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Cat-Scratch Disease in an AIDS Patient Presenting with Generalized Lymphadenopathy: An Unusual Presentation with Delayed Diagnosis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 44
Final Diagnosis: Cat-scratch disease
Symptoms: Lymfadenopathy
Medication: —
Clinical Procedure: Lymph node biopsy
Specialty: Infectious Diseases

Objective: Unusual clinical course

Background: *Bartonella* infection is the causative organism of cat-scratch disease (CSD), which typically presents with self-limited localized lymphadenopathy. In HIV-infected patients, *Bartonella* infection can cause systemic illnesses with significant morbidity and mortality manifesting as bacillary angiomatosis (BA), hepatic peliosis, splenitis, bacteremic febrile illness, and other organ involvement. To the best of our knowledge, there have been no reports of HIV-infected patients presenting with generalized lymphadenopathy caused by *Bartonella* infection. We report an unusual case of CSD presenting with generalized lymphadenopathy in an AIDS patient with advanced immunosuppression.

Case Report: A 44-year-old woman with AIDS, advanced immunosuppression, and intermittent adherence to antiretroviral therapy and medical care, presented with cough and increased generalized tender lymphadenopathy. A lymph node biopsy 1 year earlier was non-diagnostic for tuberculosis, fungal infection, and lymphoproliferative disorders. She remained with generalized lymphadenopathy. A repeat biopsy with the addition of Warthin-Starry silver staining suggested the diagnosis of cat-scratch lymphadenitis. She responded well to a long course of azithromycin antibiotic therapy, with the resolution of lymphadenopathy.

Conclusions: Cat-scratch disease may present with prolonged generalized lymphadenopathy, an unusual presentation in HIV patients with advanced immunosuppression. Awareness of the possibility of CSD in a similar clinical scenario may prompt early recognition and management of this disease.

MeSH Keywords: Angiomatosis, Bacillary • Cat-Scratch Disease • HIV Infections • Lymphadenitis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/909325

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Background

Cat-scratch disease (CSD) is an illness caused by *Bartonella henselae* infection following cat exposure, usually a cat-scratch or bite, most commonly occurring in children and young adults; with the median age of 21 years [1,2]. Typical CSD in immunocompetent patients presents as a regional lymphadenopathy accompanied by fever and other systemic symptoms of malaise, fatigue, and night sweats and is usually benign and self-limited. About 10% of patients have atypical CSD, mainly in older adults with manifestations including Parinaud oculoglandular syndrome, neuroretinitis, granulomatous hepatitis, erythema nodosum, and, rarely, endocarditis, osteomyelitis, myalgias, and arthropathy [3,4].

Bartonella infections caused by *B. henselae* or *B. quintana* in immunocompromised patients primarily present as a systemic illness that may be characterized by angioproliferative lesions involving the skin, liver, and spleen. Bacillary angiomatosis (BA) lesions and fever are the most common manifestations of *B. henselae and B. quintana* in HIV/AIDS patients [5], with clinical manifestations, including cutaneous vascular lesions, subcutaneous nodules, and vascular-proliferative disease, affecting the liver and spleen, and systemic illness with fever, bacteremia, and weight loss [6,7].

Isolation of *Bartonella* bacteria from blood and tissue is difficult, requiring prolonged incubation. The organisms can be seen on Warthin-Starry staining of histopathologic specimens, and PCR assay can be used in detecting *Bartonella* DNA in tissue [8,9].

We report a case of prolonged generalized lymphadenopathy of more than 1-year duration in an AIDS patient on intermittent antiretroviral therapy (ART) and *Mycobacterium avium complex* (MAC) prophylaxis.

Case Report

A 44-year-old woman was admitted with a few days' history of cough, whitish sputum production, and acute increase in painful, enlarged neck lymph nodes. She was diagnosed with AIDS 7 years earlier and had previously been treated for oral thrush, genital herpes simplex infection, syphilis, and recurrent episodes of *Pneumocystis jirovecii* pneumonia (PCP). She received ART with a combination of rilpivirine/emtricitabine/tenofovir and raltegravir in addition to trimethoprim sulfamethoxazole and weekly azithromycin for PCP and MAC prophylaxis, respectively. She reported intermittent adherence to her medications and medical care. She reported stopping her ART and PCP prophylaxis 2 months prior to admission and then resuming her medications 6 weeks later. One year earlier, she was evaluated at a different facility for enlarged lymph nodes and underwent right epitrochlear lymph node biopsy that revealed non-necrotizing granuloma with negative fungal and mycobacterial stains and cultures. She remained with generalized lymphadenopathy with occasional febrile episodes and unquantified weight loss.

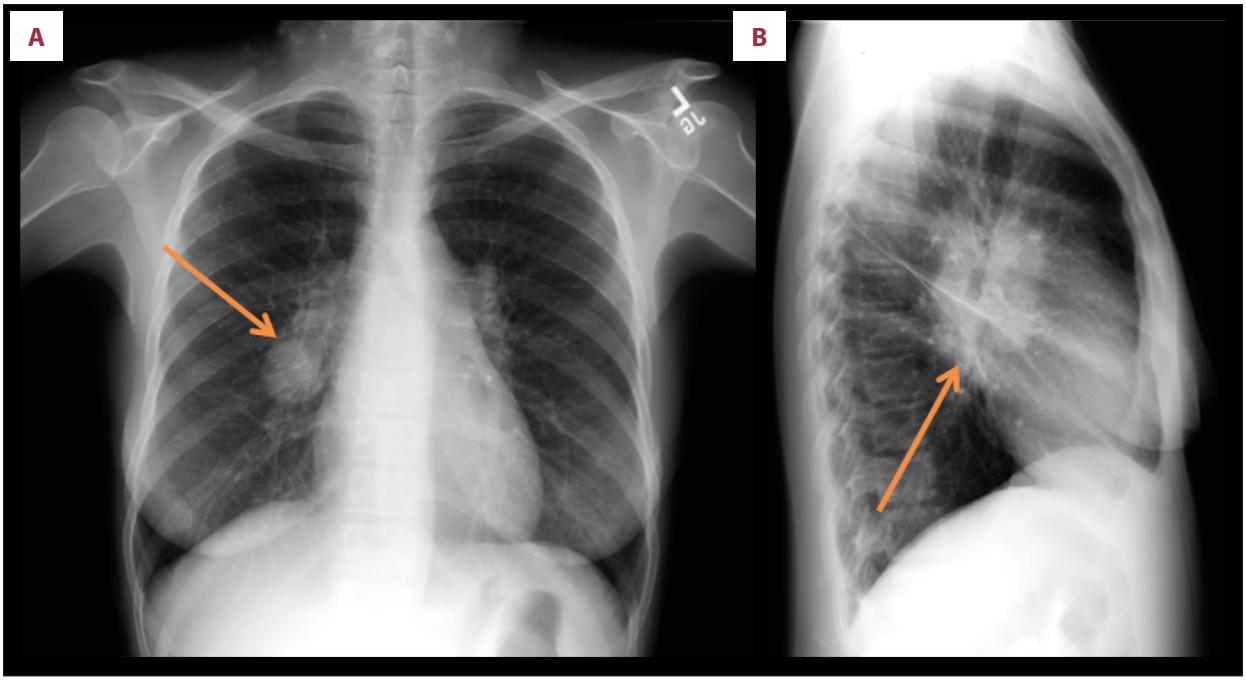

Figure 1. Chest X-ray at presentation: (**A**) Frontal view, right hilar (arrow) opacities suggestive of lymphadenopathy; (**B**) Lateral view, subcarinal (arrow) opacities suggestive of lymphadenopathy.

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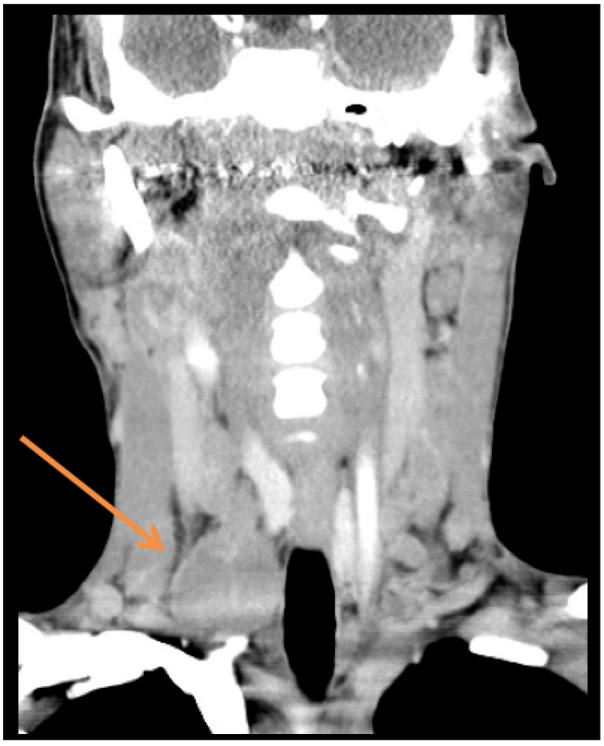

Figure 2. At presentation, contrast-enhanced CT scan of the neck, revealing bilateral cervical lymphadenopathy; the largest node was in the right supraclavicular region (arrow) with central low attenuation relative to periphery with enhancement.

On presentation, she was afebrile. Results of a physical exam were significant for diffusely enlarged and tender anterior and posterior cervical lymphadenopathy, and bilateral epitrochlear, axillary, and inguinal lymphadenopathy. Laboratory findings were significant for a CD4 count of 77 (4%), HIV viral load 1370 copies/ml, and elevated LDH 450U/L. The result of a TB QuantiFERON test was negative. A chest x-ray was suggestive of hilar and subcarinal adenopathy (Figure 1A, 1B). A computed tomography (CT) scan of the neck and chest showed extensive cervical lymphadenopathy, nodes in the suboccipital region on the left, supraclavicular, axillary, subpectoral, paratracheal, and hilar lymphadenopathy, as well as celiac adenopathy in the visualized portion of the upper abdomen (Figure 2). The largest nodal mass in the subcarinal region measured 4×2.6 cm (Figures 3A–3C).

The patient received a 5-day course of azithromycin for bronchitis and an outpatient lymph node biopsy was scheduled for 2 weeks later. At the time of biopsy, she felt clinically improved, with decrease in cervical adenopathy and tenderness. A cervical lymph node biopsy showed necrotizing granuloma with palisaded epithelioid cells, partially preserved nodular pattern, thickened capsule, and vascular proliferation. Warthin-Starry staining revealed clumps of pleomorphic bacilli, consistent with *Bartonella* species, favoring cat-scratch lymphadenitis. She reported having a 2-year-old pet cat at home. She was started on a 12-week course of oral azithromycin 600 mg daily.

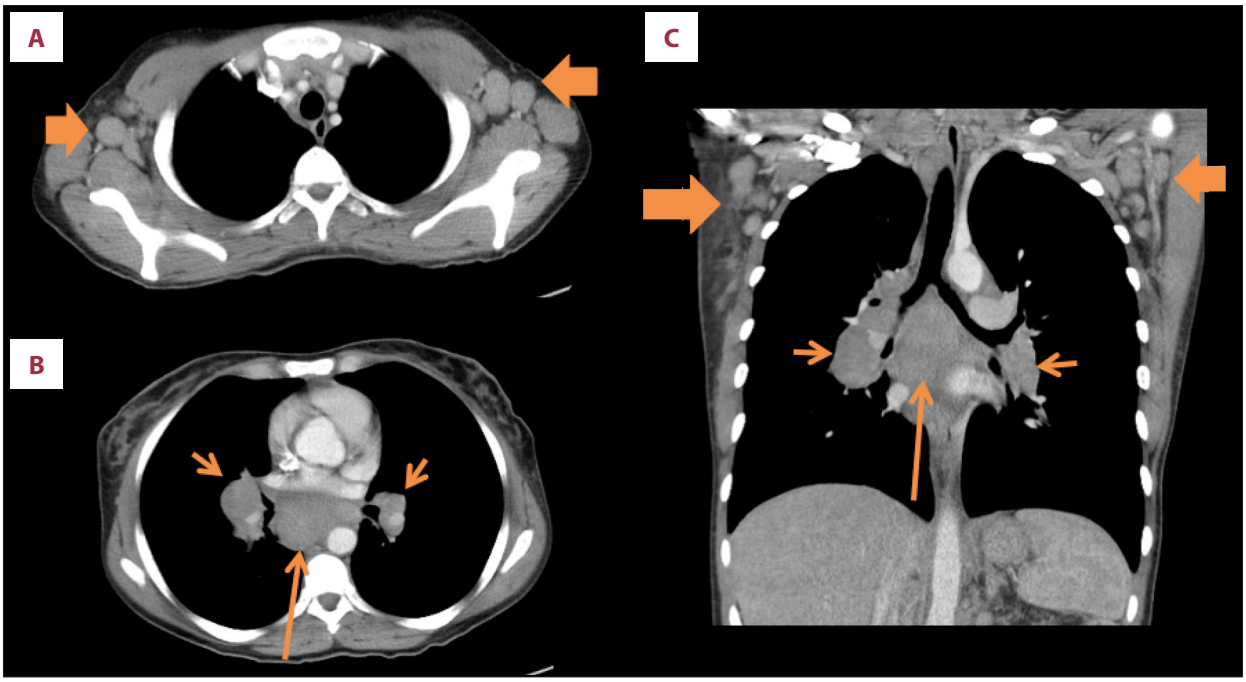

Figure 3. At Presentation, selected axial (**A, B**) and coronal (**C**) images from contrast-enhanced CT scan of the chest, demonstrating bilateral axillary (thick arrows), subcarinal (long arrows), and right hilar larger than left (short arrows) lymphadenopathy.

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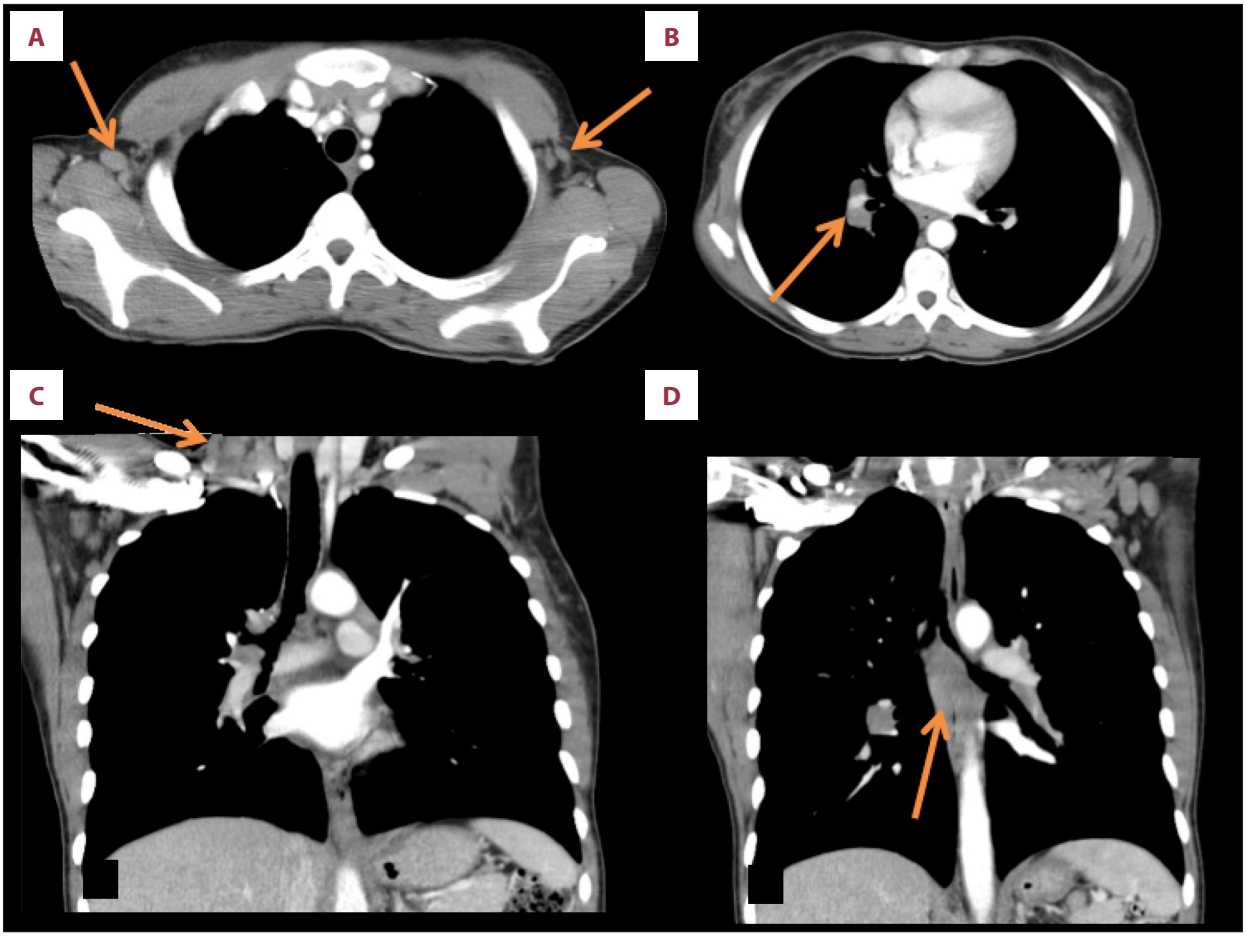

Figure 4. One week after start of treatment, selected axial (**A, B**) and coronal (**C, D**) contrast-enhanced CT scan of the chest, demonstrating significant reduction in size of the right supraclavicular (arrow in **C**), bilateral axillary, hilar, and subcarinal lymphadenopathy, indicating a favorable response to treatment.

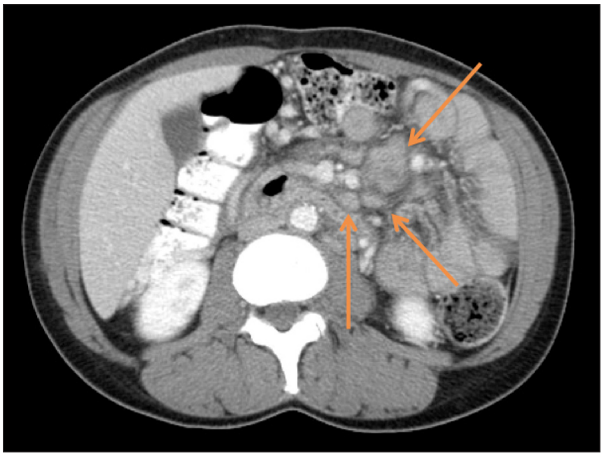

Figure 5. One week after start of treatment, Axial contrast-enhanced CT image at level of lower pole of kidneys, demonstrating sub-centimeter and enlarged mesenteric lymph nodes (arrows).

One week after starting the antibiotic course, a repeat chest CT and an abdomen CT revealed significantly decreased bilateral axillary, hilar, and mediastinal adenopathy (Figure 4). The dominant nodal mass in the subcarinal region measured 1.9 cm compared to 4 cm on the previous CT exam. There was extensive adenopathy in the region of the celiac axis, superior mesenteric artery and small bowel mesentery (Figure 5). She continued to improve clinically, with resolution of cervical, axillary, epitrochlear, and inguinal adenopathy. A planned repeat CT of chest and abdomen at the end of the 12-week azithromycin course was not done as the patient was lost to follow-up.

Discussion

Cat-scratch disease (CSD) is usually caused by *Bartonella henselae* [10–12] and cats are the main reservoir for the organism. The disease is linked to cat or flea exposure and in immunocompetent human hosts it is typically a local infection that manifests as cutaneous lesions at the site of inoculation and

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tender regional lymphadenopathy [13]. Localized disease is generally a self-limited illness. Generalized lymphadenopathy is rare. In a review of 1200 patients with CSD by Carithers, all patients in the series had lymphadenopathy; 85% had single-node involvement and the remainder had regional lymph node involvement, usually with only 2, occasionally 3, and rarely 4 or more nodes enlarged. None of the patients in this series had generalized lymphadenopathy [14]. In some individuals, CSD can include visceral organ involvement, an important manifestation in children, mainly the affecting the liver and spleen [15–17]. The diagnosis of CSD is often made presumptively based on characteristic clinical features and a history of recent cat or flea contact. Treatment, when indicated, is typically a 5-day course of azithromycin [18].

Bartonella infections in HIV-infected patients can cause serious morbidity and mortality, especially in those with significant immunosuppression [19]. Two species cause clinical infections in HIV-infected patients: *Bartonella henselae*, usually in patients who have a history of cat exposure, and *Bartonella quintana,* usually in homeless individuals with body lice. The clinical manifestations include BA, lesions involving the liver (hepatic peliosis) [20], splenitis, osteomyelitis, bacteremia, subcutaneous masses, and hemophagocytic lymphohistiocytosis [21,22]. BA is a common presentation in HIV-infected individuals with advanced immunosuppression, characterized by violaceous, friable, and vascular lesions that bleed profusely with trauma. These lesions most frequently involve the skin but can also involve internal organs, including the liver and spleen [23]. Constitutional symptoms are reported by almost all patients with BA.

Definitive diagnosis can be challenging since *Bartonella* species generally do not grow in routine cultures and isolation of the fastidious, slow-growing, gram-negative organism is difficult, requiring extended incubation with specific growth conditions [24]. The sensitivity of culture for *Bartonella henselae* from blood or lymph nodes has been reported to be as low as 20% [8]. Detection of *Bartonella* DNA in tissue specimens via polymerase chain reaction (PCR) assay is diagnostic, but the sensitivity is very low, especially when the duration of illness is more than 6 weeks [25]. Histopathological features in lymph nodes consistent with CSD include granuloma formation, stellate abscesses, and lymphocytic infiltrates. Warthin-Starry silver staining of tissue samples identifies the characteristic dark-staining masses of small curved bacteria. Treatment in immunocompromised patients with doxycycline or daily macrolide is generally for at least 3 months [26].

Our patient, with advanced immunosuppression, presented with extensive generalized lymphadenopathy, raising the possibility of lymphoproliferative disorders, fungal infections, and tuberculosis in the differential diagnosis. She had no skin lesions, subcutaneous masses, or involvement of liver and spleen on CT scans, as might be expected in HIV-infected patients with *Bartonella* infection. One year prior to presentation, she had a lymph node biopsy that revealed necrotizing granuloma with negative fungal and mycobacterial stains and no evidence for lymphoproliferative disorders. A diagnosis of CSD was not made at that time as Warthin-Starry stain and *Bartonella* PCR were not performed. Warthin-Starry stains are not routinely performed on histologic specimens unless specifically asked for by clinicians. Our patient's clinical presentation with prolonged generalized lymphadenopathy of over 1-year duration, neither typical of self-limited CSD nor of BA and other manifestations described in HIV-infected patients, is likely due to her intermittent adherence to ART and past exposure to macrolide therapy taken for MAC prophylaxis. Warthin-Starry staining on the second lymph node biopsy revealed typical findings on histopathology for CSD, and the patient responded well to azithromycin antibiotic therapy.

Conclusions

Cat-scratch disease may present with prolonged generalized lymphadenopathy, which is an unusual presentation in HIV patients with advanced immunosuppression. Awareness of the possibility of CSD in a similar clinical scenario may prompt early recognition and management of this disease.

Acknowledgements

Genna Pearl, MD, St. George's University School of Medicine reviewed and searched the literature.

Conflicts of interest

None.

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