Portal Vein and Bone Involvement in Disseminated Cat-Scratch Disease: Report of 2 Cases

Cat-scratch disease (CSD) is a common cause of regional lymphadenopathy. We describe 2 children with an unusual presentation of disseminated CSD, the first one presenting with persistent fever, multilocular abscesses in liver and spleen as well as osteolytic lesions in the lumbar spine and the second one with portal vein thrombosis and severe ascites.

Cat-scratch disease (CSD) caused by the fastidious growing gram-negative rod Bartonella henselae is a common cause of subacute regional lymphadenopathy in children and adults, with typical clinical manifestations. It is usually a benign, self-limited disease. Three to 10 days after a scratch or bite by a cat, the patient may develop pustules or papules at the primary site of injury. After 2–3 weeks, regional lymph nodes enlarge and persist for several weeks to months. Usually no antibiotic therapy is required, and surgical resection of the lymph nodes is rarely necessary. If CSD is clinically suspected by the typical lymphadenopathy and a history of cat exposure, the diagnosis is usually confirmed by serology [1–4]. In cases with atypical clinical manifestations or low antibody levels against B. henselae, suspected CSD should be proved by serological follow-up, by molecular or histopathological investigations of the affected tissue, or both.

Disseminated CSD, in contrast, presents with a large variety of clinical symptoms [5] and may be difficult to diagnose. It has been described in immunocompetent and immunocompromised patients. Clinical manifestations include persistent fever, Parinaud’s oculoglandular syndrome, various skin lesions, hepatic and splenic abscesses, arthritis, pneumonia, pleural effusion, thrombocytopenic purpura, and osteolytic lesions. Neurological complications can present as encephalitis, meningitis, optic neuritis, convulsion, radiculitis, paraplegia, and cerebral arteritis [6–22]. Here we report 2 cases of disseminated CSD in immunocompetent children with hepatosplenic manifestations and the rare symptoms of bone and portal vein involvement.

Three weeks after a bout of measles with an uneventful course, a previously healthy 12-year-old girl developed fever (38°C–40°C for 4 weeks), enlarged submandibular and axillary lymph nodes 1 cm in diameter, severe diffuse abdominal pain not related to meals or time of day, back pain, diffuse myalgia, weight loss of 6 kg within 4 weeks, and hepatosplenomegaly. There was no history of cat or dog contact. At admission, the patient’s white blood cell count was 5900/mm³, C-reactive protein level was 7.7 mg/dL, and the erythrocyte sedimentation rate was 57 mm/h. Liver function tests were slightly elevated, with an alanine transferase of 46 U/L and an aspartate transferase of 28 U/L. Serological tests were performed that showed negative results for cytomegalovirus, Epstein-Barr virus, hepatitis A and C virus, Salmonella typhi, Salmonella paratyphi, Brucella abortus, and Entamoeba histolytica. Likewise, the anti-streptolysin O titer, antinuclear antibodies, and antimitochondrial antibodies were all within normal limits. Rheumatoid factor was negative. Serological investigations for hepatitis B revealed a chronic persistent hepatitis B infection (HBs antigen and anti-HBc immunoglobulin [Ig] G positive and anti-HBc IgM and HBe antigen negative). High titers of antibodies to B. henselae (IgM 1:1024 and IgG 1:8000) were found by immunofluorescence assay 3 weeks after onset of the illness. Analysis of magnetic resonance images taken of the abdomen showed multiple abscesses in the liver and spleen (figure 1). A ¹⁸F-fluorodeoxyglucose positron emission tomography scan showed multiple spots of hyperactivity in the lumbar vertebra (figure 2) corresponding to spondylitis, which was confirmed by magnetic resonance imaging scan as osteolytic lesions in the lumbar vertebra (figure 1). After 3 weeks of therapy with erythromycin, the patient clinically improved. Abdominal pain and back pain decreased; the girl was afebrile and in good general condition. Three months later, the abdominal pain was completely resolved. After a follow-up period of 15 months, the girl was doing clinically well, and sonography indicated that the hepatic and splenic abscesses had disappeared. Titer to B. henselae decreased in the follow-up, as shown in table 1.

A previously healthy 2.5-year-old boy with a history of cat contact presented for routine physical examination. He was in good general condition and afebrile, with mild abdominal tenderness in the paraumbilical area. Splenomegaly 10 cm in dia-

![Figure 1](image-url). Magnetic resonance image scan showing multiple abscesses in liver and spleen and an osteolytic lesion in the lumbar vertebra (arrow) in patient 1.
Figure 2. Bone scan showing multiple spots of hyperactivity in the lumbar spine of patient 1.

Table 1. *Bartonella henselae* antibody titers and serological follow-up in patients 1 and 2.

<table>
<thead>
<tr>
<th>Time of serum collection after onset of illness</th>
<th><em>B. henselae</em> titer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgG</td>
</tr>
<tr>
<td>Patient 1</td>
<td></td>
</tr>
<tr>
<td>3 Weeks</td>
<td>8000</td>
</tr>
<tr>
<td>3 Months</td>
<td>4000</td>
</tr>
<tr>
<td>6 Months</td>
<td>2000</td>
</tr>
<tr>
<td>25 Months</td>
<td>256</td>
</tr>
<tr>
<td>Patient 2</td>
<td></td>
</tr>
<tr>
<td>6 Weeks</td>
<td>1024</td>
</tr>
<tr>
<td>4 Months</td>
<td>512</td>
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</table>

Fever and abdominal pain may be leading symptoms in disseminated CSD. In a recently published study, Arisoy et al. [9] described 19 children with hepatosplenic CSD. Fever (100%) and abdominal pain (68%) were the 2 most frequent symptoms. The initial diagnosis of fever of unknown origin was made in 79% of the children. Dunn et al. [6] reported a series of 11 children with hepatosplenic CSD. Fever for >2 weeks was found in 72% of the patients, and 64% of the children complained of abdominal pain. In typical CSD, regional lymphadenopathy is a characteristic feature and one of the major diagnostic criteria. In disseminated CSD, however, lymphadenopathy can be absent [6, 8, 15]. In the study of Dunn et al. [6], approximately half the children showed lymphadenopathy, and in a recently reported series of 9 cases of disseminated CSD, only 4 patients had peripheral lymphadenopathy [15].

The first patient of our report showed the most frequent symptoms of disseminated CSD: fever and abdominal pain. She also had peripheral lymphadenopathy and bone involvement, a symptom that was first described in 1954 [16] and that is rarely seen in disseminated CSD. A recently published review [17] of the literature reports ~15 cases of CSD associated with osteomyelitic lesions. Bone involvement as a consequence of *B. henselae* infection usually presents with localized pain without erythema, swelling, or tenderness and appears only in <1% of CSD cases [18]. An even more atypical course of the disease was observed in the second patient. Splenomegaly found on routine physical examination and slight abdominal tenderness were the leading signs. The delayed onset of ascites 3 weeks after onset of the illness and the extrahepatic portal vein thrombosis are very rare complications. To our knowledge, this is only the second report of portal vein involvement in disseminated CSD [19]. These sequelae can be explained by the pressure of the enlarged abdominal lymph nodes to the portal vein and subsequent deceleration of the blood flow. A thrombophilic disorder was excluded in this patient. In 1996, Zinzindohoue et al. [19] described portal vein involvement due to disseminated CSD in a 16-year-old boy. This patient had symptoms of portal hypertension, which were caused by an abscess behind the por-
Antimicrobial treatment differed in our patients. The first patient received erythromycin for 3 weeks and clinically improved, but they still had persisting, high levels of IgG. Approximately 15 months after onset of the disease, the first patient had an IgG titer of 1:256. In several cases in the literature, very high IgG and IgM titers are reported at the time of diagnosis [6, 9, 11, 13–15, 20], but serological follow-up after recovery is not well known. Waldvogel et al. [20] described the titer course of a patient with disseminated CSD, but within a period of 5 months, no significant decrease could be observed. The sensitivity of the immunofluorescence assay in CSD ranges from 83% to 100% [1–4] but has less satisfying specificity. Especially high titers to \( B. \text{henselae} \) are diagnostic key findings, and serological testing is a method to confirm clinically suspected CSD within 48 h [2, 4]. PCR analysis is a helpful tool to confirm the diagnosis. Sensitivity of PCR assays varies depending on the primers used for amplification and the preparation of the specimen [21]. Formalin-fixed, paraffin-embedded specimens seem to be less suitable for PCR analysis than fresh or frozen specimens. However, obtaining clinical specimens is always combined with invasive procedures.

Antimicrobial treatment differed in our patients. The first patient received erythromycin for 3 weeks and clinically improved after treatment and was completely recovered after 3 months. The second patient received no antibiotic treatment. He also clinically improved, but the length of recovery—5 months—was significantly longer. For typical CSD, one study showed a faster decrease of peripheral lymph node enlargement during azithromycin therapy during the first 30 days [22]. But after 1 month, there was no difference in the outcome of antibiotic treated and untreated patients. There are many case reports in the literature with empirical antibiotic treatment for disseminated CSD, including erythromycin, tetracycline, gentamicin, rifampin, ciprofloxacin, and other drugs [23]. But there are no prospective controlled clinical trials to prove the effectiveness of an antimicrobial therapy for disseminated CSD. Therefore, the use of antibiotics in a patient with disseminated CSD has to be decided on a case-by-case basis. A general recommendation of a specific antibiotic as drug of choice at this time remains questionable.

Diagnosis and treatment of disseminated CSD remains difficult. The broad range of clinical symptoms and the unspecific course of the disease may cause problems in recognizing CSD and lead to misdiagnosis. Therefore, disseminated CSD has to be taken into account in children presenting with a systemic illness, and \( B. \text{henselae} \) infection should be considered in the initial evaluation of prolonged fever, especially in children with a history of exposure to cats.

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References

10. Hayem F, Chacar S, Hayem G. \( \text{Bartonella henselae} \) infection mimicking...
Thiabendazole for the Treatment of Strongyloidiasis in Patients with Hematologic Malignancies

A total of 21 patients with hematologic malignancies were given thiabendazole for treatment of strongyloidiasis. Fifteen patients were cured. Since there were no relapses, it is unlikely that maintenance therapy has a role in the management of strongyloidiasis in this population of patients.

Thiabendazole has been considered the mainstay of treatment for strongyloidiasis for decades, with a clinical efficacy of ~90% in the immunocompetent host [1]. Nevertheless, information regarding its use in immunosuppressed patients is limited to anecdotal reports of patients treated for the disseminated syndrome [2, 3], with little being known about the best therapeutic regimen and its efficacy. In this study, we report the treatment response to thiabendazole in 21 cases of strongyloidiasis diagnosed in a cohort of 163 patients with hematologic malignancies. All patients were screened for strongyloidiasis by examination of 3 stool samples with use of the direct and Baermann-Moraes methods [4]. Patients with strongyloidiasis were treated with thiabendazole, 25 mg/kg, given twice daily for 3 days (maximum dose, 3000 mg/day), and they were subsequently monitored with monthly stool examinations. Patients with >3 negative stool samples after treatment were considered to be cured. The definition of disseminated strongyloidiasis was the same as that in our previous report [5].

From April 1995 through December 1997, 163 consecutive patients with hematologic malignancies were evaluated, and 22 (13%) had strongyloidiasis. One patient was excluded because he died of uncontrollable acute leukemia before the beginning of treatment. The median age of the 21 patients was 46 years (range, 12–76 years), and the male:female ratio was 16:5. Six patients had acute leukemia, 7 had chronic leukemia, 6 had lymphoma, and 2 had multiple myeloma. Corticosteroids were being used by 17 (81%) of the patients. Symptoms attributable to strongyloidiasis were present in 17 patients (81%), and cough was the most frequent symptom (7 patients), followed by diarrhea and abdominal pain (6 patients each). Four patients (19%) were asymptomatic. The median number of samples examined was 2 (range, 1–6), and the median number of positive stool samples was 1 (range, 1–3).

One patient complained of dizziness, but all patients took the full dose of thiabendazole. The median follow-up was 14 months (range, 1–29 months). Eighteen patients (86%) were shown to be free of infection by all subsequent stool examinations (median, 4 examinations; range, 1–12 examinations). Fifteen patients (71%) had >3 negative examination results and were considered to be cured. Of the 3 patients for whom <3 examinations were performed, 2 died of acute leukemia in relapse and 1 died of sepsis of cutaneous origin. Three patients remained infected after 1 course of thiabendazole (cure rate in 15 of 18 patients, 82%). Of the 3 patients for whom therapy failed, 1 was cured after a 10-day course of treatment with thiabendazole, whereas the other 2 died during relapse of their underlying diseases, before the results of a second course of treatment could be evaluated. Ten patients are still alive. One patient was lost to follow-up and was censored after the last...