HIV/AIDS

BRIEF REPORTS

HIV and Leishmania Coinfection: A Review of 91 Cases with Focus on Atypical Locations of Leishmania

A retrospective study was conducted in France in 1998 to determine the clinical features of visceral leishmaniasis (VL) in 91 patients infected coomitantly with human immunodeficiency virus. Our data suggest that the clinical manifestations of VL may be influenced by the immunological status, with atypical locations of Leishmania amastigotes more frequently found in severely immunocompromised patients. In such patients, the involvement of atypical locations may lead to the discovery of VL.

Visceral leishmaniasis (VL) is a severe disease that is the third most frequent opportunistic infection among HIV-infected individuals in certain areas of Spain and Portugal [1]. Nevertheless, VL is not an AIDS-defining criterion [2]. As recently stressed by Albrecht [3], the existence of subclinical or occult disease may result in underestimation of the true incidence of VL. In addition, Leishmania amastigotes may be found in unexpected locations in HIV-infected individuals [4, 5]. We have studied the clinical presentation of VL in a large series of HIV-infected individuals, focusing on atypical locations of Leishmania amastigotes.

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without such amastigotes (36 ± 47 cells/mm³ vs. 67 ± 75 cells/mm³, respectively; \( P = .06 \)).

For 15 patients, the diagnosis of VL was established only when *Leishmania* amastigotes were found unexpectedly in atypical locations, after discovery of *Leishmania* infection initiated the diagnostic procedure. Endoscopic examination of these patients was performed because of the following clinical signs: diarrhea, epigastralgia, or dry cough. The main clinical characteristics of the patients are presented in table 1. For 12 patients, the diagnosis of VL was confirmed by the presence of amastigotes on bone marrow smears. For the other 3 patients, bone marrow smears were negative, but the diagnosis of VL was made later. For patient 2, the indirect immunofluorescence (IFAT) for *Leishmania* species was positive, and later explorative splenectomy revealed the presence of *Leishmania infantum* MON-1 [6]. ELISA and IFAT were negative for patients 7 and 13. At follow-up, patient 7 had clinical relapse of VL with patient 13 revealed disseminated *Leishmania* infection in the bone marrow, lymph nodes, liver, spleen, and gastrointestinal tract. For the 16 other patients who had *Leishmania* infection in atypical locations, the diagnosis of VL was made concomitantly with a reference diagnosis procedure—that is, by demonstration of amastigotes on bone marrow smears.

This series reports half of the cases of coinfection diagnosed in France during the study period [8]. The clinical manifestations of VL in HIV-infected patients did not differ significantly from those in immunocompetent individuals [9]. However, our data suggest that the clinical manifestations of VL in HIV-infected patients may be influenced by the patients’ immunological status; patients with a CD4 count of <50 cells/mm³ have a lower frequency of the clinical triad of fever, splenomegaly, and hepatomegaly and, conversely, findings of *Leishmania* amastigotes in atypical locations were more frequent. *Leishmania* amastigotes were present in atypical locations in one-third of the patients, and because systematic searches were not done, their numbers were probably underestimated. That they were significantly more frequent in severely immunocompromised patients supports the role of the response of the immune system in expression of the disease [4].

Discovery of amastigotes in an atypical site led to the diagnosis of VL in 15 patients. Involvement of the gastrointestinal tract or the respiratory tract is not uncommon in HIV-infected patients [4, 5, 7]. In the literature, the frequency and clinical significance of VL in atypical locations are not clearly described. *Leishmania* species can invade many tissues asymptptomatically [4]. However, parasitization should be considered in those cases in which digestive tract symptoms are present. Diarrhea has been reported in 40% of immunocompetent patients with VL who live in Sudan, 50% of those who live in India, and 60% of those who live in Brazil [10]. Nevertheless, in these countries, diarrhea may result from other diseases. In our series, perendoscopic gastrointestinal biopsies led to the unexpected diagnosis of VL in 12 patients. Endoscopy, which was performed because of the clinical symptoms, revealed no pathogens, other than *Leishmania* species, in 11 patients (table 1). We cannot exclude all biases, in particular other undiagnosed conditions causing diarrhea or epigastralgia. However, our data suggest that *Leishmania* parasitization of the digestive tract can be symptomatic in severely immunocompromised HIV-infected patients.

Even in areas where *Leishmania* infection is endemic, the diagnosis of VL is not yet systematically considered by physicians caring for HIV-infected patients. In 5 patients (patients 3, 5, 10, 12, and 14; table 1), the clinical triad of fever, splenomegaly, and hepatomegaly was present with pancytopenia, suggesting that a diagnosis of VL could have been evoked prior

### Table 1. Main clinical characteristics of 15 human immunodeficiency virus-infected patients with visceral leishmaniasis (VL) diagnosed after the accidental discovery of amastigotes in an atypical location.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Amastigote location</th>
<th>Year VL was diagnosed</th>
<th>Resides in area where <em>Leishmania</em> infection is endemic</th>
<th>CD4 count, cells/mm³</th>
<th>Fever</th>
<th>Splenomegaly</th>
<th>Hepatomegaly</th>
<th>PMN, cells/mm³</th>
<th>Hb, m/L</th>
<th>PLT, cells/mm³</th>
<th>Amastigotes on bone marrow smears</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Stomach</td>
<td>1988</td>
<td>No</td>
<td>10</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3500</td>
<td>6.9</td>
<td>97,000</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>Skin</td>
<td>1991</td>
<td>Yes</td>
<td>150</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>5000</td>
<td>7.3</td>
<td>493,000</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>Lung</td>
<td>1991</td>
<td>Yes</td>
<td>18</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1500</td>
<td>5.0</td>
<td>71,000</td>
<td>Positive</td>
</tr>
<tr>
<td>4</td>
<td>Colon</td>
<td>1993</td>
<td>Yes</td>
<td>102</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>2800</td>
<td>5.2</td>
<td>292,000</td>
<td>Positive</td>
</tr>
<tr>
<td>5</td>
<td>Duodenum</td>
<td>1993</td>
<td>Yes</td>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1200</td>
<td>7.1</td>
<td>68,000</td>
<td>Positive</td>
</tr>
<tr>
<td>6</td>
<td>Colon</td>
<td>1993</td>
<td>Yes</td>
<td>60</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>1800</td>
<td>6.8</td>
<td>146,000</td>
<td>Positive</td>
</tr>
<tr>
<td>7</td>
<td>Colon</td>
<td>1994</td>
<td>No</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>4000</td>
<td>7.9</td>
<td>145,000</td>
<td>Negative</td>
</tr>
<tr>
<td>8</td>
<td>Lung, esophagus</td>
<td>1994</td>
<td>No</td>
<td>10</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>1600</td>
<td>8.8</td>
<td>265,000</td>
<td>Positive</td>
</tr>
<tr>
<td>9</td>
<td>Stomach</td>
<td>1995</td>
<td>Yes</td>
<td>88</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>1800</td>
<td>5.5</td>
<td>149,000</td>
<td>Positive</td>
</tr>
<tr>
<td>10</td>
<td>Duodenum</td>
<td>1995</td>
<td>Yes</td>
<td>13</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1300</td>
<td>6.0</td>
<td>90,000</td>
<td>Positive</td>
</tr>
<tr>
<td>11</td>
<td>Duodenum</td>
<td>1996</td>
<td>Yes</td>
<td>15</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>6500</td>
<td>6.0</td>
<td>52,000</td>
<td>Positive</td>
</tr>
<tr>
<td>12</td>
<td>Duodenum</td>
<td>1996</td>
<td>No</td>
<td>19</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>2500</td>
<td>6.6</td>
<td>48,000</td>
<td>Positive</td>
</tr>
<tr>
<td>13</td>
<td>Colon</td>
<td>1996</td>
<td>No</td>
<td>10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1900</td>
<td>6.2</td>
<td>51,000</td>
<td>Negative</td>
</tr>
<tr>
<td>14</td>
<td>Colon</td>
<td>1996</td>
<td>No</td>
<td>6</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>1900</td>
<td>6.1</td>
<td>119,000</td>
<td>Positive</td>
</tr>
<tr>
<td>15</td>
<td>Lung</td>
<td>1997</td>
<td>Yes</td>
<td>15</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>3400</td>
<td>8.3</td>
<td>175,000</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Note. HB, hemoglobin; PLT, platelets; PMN, polymorphonuclear neutrophils.

* Patients 3, 6, and 15 were found to have concomitant *Cryptosporidium, Histoplasma capsulatum,* and *Pneumocystis carinii* infections, respectively.
to endoscopy. Conversely, our data suggest that it is not unusual for major clinical signs to be absent. Occult forms of VL, for which neither major clinical signs nor hematologic abnormalities were observed, were found in patients 1, 2 and 7. Although previously reported [4], the prevalence of this atypical form of VL was unclear. Most studies have shown that, among HIV-infected patients, the sensitivity of IFAT and ELISA is low [3, 4]. However, western blotting is more sensitive and may help discriminate asymptomatic carriage of Leishmania infection from acute VL [11]. For areas where Leishmania infection is endemic, we have recently proposed the use of systematic investigation consisting of western blotting and careful follow-up of patients with a serologic profile of latent infection [11]. This approach might allow for earlier systematic diagnosis of VL, rather than merely fortuitous diagnosis.

In conclusion, our data suggest that, in HIV-infected patients, clinical presentation of VL may be influenced by CD4 count. The clinical manifestations may be typical of VL or nonspecific (e.g., diarrhea), and the illness may become more atypical as the CD4 count decreases. Physicians in areas where Leishmania infection is endemic should be encouraged to test for such infection by use of western blotting and to consider a diagnosis of VL more routinely for HIV-infected patients.

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References

Prolonged Suppression of Human Immunodeficiency Virus Type 1 RNA during Dual Nucleoside Reverse-Transcriptase–Inhibitor Therapy in Clinical Practice

Because there is limited information about suppression of virus loads (determined by current “ultrasensitive” assays) in patients receiving nucleoside reverse-transcriptase inhibitors (NRTIs) alone, we reviewed our experience in clinical practice with patients who had virus loads of <25 copies/mL after >1 year of treatment with dual NRTIs.

The outcomes achieved with highly active 3-drug antiretroviral therapy are better than those achieved with less aggressive...