**Figure 2.** The C-Reactive Protein and Erythrocyte Sedimentation Rate test values increased, and the remaining blood test indexes were roughly in the normal range.

sequencing, the patient was diagnosed with cat-scratch disease. Therefore, azithromycin was administered according to the Sanford Guide to Antimicrobial Therapy (version 50), but the ulceration of lymph nodes did not improve significantly. After excluding surgical contraindications, the wound was repaired and parts of the excised lymph nodes were sent for examination again (Figure 1C, D). The tissues stained positively for Warthin-Starry silver staining (Figure 1E, F, G). After 2 months, the patient recovered. The study was reviewed and approved by the Ethics Committee of Jiangsu North Subei People's Hospital, and the patient's consent was obtained.

### 3. Discussion

#### 3.1. Diagnosis of cat-scratch disease

Cat-scratch disease is observed globally, and had an incidence of approximately 6.4/100000 in the southern states of the United States between 2005 and 2013 [6]. The pathogen of cat-scratch disease is *B. henselae*, which is an aerobic bacterium. It is mainly transmitted by cats [7]. It is characterized by enlarged lymph nodes in the local drainage area after infection and systemic symptoms, such as low fever, headache, chills, fatigue, nausea and vomiting. *B. henselae* is difficult to cultivate, and the imaging manifestations of patients are non-specific. Therefore, pathology is important for the diagnosis of the disease. Early pathology of cat-scratch disease is mainly characterized by the proliferation of reactive tissue cells and lymphoid follicles, followed by star-shaped and fissure-shaped granulomas, formation of small abscesses, and finally, the fusion, fibrosis and disappearance of the abscesses [8]. The use of Warthin-Starry silver staining to stain black rod-like bodies is of great help in diagnosis. Specific monoclonal antibody or PCR can be used for definite diagnosis, and PCR detection of lymph node pus aspirate has the highest sensitivity [9]. The pathology of lymph node puncture in our patient showed granulomatous inflammation and no micro-abscesses. Based on the symptoms, the pathologist concluded that it may not be a tuberculosis infection. For diagnosis of the punctured tissue, pus was subjected to sequencing, which helped make an informed diagnosis of cat-scratch disease. Upon Warthin-Starry silver staining, clustered, black and short Corynebacteria were found. The diagnosis was further confirmed by the pathological staining report.

#### 3.1.1. Multidisciplinary management of cat-scratch disease

Lymphadenitis is a self-limiting disease, which usually subsides within 3 months. It is recommended to be treated with azithromycin or doxycycline, and patients involving tissues and organs should be treated with doxycycline combined with rifampicin. Mild cases only require supportive care. A large number of individuals with a history of extensive exposure to cats and arthropod have been reported in the literature to have *B. henselae* bacteremia, which is associated with tick exposure, and because of the presence of *B. henselae* DNA in ticks, ticks may serve as an important ecological reservoir for the Bartonella species [10, 11]. More than 80% of patients with confirmed cat scratch disease typically have a history of exposure to cats, with a median total duration of fever of 4 weeks [12]. However, in some immunocompromised patients, the recovery is delayed and accompanied by serious infections of the bone marrow, eyes, liver and spleen. The onset symptoms in such patients are not typical, and require multidisciplinary comprehensive management [13, 14, 15]. Our patient had a chronic history of bronchiectasis and was immunocompromised. While waiting for the test results, multiple lymph nodes fester. Since the patient's lymph node infection enters the suppurative stage from the serious stage, the lymph node capsule is pierced, and the inflammation affects the surrounding tissues. At this time point, the patient's lymph nodes are red and swollen to a wide range with obvious tenderness, the pus diffuses into the surrounding tissues, and the pus must be drained quickly. After Multidisciplinary Treatment consultation with hematology, imaging, pathology, infection, burn and plastic, respiratory and other departments, wound repairing was performed and anti-infection treatment

was administered to avoid further progress of ulceration. According to the prognosis of the patient, timely debridement is necessary.

### 4. Conclusion

Cat-scratch lymphadenitis needs to be considered in patients with enlarged lymph nodes and with a history of cat contact. Multidisciplinary treatment is important for the management of the cat-scratch disease. Serological and PCR testing may be a more rapid and sensitive diagnostic tool. If no relevant detection conditions are available, metagenomic sequencing is a comprehensive and reliable diagnostic method for cat scratch disease. In addition, clinicians, microbiologists, and pathologists should consider the possibility of *B. henselae* infection when dealing with any patient with lymphadenopathy in any location.

### Declarations

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The authors declare no conflict of interest.

#### Additional information

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### References

- [1] R. Maini, S. Nagalli, Lymphadenopathy. 2021 Nov 25, in: StatPearls [Internet], StatPearls Publishing, Treasure Island (FL), 2022.
- [2] A.K. Leung, W.L. Robson, Childhood cervical lymphadenopathy, *J. Pediatr. Health Care* 18 (2004) 3–7.
- [3] A. Álvarez-Fernández, M. Baxarias, D. Prandi, E.B. Breitschwerdt, L. Solano-Gallego, Bartonella henselae antibodies in serum and oral fluid specimens from cats, *Pathogens* 10 (2021) 329.
- [4] K. Baranowski, B. Huang, Cat scratch disease, in: StatPearls [Internet], StatPearls Publishing, Treasure Island (FL), 2021.
- [5] Z. Habet-Wilner, O. Trivizki, M. Goldstein, A. Kesler, S. Shulman, J. Horowitz, R. Amer, et al., Cat-scratch disease: ocular manifestations and treatment outcome, *Acta Ophthalmol* 96 (2018) e524–e532.
- [6] C.C. Nawrocki, R.J. Max, N.S. Marzec, C.A. Nelson, Atypical manifestations of cat-scratch disease, United States, 2005–2014, *Emerg. Infect. Dis.* 26 (2020) 1438–1446.
- [7] C.A. Nelson, A.R. Moore, A.E. Perea, P.S. Mead, Cat scratch disease: U.S. clinicians' experience and knowledge, *Zoonoses Public Health* 65 (2018) 67–73.
- [8] Y. Chen, Y.B. Fu, X.F. Xu, Y. Pan, C.Y. Lu, X.L. Zhu, Q.H. Li, R.S. Yu, Lymphadenitis associated with cat-scratch disease simulating a neoplasm: imaging findings with histopathological associations, *Oncol. Lett.* 15 (2018) 195–204.
- [9] S. Goaz, M. Rasis, I. Binsky Ehrenreich, L. Shapira, O. Halutz, et al., Molecular diagnosis of cat scratch disease: a 25-year retrospective comparative analysis of various clinical specimens and different PCR assays, *Microbiol. Spectr.* 10 (2022), e0259621.
- [10] R.G. Maggi, M. Ericson, P.E. Mascarelli, J.M. Bradley, E.B. Breitschwerdt, Bartonella henselae bacteremia in a mother and son potentially associated with tick exposure, *Parasites Vectors* 6 (2013) 101.
- [11] M.R. André, P. Neupane, M. Lappin, B. Herrin, V. Smith, et al., Using proteomic approaches to unravel the response of ctenocephalides felis felis to blood feeding and infection with Bartonella henselae, *Front. Cell. Infect. Microbiol.* 12 (2022), 828082.

- [12] M. Landes, Y. Maor, D. Mercer, Z. Habet-Wilner, E. Bilavsky, B. Chazan, M. Giladi, et al., Cat scratch disease presenting as fever of unknown origin is a unique clinical syndrome, *Clin. Infect. Dis.* 71 (2020) 2818–2824.
- [13] C. Tolou, L. Mahieu, G. Martin-Blondel, P. Ollé, F. Matonti, S. Hamid, X. Benouaich, A. Debard, M. Cassagne, V. Soler, Posterior segment involvement in cat-scratch disease: a case series, *J. Fr. Ophthalmol.* 38 (2015) 974–982.
- [14] R.C. Charles, M. Sertic, A.M. Neilan, A.R. Sohani, Case 11-2021: a 39-year-old woman with fever, flank pain, and inguinal lymphadenopathy, *N. Engl. J. Med.* 384 (2021) 1448–1456.
- [15] A. Johnson, Ocular complications of cat scratch disease, *Br. J. Ophthalmol.* 104 (2020) 1640–1646.