Bartonella henselae Infection as a Cause of Fever of Unknown Origin

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Received 12 October 1999/Returned for modification 18 January 2000/Accepted 8 February 2000

Fourteen of 41 patients (34%) with a serological diagnosis of Bartonella henselae infection were found to have prolonged fever or fever of unknown origin, suggesting that generalized systemic B. henselae infection is not rare in immunocompetent healthy individuals.

The clinical spectrum of Bartonella henselae infection varies, ranging from classic cat scratch disease with only lymphadenopathy to severe systemic disease. In general, immunocompetent individuals tend to develop classic cat scratch disease, while immunocompromised individuals tend to have systemic disease (1). We report the prevalence of systemic B. henselae infection among otherwise healthy individuals.

Between 9 July 1996 and 7 January 1999, a total of 119 patients (80 children and 39 adults) suspected of having cat scratch disease because of either lymphadenopathy or fever of unknown origin and pet ownership were referred to us for serological diagnosis. All the patients had no underlying diseases. Sera from 33 hospitals located in central and southwestern areas of Japan were included in this study, and referring doctors included pediatricians, physicians, surgeons, otolaryngologists, ophthalmologists, dentists, radiologists, and pathologists. Serological diagnosis using the indirect fluorescent-antibody (IFA) method (4, 6) was made on the basis of either elevated titers of immunoglobulin M (IgM) (≥1:20) or IgG (≥1:256) antibodies or a fourfold rise in IgG titer between acute- and convalescent-phase sera. The sensitivity and specificity of our IFA method were 87 and 97.7%, respectively.

The 119 patients were categorized into four groups by clinical features (Table 1). Group 1 included patients with regional lymphadenopathy and mild symptoms, with no fever or a fever lasting less than 7 days, indicating classic cat scratch disease. Group 2 included patients with regional lymphadenopathy and a prolonged fever, lasting more than 7 days. Group 3 included patients without lymphadenopathy and with a fever lasting less than 7 days. Group 4 included patients without lymphadenopathy and with a fever lasting more than 7 days. The numbers of patients in the groups were 90, 16, 2, and 11, respectively. There were no differences between the groups in terms of age, sex, or exposures to cats.

Of the 119 patients, 41 (31 children and 10 adults) were serologically positive for B. henselae, whereas 78 were serologically negative. Out of the 41 patients who tested positive for IFA, 27 (18 children and 9 adults) were from group 1, 6 (all children) were from group 2, and 8 (7 children and 1 adult) were from group 4.

Table 2 summarizes the clinical features for the 14 patients from groups 2 and 4 (fever lasting more than 7 days) who tested positive for IFA. The maximum temperature of these patients ranged from 39.0 to 40.5°C. Despite a prolonged fever, they were otherwise in good condition. It is noteworthy that 8 (7 children) of the 14 patients had no lymph node swelling, even though they had a prolonged fever, lasting from 7 to 25 days. Of these eight, three had hepatic granuloma and/or splenic granuloma. By using PCR analysis (5), we were able to confirm that one patient had septicemia, whereas we could not confirm septicemia for three patients. The other six patients had regional lymphadenopathy accompanied by a prolonged fever, lasting from 9 to 30 days, and PCR analysis confirmed septicemia in one patient.

B. henselae has been reported as a cause of fever with bacteremia or fever of unknown origin in both immunocompetent and immunocompromised hosts (2, 3, 7). Previous reports indicated that B. henselae infection may cause fever of unknown origin without regional lymphadenopathy or hepatosplenic involvement (2, 3, 7) and is one of the most common infectious diseases in children (2). Our findings support previous reports and suggest that generalized systemic B. henselae infection is not rare in healthy individuals and that children seem to be more prone to develop a prolonged fever or fever of unknown origin.

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If a patient with prolonged fever or fever of unknown origin,
irrespective of lymphadenopathy, owns a pet, especially a cat or dog, or has a history of pet contact, the possibility of *B. henselae* infection should be considered.

We thank the referring doctors for allowing us to analyze blood samples from patients suspected of having cat scratch disease.

**REFERENCES**


**TABLE 2. Clinical features for patients with prolonged fever (≥7 days)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Regional lymphadenopathy</th>
<th>Duration of fever (days)</th>
<th>Symptom(s)</th>
<th>IFA titer IgM</th>
<th>PCR result*</th>
<th>Pet ownership</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>F</td>
<td>–</td>
<td>15</td>
<td>Malaise&lt;sup&gt;cd&lt;/sup&gt;</td>
<td>1,024</td>
<td>ND</td>
<td>Cat&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>15</td>
<td>10</td>
<td>F</td>
<td>–</td>
<td>10</td>
<td>Malaise</td>
<td>512</td>
<td>+, granuloma&lt;sup&gt;fg&lt;/sup&gt;</td>
<td>Cat&lt;sup&gt;e&lt;/sup&gt;, dog&lt;sup&gt;e&lt;/sup&gt;</td>
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<tr>
<td>36</td>
<td>9</td>
<td>F</td>
<td>–</td>
<td>14</td>
<td>Headache, back pain</td>
<td>80 1,024</td>
<td>ND</td>
<td>Cat</td>
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<tr>
<td>44</td>
<td>25</td>
<td>F</td>
<td>–</td>
<td>14</td>
<td>Abdominal pain</td>
<td>80 1,024</td>
<td>+, granuloma&lt;sup&gt;fg&lt;/sup&gt;</td>
<td>Dog</td>
</tr>
<tr>
<td>77</td>
<td>9</td>
<td>F</td>
<td>–</td>
<td>20</td>
<td>–</td>
<td>160 2,048</td>
<td>+, PB</td>
<td>Cat</td>
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<tr>
<td>87</td>
<td>9</td>
<td>M</td>
<td>–</td>
<td>14</td>
<td>Malaise, weight loss</td>
<td>320 2,048</td>
<td>ND</td>
<td>Cat</td>
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<tr>
<td>88</td>
<td>4</td>
<td>F</td>
<td>–</td>
<td>25</td>
<td>–</td>
<td>4,096</td>
<td>–, PB</td>
<td>Cat</td>
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<tr>
<td>107</td>
<td>9</td>
<td>F</td>
<td>–</td>
<td>7</td>
<td>Sore throat</td>
<td>40 1,024</td>
<td>–, PB</td>
<td>Cat</td>
</tr>
<tr>
<td>21</td>
<td>10</td>
<td>M</td>
<td>+</td>
<td>10</td>
<td>Sore throat</td>
<td>1,024</td>
<td>ND</td>
<td>Dog</td>
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<tr>
<td>23</td>
<td>9</td>
<td>F</td>
<td>+</td>
<td>24</td>
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<td>ND</td>
<td>Cat</td>
</tr>
<tr>
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<td>1</td>
<td>M</td>
<td>+</td>
<td>14</td>
<td>–</td>
<td>512</td>
<td>ND</td>
<td>Cat</td>
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<tr>
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<td>5</td>
<td>F</td>
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<td>20 512</td>
<td>ND</td>
<td>Cat</td>
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<td>74</td>
<td>11</td>
<td>F</td>
<td>+</td>
<td>11</td>
<td>Malaise, headache</td>
<td>320 1,024</td>
<td>+, PB</td>
<td>Cat, dog</td>
</tr>
<tr>
<td>117</td>
<td>9</td>
<td>F</td>
<td>+</td>
<td>30</td>
<td>Malaise</td>
<td>40 1,024</td>
<td>–, PB; +, pus</td>
<td>Cat, dog</td>
</tr>
</tbody>
</table>

<sup>a</sup> F, female; M, male.
<sup>b</sup> –, absent; +, present.
<sup>c</sup> +, positive; –, negative; ND, not done. The tissue tested was granuloma peripheral blood cells (PB) or pus.
<sup>d</sup> Multiple hypoechoic lesions in the liver were found by echocardiography.
<sup>e</sup> No ownership, but a positive history of pet contact.
<sup>f</sup> Hepatic hypoechoic lesions and splenic granuloma were seen in resected tissue.
<sup>g</sup> Histopathological diagnosis was obtained from resected tissue.