Bartonella henselae Diagnosed Using Molecular Studies on a Fine Needle Aspiration Specimen

Elina Shkolnik, DO MS; Tara Hajarat, MD; Marino E. Leon, MD

University of Florida College of Medicine, Department of Pathology, Immunology, and Laboratory Medicine

Introduction

Lymph node enlargement is caused by a variety of pathogens. The most common etiological agents are fastidious bacteria with Bartonella species being the most common. Bartonella species are intracellular Gram-negative bacteria capable of producing several diseases in humans. The three most common diseases are cat scratch disease (CSD), caused by *B. henselae;* trench fever, caused by *B. Quintana;* and Carrion's Disease, caused by *B. bacilliformis*. Signs and symptoms can include fatigue, fever, headache, lymphadenopathy, malaise, among others. *Bartonella henselae* lymphadenitis, or cat-scratch lymphadenitis (CSL), is classically associated with microabscesses, occasional giant cells, and extension of the inflammatory infiltrate into perinodal soft tissue. These organisms are rarely isolated by conventional techniques of cell culture. In cases where clinical suspicion is present and biopsy findings are non-specific or inconclusive, there is utility for molecular testing for detection of *B. henselae* to aid in conformation of diagnosis.

Case Presentation

The patient is a 13-year-old male with a past medical history of asthma, eczema, and cyclic neutropenia, who presented to the Emergency Department at the University of Florida Health Shands Hospital with a right submandibular mass and lymphadenopathy of one month duration. The patient reported that the mass was initially soft and tender with some pain when swallowing but over time had decreased in size and had become hard in nature. He had no fever or pharyngitis and denied having mouth sores or dental pain. He had mild leukopenia and neutropenia. The patient was placed on amoxicillin for ten days without improvement of symptoms. He had no sick contacts or travel history. He did however report that his household has 5 cats present that are both indoor and outdoor . On physical examination, the mass had red and blue discoloration. On CT, there were several enlarged lymph nodes. An infectious work-up was performed including testing for CMV, EBV and Bartonella. Aerobic and anaerobic cultures as well as fungal cultures were negative.

Case Presentation (Continued)

Serology detected elevated titers of IgM and IgG antibodies for *Bartonella henselae.* A neck ultrasound was performed showing multiple enlarged lymph nodes with the largest measuring 2.7 x 2.3 x 2.1 cm. A computed tomography (CT) scan demonstrated a right submandibular lesion with a solid multiseptated component with mass effect in the right submandibular gland and a large inferior cystic component (Figure 1).

Subsequently, a fine needle aspiration (FNA) for definitive diagnosis was performed. FNA material showed acute inflammation and necrotic debris (Figure 2). Due to clinical suspicion, molecular testing was requested for *Bartonella henselae* and sent to the University of Washington Medical Center. A PCR based assay targeting 16S rRNA and the riboflavin synthase gene (ribC) was used; these molecular studies were positive for *Bartonella henselae.*

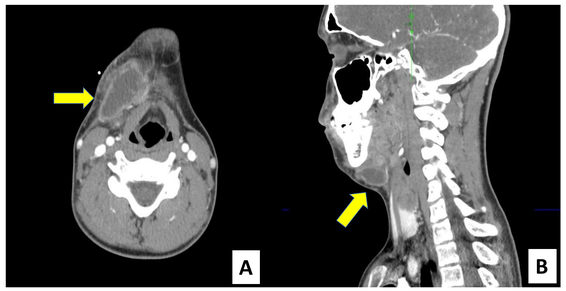

Figure 1: CT maxilla/facial (A) coronal at the level of the right submandibular space; (B) sagittal

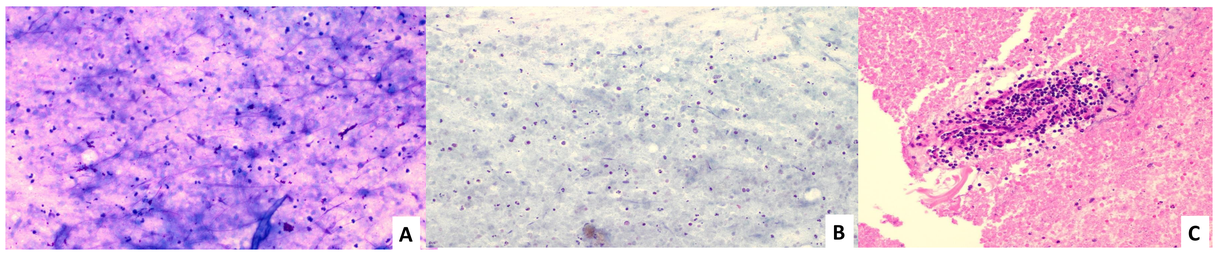

Figure 2: FNA of the lymph node (A) Romanosky-type (Diff Quik;20x). (B) Papanicolaou 10x. (C) Cell block slide H&E 20x.

Discussion and Conclusion

Lymphadenopathy has multiple etiologies including malignancy, infection, and autoimmune disorders. Infectious lymphadenopathy may be caused by bacteria, viruses, fungus, and other infectious agents. Infectious causes have clinical presentations that are often similar to other pathological processes. *Bartonella henselae*, the primary causative agent of cat-scratch disease (CSD), is the most common organism responsible for infectious lymphadenopathy in adults and children. Bacterial lymph node enlargement diagnosis is difficult and often requires a biopsy to obtain lymph node material. Culture techniques were the first method used for the diagnosis of infectious lymph node enlargement. However, due to difficulty in culturing these organisms, additional techniques are used.

Discussion and Conclusion (Continued)

Serological analysis by immunofluorescence or enzyme-linked immunosorbent assay is a useful noninvasive diagnostic method for the diagnosis of CSD, but specificities and sensitivities may vary according to the antigens used and disease case definition. Therefore, molecular techniques have become a useful tool for diagnosis and have been the gold standard for the diagnosis of infectious lymphadenitis. 16S rRNA sequences and genes such as the riboflavin synthase gene are used as a target for PCR.

Testing for Bartonella species is appropriate in patients with exposure history and symptoms of cat scratch disease. Serology may be useful to confirm diagnosis including current and past exposure. After infection, serologic results may be positive for years, even after treatment. Low sensitivity and cross-reactivity between Bartonella species may create an additional diagnostic challenge some cases. Combining testing for both IgG and IgM antibody titers increases the sensitivity of detecting acute infection. For cases of cat scratch lymphadenitis which lack specific clinical and cytologic features, a low threshold for *B. henselae* molecular testing on tissue is warranted in the appropriate clinical context. *Bartonella spp.* have been detected by using PCR-based assays that target conserved binding sites flanking regions of the rRNA gene and organism-specific gene targets such as the riboflavin synthase gene *ribC*.

Selected References

- Allizond V, et al. (2019) Serological and molecular detection of *Bartonella henselae* in specimens from patients with suspected cat scratch disease in Italy: A comparative study. PLoS ONE 14(2)
- Jabcuga C, et al. Broadening the Morphologic Spectrum of Bartonella henselae Lymphadenitis: Analysis of 100 Molecularly Characterized Cases. The American Journal of Surgical Pathology 40(3):p 342-347, March 2016
- Prudent E, et al.Molecular strategy for the diagnosis of infectious lymphadenitis. Eur J Clin Microbiol Infect Dis 37, 1179–1186 (2018)