Highly Elevated Serum Ferritin Levels Are a Diagnostic Marker in Babesiosis

To the Editor—Babesiosis is a tick-borne zoonosis most commonly caused by Babesia microti and is transmitted by Ixodes species ticks [1, 2]. Babesia presents as a febrile undifferentiated malaria-like illness with a variety of nonspecific clinical and laboratory abnormalities [3]. Nonspecific laboratory abnormalities have been described in babesiosis, for example, leukopenia, relative lymphopenia, atypical lymphocytes, thrombocytopenia, elevated serum aminotransferases, and elevated lactate dehydrogenase (LDH) levels [4, 5].

Mildly elevated serum ferritin levels may occur as part of the “acute-phase response.” Acute-phase ferritin elevations are only mildly elevated (<2 times normal) and normalize rapidly in a few days. However, highly and persistently elevated serum ferritin levels (>2 times normal) have been associated with several systemic noninfectious and infectious disorders [6–8]. Among noninfectious disorders, highly elevated ferritin levels may be due to hemophagocytic syndrome, malignancies, myeloproliferative/myelodysplastic disorders, rheumatic/inflammatory disorders (rheumatoid arthritis, adult Still disease, systemic lupus erythematosus, temporal arteritis, Kawasaki disease), liver disease (hemochromatosis, cirrhosis, chronic active hepatitis, α-1 antitrypsin deficiency), and renal disease (acute/chronic renal failure), as well as other miscellaneous causes (eg, anemia of chronic disease, sickle cell anemia, blood transfusions) [6, 7]. Among infectious diseases, highly and persistently elevated serum levels have been reported with Legionnaire’s disease and West Nile encephalitis, human immunodeficiency virus, tuberculosis, and malaria [6, 7, 9, 10]. In contrast to acute-phase ferritin elevations, highly elevated ferritin levels due to systemic diseases are very highly elevated and remain elevated for days.

Highly elevated serum ferritin levels have not been reported in babesiosis. Recently, in hospitalized adults with babesiosis, we noted elevated ferritin levels. All were smear positive for babesiosis. None of our babesiosis patients had other infectious or noninfectious disorders associated with elevated ferritin levels. In our babesiosis patients, the age range was 34–95 years with a male predominance. Two cases were acquired by blood transfusion and 2 were asplenic. Five (5/10) had temperatures of >39°C and all (5/5) of these had a pulse temperature deficit (ie, relative bradycardia). Physical findings were limited to mild splenomegaly and none had a rash. In

![Figure 1](https://via.placeholder.com/150)

Figure 1. Time course of elevated serum ferritin levels in an adult with babesiosis.
our babesiosis patients, laboratory abnormalities included leukopenia, relative lymphopenia, atypical lymphocytes, mildly elevated aminotransferases, and elevated serum LDH levels. In babesiosis patients with ferritin levels examined (8/10), all (8/8) were highly elevated (>2 times normal), ranging from 1130 ng/mL to 3694 ng/mL (n < 235 ng/mL) (Table 1). One patient had elevated serum ferritin levels that persisted for 4 weeks (Figure 1).

In reviewing our recent babesiosis experience in admitted adults, we observed highly and persistently elevated serum ferritin levels (>2 times normal). None of our babesiosis patients had other disorders associated with elevated ferritin levels. In babesiosis, serum ferritin levels were elevated during the first week of illness, usually persisting for 1–2 weeks, but in some patients ferritin levels remained elevated for 3–4 weeks. In our experience, highly elevated ferritin levels are another nonspecific laboratory abnormality in acute babesiosis in hospitalized adults. To the best of our knowledge, highly elevated serum ferritin levels have not been previously reported in babesiosis.

Note
Potential conflicts of interest. All authors: No potential conflicts of interest.

Abbreviations: bpm, beats per minute; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; LDH, lactate dehydrogenase; NA, not available; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; WBC, white blood cell.

* Relative bradycardia present in those with temperature >39°C.

Table 1. Clinical Features in Adults Hospitalized With Babesiosis

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age, y</th>
<th>Gender</th>
<th>Peak Fever</th>
<th>Pulse, bpm</th>
<th>Splenomegaly</th>
<th>Admission WBC Count (3.9–11 K/µL)</th>
<th>Admission % Lymphocytes (&gt;21%)</th>
<th>Atypical Lymphocytes</th>
<th>Hb/Hct (12.7–18 g/dL)</th>
<th>Admission Platelet Count (160–392 k/µL)</th>
<th>Admission ESR (1–16 mm/h)</th>
<th>Admission SGOT (4–36 IU/L)</th>
<th>Admission SGPT (4–36 IU/L)</th>
<th>Admission LDH (100–250 IU/L)</th>
<th>Admission Ferritin Level (14–235 ng/mL)</th>
<th>Degree of Parasitemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>M</td>
<td>39.4°C</td>
<td>98*</td>
<td>Mild</td>
<td>3.3</td>
<td>32</td>
<td>2%–7%</td>
<td>10.6/11.7</td>
<td>66</td>
<td>97</td>
<td>92</td>
<td>NA</td>
<td>525</td>
<td>1326</td>
<td>1%</td>
</tr>
<tr>
<td>2</td>
<td>85</td>
<td>M</td>
<td>37.7°C</td>
<td>79</td>
<td>Mild</td>
<td>7.6</td>
<td>9</td>
<td>1%</td>
<td>10.5/12.6</td>
<td>92</td>
<td>NA</td>
<td>24</td>
<td>13</td>
<td>336</td>
<td>NA</td>
<td>1.5%</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>M</td>
<td>37.3°C</td>
<td>94</td>
<td>Mild</td>
<td>5.5</td>
<td>9</td>
<td>1%</td>
<td>9.9/12.8</td>
<td>40</td>
<td>NA</td>
<td>82</td>
<td>122</td>
<td>643</td>
<td>&gt;1300</td>
<td>3%</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>M</td>
<td>39.4°C</td>
<td>100*</td>
<td>Asplenic</td>
<td>20</td>
<td>11</td>
<td>1%–4%</td>
<td>5.9/9.5</td>
<td>208</td>
<td>100</td>
<td>92</td>
<td>115</td>
<td>722</td>
<td>3945</td>
<td>5%</td>
</tr>
<tr>
<td>5</td>
<td>87</td>
<td>M</td>
<td>38.1°C</td>
<td>79</td>
<td>Mild</td>
<td>3.3</td>
<td>16</td>
<td>1%–2%</td>
<td>9.0/9.6</td>
<td>70</td>
<td>99</td>
<td>34</td>
<td>24</td>
<td>330</td>
<td>1130</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>6</td>
<td>62</td>
<td>M</td>
<td>39.5°C</td>
<td>86*</td>
<td>Mild (with infarct)</td>
<td>2.9</td>
<td>13</td>
<td>3%</td>
<td>10.6/8.4</td>
<td>74</td>
<td>84</td>
<td>67</td>
<td>52</td>
<td>737</td>
<td>1885</td>
<td>2%</td>
</tr>
<tr>
<td>7</td>
<td>64</td>
<td>M</td>
<td>37.5°C</td>
<td>115</td>
<td>None</td>
<td>5.3</td>
<td>9</td>
<td>4%</td>
<td>8.4/10.9</td>
<td>157</td>
<td>82</td>
<td>79</td>
<td>93</td>
<td>459</td>
<td>NA</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>M</td>
<td>39.6°C</td>
<td>94*</td>
<td>None</td>
<td>2.8</td>
<td>17</td>
<td>3%</td>
<td>9.2/13.9</td>
<td>69</td>
<td>100</td>
<td>33</td>
<td>27</td>
<td>544</td>
<td>2970</td>
<td>4.5%</td>
</tr>
<tr>
<td>9</td>
<td>95</td>
<td>F</td>
<td>39.7°C</td>
<td>110*</td>
<td>Mild</td>
<td>6.5</td>
<td>12</td>
<td>NA</td>
<td>9.1/10.2</td>
<td>66</td>
<td>NA</td>
<td>28</td>
<td>22</td>
<td>364</td>
<td>606</td>
<td>1%</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>F</td>
<td>38°C</td>
<td>72</td>
<td>Asplenic</td>
<td>5.8</td>
<td>2</td>
<td>2%</td>
<td>9.9/13</td>
<td>95</td>
<td>85</td>
<td>21</td>
<td>17</td>
<td>222</td>
<td>539</td>
<td>1%</td>
</tr>
</tbody>
</table>

Numbers within parentheses are normal ranges.

Abbreviations: bpm, beats per minute; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; LDH, lactate dehydrogenase; NA, not available; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; WBC, white blood cell.


References

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Clinical Infectious Diseases® 2015;60(5):827–9
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DOI: 10.1093/cid/ciu960