Vertebral Osteomyelitis Due to *Bartonella henselae* in Adults: A Report of 2 Cases

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We describe 2 adult patients (1 of whom was infected with human immunodeficiency virus) with osteomyelitis due to *Bartonella henselae*. Diagnosis was established on the basis of direct identification of the microorganism in one case and seroconversion in the other. Both patients recovered completely within 3 months.

*Bartonella henselae* was first identified as the etiological agent of bacillary angiomatosis and peliosis in AIDS patients [1]. It is now widely accepted that *B. henselae* also is the cause of cat-scratch disease [2]. Typical cat-scratch disease presents as a lymphadenopathy in a patient with a history of cat contact. New diagnostic procedures, such as PCR analysis of biopsy samples and lymph node aspirates [3, 4] and serological assays [5], have made the identification of *B. henselae* in a number of atypical cases of cat-scratch disease easier. We report 2 cases of cat-scratch disease in adults who presented with vertebral osteomyelitis that was caused by infection with *B. henselae*.

**Case 1.** A previously healthy 28-year-old man was admitted to the hospital because of fever and right upper quadrant abdominal pain. He was a gardener and had a 3-month-old kitten. He had been well until 3 days before admission. The patient presented with intermittent fever (≤39°C) and sweats. Physical examination revealed no abnormality, except a tenderness in the right upper quadrant. There was no lymphadenopathy. His WBC count and liver function test results were normal. His serum C-reactive protein level and erythrocyte sedimentation rate were 224 mg/L and 58 mm/h, respectively. Culture of blood yielded negative results. Findings of abdominal ultrasonography and CT were normal. Esogastroduodenal endoscopy revealed no abnormality. Because of spontaneous improvement in his clinical condition, the patient was discharged after a 1-week hospital stay.

He was readmitted 2 days later because of fever, sweats, and low back pain. Findings of physical examination were unchanged, except for the presence of splenomegaly. A second CT of the abdomen revealed small focal lesions scattered in the liver. A bone marrow aspirate specimen revealed a slight excess of plasmocytes. A technetium bone scan demonstrated increased uptake in the body of the L1 vertebra. MRI of the spine showed a low signal intensity from the L1 vertebral body on T1-weighted imaging and hyperintensity on T2-weighted sequences (figure 1). These abnormalities were enhanced when contrast medium was used. Of interest, the maximum of intensity of backache was not at the L1 level, which demonstrated a dissociation between the clinical symptoms and MRI data. Histopathological study of a radiographically guided bone biopsy of the L1 body showed multiple foci of polymorphonuclear infiltration and medullar hyperplasia; results of Warthin-Starry silver staining were negative. Cultures of bone marrow for pyogenic bacteria, mycobacteria, and fungi yielded negative results. PCR analysis [6] of a sample from the L1 body was positive for *B. henselae*, and serologic analysis for *B. henselae* yielded positive results (indirect immunofluorescence assay: IgG titer, 2048; IgM titer, 80).

Treatment with ciprofloxacin was given for 3 weeks, in combination with amikacin during the first week. Fever resolved completely within 1 week after the beginning of antimicrobial therapy. However, the impact of antibiotic therapy was difficult to evaluate, because fever had begun to diminish the day before the treatment was introduced. The backache completely disappeared within 3 months, and the patient returned to work 3 months after the beginning of the illness. Three years later, the patient was healthy and had no symptoms.

**Case 2.** A 30-year-old man was admitted to the hospital because of fever, myalgia, backache, and sweats. He had been seropositive for HIV since 1997 and had never developed opportunistic infections. He started antiretroviral therapy ( stavudine, didanosine, and ritonavir) in January 1998. At this time, his CD4 cell count was 230 cells/mm³, and his HIV load was 108,333 copies/mL. Because of hepatitis C virus infection, treat-
ment with IFN-α (3 × 10⁶ IU 3 times per week) was begun in December 1998.

Seven weeks after IFN therapy was started, the patient complained of fever, diffuse backache, and myalgia. Physical examination showed nuchal stiffness, without any other sign of meningeal irritation. The other findings of the physical examination were normal. IFN therapy was stopped. WBC and platelet counts were normal. Electrolyte and creatinine blood levels were within the normal range. γ-Glutamyltransferase and alanine aminotransferase levels were 3 and 1.5 times the upper limits of the normal range, respectively, whereas bilirubin, alkaline phosphatase, and aspartate aminotransferase levels were normal. The CD4 cell count and HIV RNA load at the time of hospitalization were 731 cells/mm³ and <50 copies/mL, respectively. The serum C-reactive protein level was 64 mg/L. Cultures of blood and urine yielded negative results. Results of chest radiography were normal. CT of the abdomen showed scattered hypodense foci in the spleen (figure 2) and hepatomegaly. MRI of the spine showed diffuse changes of several vertebral bodies characterized by subtle, diffuse low signal intensity on T1-weighted sequences and hyperintensity on T2-weighted sequences; these abnormalities were enhanced when contrast medium was used. In addition, nodules could be detected in the vertebral bodies of T12 and S1, which demonstrated contrast-enhanced hypointense and hyperintense signals on T1- and T2-weighted images, respectively (figure 2). Histopathological study of a sample obtained by radiographically guided bone biopsy of the contrast-enhanced nodule of T12 showed an intense histiocytic and eosinophilic inflammatory reaction. Cultures results continued to be negative. Empirical antituberculous treatment was initiated with isoniazid, pyrazinamide, and ethambutol.

Fever completely resolved within 10 days of the beginning of the antituberculous therapy, and the patient returned to regular activity 1 month later. Cultures of blood, sputum, and urine samples did not yield mycobacteria, which made the diagnosis of tuberculosis unlikely. Several months later, a new medical interview revealed that the patient had been scratched by a kitten several times within the weeks preceding admission. A retrospective search for anti–B. henselae antibodies was done in stored serum samples that had been obtained 2 months before admission (at the time IFN therapy was started) and at 6 weeks and 1 year after admission to the hospital. Results of an indirect immunofluorescence assay were negative for the first serum sample and were positive for the second and third samples (IgG titer, 256). One year later, treatment with a combination of IFN and ribavirin was given for 6 months without any problem. At 2-year follow-up, the patient did not report any symptoms, and findings of a physical examination were normal.

Discussion. The diagnosis of cat-scratch disease in case 1 was established definitively by PCR detection of B. henselae DNA in a vertebral biopsy sample. In case 2, the diagnosis was strongly suggested by the demonstration of seroconversion. Serological detection of specific anti–B. henselae IgM could not...
be done because of a limited amount of available serum. In case 1, the diagnosis was established late in the course of the disease as fever started to diminish. In case 2, the diagnosis was done retrospectively, and the patient recovered while he was receiving empirical antituberculous therapy. These particular conditions make difficult any assumption about the effect of antibiotic therapy on the course of the disease.

Cat-scratch disease, which usually presents as regional lymphadenopathy, may be responsible for atypical manifestations involving the eye, the central nervous system, the skin and soft tissues, the liver, and the spleen. Cases of bone involvement in patients with cat-scratch disease are rare. According to 3 independent series totaling 1443 patients [7–9], the prevalence can be estimated at ~0.1% of cases (2/1443). In another series, 5 cases of osteomyelitis were reported among 1852 cases, which suggests a prevalence of 0.3% [10]. However, these percentages come from relatively old series in which the diagnosis of cat-scratch disease was established by clinical or histological criteria. Our report suggests that the routine use of new diagnostic tools (e.g., PCR or serologic analyses) and modern imaging techniques (MRI or CT) would significantly increase this percentage.

To our knowledge, reports of 23 cases of cat-scratch disease with bone involvement have been published [11–30]. Only 4 of the 23 cases occurred in adults [14, 15, 21, 22]. The locations reported thus far are the spine (10 cases), the limbs (5 cases), the pelvis (2 cases), the sternum (2 cases), and the skull (2 cases). The clinical and radiological presentation includes localized pain and classical signs of osteomyelitis, such as osteolysis and periosteal reaction. The contiguous development of a soft tissue abscess is frequent. Bone involvement with *B. henselae* may occur as a direct extension from an infected lymph node [13] or via hematogenous spread from the initial inoculation site or infected lymph node [18]. Hepatic and splenic involvement in both cases presented in this report suggests that bone lesions were part of a multiple-organ infection with hematogenous spread.

Figure 2. Case 2: T1-weighted (A), enhanced T1-weighted (B), and T2-weighted (C) MRI images of the lumbar spine, showing 2 nodular lesions in the bodies of T12 and S1 (arrows); multiple splenic defects were seen on a CT scan (D). Diagnosis of *Bartonella henselae* infection was made by seroconversion.
MRI presentation of bone involvement in cat-scratch disease has been described in 3 reports [21, 24, 29]. These reports, as well as the present study, show that bone involvement with B. henselae presents as contrast-enhanced hypointense and hyperintense images on T1- and T2-weighted sequences, respectively. These abnormalities may be diffuse or nodular and, in some cases, may involve asymptomatic anatomic sites. In case 1, the most severe MRI abnormalities was found in the L1 body, whereas back pain was diffuse to the lumbar spine. In some cases, a paravertebral abscess may be associated. Our report illustrates the large spectrum of MRI presentation of spine localization of cat-scratch disease.

In HIV-infected patients, B. henselae infection may present as classical cat-scratch disease with some alterations in the histopathologic findings of the lymphadenopathy or the so-called bacillary angiomatosis [30–33]. In case 2, there was no cutaneous lesion suggesting bacillary angiomatosis, and the clinical presentation did not differ significantly from that of the case in the immunocompetent patient. This may be due to the patient’s relatively high CD4 cell count and the satisfactory control of HIV replication. The impact of IFN therapy on the clinical presentation remains undetermined.

The discovery of B. henselae as the etiologic agent of cat-scratch disease allowed for the development of diagnostic procedures such as serologic and PCR detection. Because of these recent developments in diagnostic tools, it may be anticipated that unusual clinical manifestations of cat-scratch disease will be described more frequently in the future. B. henselae must be added to the list of differential diagnoses in cryptogenetic granulomatous bone lesions.

References