Short Report: Evaluation of Serum Procalcitonin Levels for Diagnosis of Secondary Bacterial Infections in Visceral Leishmaniasis Patients

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Abstract. Secondary bacterial infections are a major complication and cause of death in children with visceral Leishmaniasis (VL). Thus, early diagnosis of bacterial infections is an important step in the treatment of patients with VL. The goal of this study was to determine if serum procalcitonin (PCT) could be used as a diagnostic marker of secondary bacterial infections in VL patients. Serum PCT was measured in 35 hospitalized patients with VL before treatment and after defervescence. The level was higher than normal (> 0.5 ng/mL) in 72% (25) of the patients. Twelve (34%) of the patients had secondary bacterial infections with PCT levels ranging from 0.1 to 12.29 ng/mL, and those without secondary bacterial infections (23) had PCT levels ranging from 0.1 to 14.58 ng/mL. The results suggest that PCT levels increase significantly in most VL patients but are not correlated with the presence of secondary bacterial infections.

Visceral leishmaniasis (VL), which is also known as kala-azar and caused by various strains of *Leishmania* spp., is characterized by fever, hepatosplenomegaly, anemia, weight loss, and neutropenia.1 In Iran, it is endemic to southern and northwestern areas, and most patients are children less than three years of age.2 Secondary bacterial infections are one of the major complications and a leading cause of death in these patients.2,3

Because of similarities in signs and symptoms of VL and bacterial infections, the coexistence of VL and bacterial infections cannot be ruled out on the basis of clinical findings. In the presence of bacterial infections, routine bacterial cultures can be negative because most patients receive antibiotic treatment for the suspected bacterial infections before the diagnosis of VL. Availability of a laboratory test for early and accurate diagnosis of bacterial infections can be crucial and can help in the appropriate use of antibiotic treatment.

Procalcitonin (PCT) is a prohormone of calcitonin that is produced by C cells of the thyroid gland and certain endocrine cells of the lung. In healthy persons, the blood level of PCT is undetectable or less than 0.5 ng/mL.4,5 In 1993, an increased level of PCT in bacterial sepsis was reported.6 During inflammatory response, the pathophysiological role of PCT is unclear and the probable sites of its origin are thought to be extra-thyroidal from all parenchymal tissues and differentiated cell types throughout the body.7 Compared with other inflammatory markers such as interleukin-6 and tumor necrosis factor, PCT is more stable and has a longer half-life.8 Its level does not increase in systemic inflammatory response because of non-bacterial causes such as autoimmune disease, viral infections, or most cases of cancer.9–11 The highest value is seen in association with gram-negative sepsis and bacterial meningitis; levels increase moderately when local bacterial infections such as otitis media in a physical examination, or clinical evidence of pneumonia and presence of infiltration in a chest radiograph; 2) severely ill appearance and suspected sepsis; 3) absolute neutrophil count less than 500/mm² and fever; and 4) an age less than one year.

For the measurement of PCT, a blood sample (2 mL clot) was collected from each patient on admission before starting any medication (PCT 1), and a second sample was collected one day after fever resolved with treatment (PCT 2). Serum was stored at –70°C. Clinical and laboratory data were extracted from the patients’ charts.

The PCT level was measured by using a two-site immunoluminometric assay (LIAISON BRAHMS PCT Quantitative Assay Kit, Reference 318.101; DiaSorin S.p.A., Saluggia, Italy) and an Automatic LIAISON® Analyzer (DiaSorin S.p.A.). Values less than 0.1 ng/mL were considered undetectable. All samples were analyzed in one day by one technician who used one kit and analyzer. Data were analyzed by using Spearman’s correlation for continuous data and the Mann-Whitney test. *P* values less than 0.05 was considered significant.
Of 35 patients, 18 were boys and 17 were girls (age range = 5–72 months, 77% of whom were ≤24 months of age). Among the 35 patients, 30 (86%) had an IFA titer ≥1:128. Four patients (11%) had a titer of 1:64 and one patient had negative IFA titer, but these five patients were positive for bone marrow Leishman bodies. All patients had fevers for an average of 21 days before admission. Complete blood counts and liver function test results were abnormal for all patients. Clinical and laboratory findings of VL patients are shown in Table 1.

Evidence of secondary bacterial infections (paraclinical and/or clinical) was found in 12 patients (34%). There were three positive blood cultures, six positive urine cultures, two positive chest radiographs for pneumonia, and one case of otitis media identified by physical examination.

The PCT 1 levels were greater than 0.5 ng/mL in the 72% of the VL patients, Table 2. We had expected to see higher PCT values in patients with superimposed bacterial infections, especially those with positive blood cultures, but we did not observe higher levels ($P = 0.056$). The PCT values in three patients with positive blood cultures (0.26, 0.32, and 1.92 ng/mL) were not significantly higher than patients with negative cultures or without localized bacterial infections. The highest PCT value (14.58 ng/mL) was seen in a patient who had no evidence of bacterial infection. The highest PCT values among the 35 patients were not significantly higher than patients with negative cultures.

In summary, our study suggests that PCT levels increase significantly in most VL patients. However, this increase did not show a correlation with secondary bacterial infection in these patients.

Inflammatory indices in visceral leishmaniasis patients with and without evidence of bacterial infection, Iran*

Table 3

<table>
<thead>
<tr>
<th>Inflammatory indices</th>
<th>Bacterial infection</th>
<th>Non-bacterial infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>PCT 1 (ng/mL)</td>
<td>&lt;0.1–12.29</td>
<td>1.81 ± 3.42</td>
</tr>
<tr>
<td></td>
<td>0.1–2.19</td>
<td>0.56 ± 0.57</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>17–140</td>
<td>53.09 ± 35.24</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>6–96</td>
<td>34.73 ± 30.24</td>
</tr>
</tbody>
</table>

*$PCT 1 = $pretreatment procalcitonin; $PCT 2 = $serum procalcitonin after defervescence; $ESR = $erythrocyte sedimentation rate; $CRP = $C-reactive protein.

were found in two patients with urinary tract infections who had negative blood cultures.

Severe disease was detected in 4 (11%) of 35 patients. Among these patients, two had PCT 1 levels less than 2 ng/mL (1.48 and 1.69 ng/mL), and two had PCT 1 levels less than 10 ng/mL (12.29 and 14.58 ng/mL). There was a marginally significant correlation between severity of disease and PCT 1 levels ($P = 0.049$). Several studies have shown an increase of PCT levels in patients with systemic parasitic diseases such as *P. falciparum* malaria, and a significant correlation between PCT values and severity of disease.\(^3\)

The only two parameters that had significant correlation with PCT 1 levels were related to degree of fever during hospitalization; i.e., those with higher body temperatures had higher PCT 1 values ($P = 0.037$) and platelet counts. Patients with platelet counts less than 100,000/mm\(^3\) had higher PCT 1 values ($P = 0.020$). It is unclear whether these two indices are indicative of a more severe systemic inflammatory reaction in these patients that causes higher PCT values.

The PCT 2 levels decreased in 80% of patients and increased or showed no changes in 20% (Table 3). Differences between PCT 1 and PCT 2 values and changes in PCT levels were calculated and compared between two groups of patients (those who received antibiotic treatment and those who did not receive antibiotic treatment). We did not find any significant correlation between changes in PCT levels and antibiotic treatment ($P = 0.29$).

In summary, our study suggests that PCT levels increase significantly in most VL patients. However, this increase did not show a correlation with secondary bacterial infection in these patients.

REFERENCES


