Clinical Significance of Splenic Tuberculosis in Patients Infected with Human Immunodeficiency Virus

Amparo González-López, Fernando Dronda, Mercedes Alonso-Sanz, Fernando Chaves, Ignacio Fernández-Martín, and Luis López-Cubero

To assess the clinical significance of splenic tuberculosis in patients infected with human immunodeficiency virus (HIV) type 1, we compared 20 patients who had splenic tuberculosis with 20 randomly selected, HIV-infected patients with culture-proven tuberculosis for whom splenic involvement had been ruled out by ultrasonography. All of the patients were male prison inmates and intravenous drug users. Statistically significant differences (P < .05) were detected between patients with splenic involvement (median CD4+ cell count, 54/mm³) and those without splenic involvement (median CD4+ cell count, 92/mm³). No specific symptoms suggesting splenic involvement were detected in the patients with splenic tuberculosis. All patients received antituberculous drugs, and none of these patients required splenectomy. The median survival was similar in both groups. Splenic tuberculosis occurs in more-severely immunocompromised HIV-infected patients, the prognosis is generally good, the clinical response to therapy is usually favorable, and splenectomy is rarely necessary.

Splenic lesions have been infrequently described in the biomedical literature [1–3]. In immunocompromised patients with AIDS, splenic lesions are predominantly due to opportunistic infections [4–18], followed in frequency by Kaposi’s sarcoma and lymphomas [19]. Tuberculosis is a prevalent disease in Spain, and its prevalence in penitentiaries is alarming [20]. However, splenic lesions due to Mycobacterium tuberculosis are infrequent. To our knowledge, only 31 separate case reports of splenic abscesses due to M. tuberculosis have appeared in the worldwide literature [6–18]; 22 cases were included in a general series on abdominal tuberculosis [21], and seven other cases were reported by Murray et al. [22]. We conducted the present study to determine the clinical significance of splenic tuberculosis in a series of HIV-infected patients.

Patients and Methods

This study was performed at the Hospital General Penitenciario in Madrid, which was a 150-bed facility. Between 1 March 1991 and 31 March 1995, 7,673 patients were admitted to this hospital. We retrospectively reviewed the charts of all patients who were infected with HIV-1 and had culture-proven tuberculosis. Cases of splenic tuberculosis were defined as those in which patients had characteristic lesions in the spleen (i.e., multiple, small [<1 cm], rounded, hypoechoic lesions) that were detected by ultrasonography (figure 1) at the time that tuberculosis was diagnosed (<30 days after diagnosis). Twenty control patients were selected randomly from a group of 68 HIV-infected patients with culture-proven tuberculosis for whom splenic involvement had been ruled out by ultrasonography. None of these patients had a concomitant condition that might also cause splenic lesions.

Ultrasonographic examinations were performed by using electronic real-time scanners with 3.5-MHz and 5-MHz linear and curve-array transducers to investigate underlying clinical conditions (e.g., hepatosplenomegaly, fever of unknown origin, abnormal liver function test results, or chronic infection due to hepatitis B and/or hepatitis C viruses). Follow-up ultrasonographic examinations were performed between 20 days and 2 years after tuberculosis was diagnosed for 13 case patients and six control patients.

We used the χ² test and/or Fisher’s exact test to assess the association between categorical variables. We used a nonparametric test or Student’s t test for continuous variables; means (± SE) and median-interquartile ranges are reported. We calculated survival with a logrank test. P values of <.05 were considered statistically significant.

Results

During the study period, 88 of the 483 patients at the hospital who had culture-proven tuberculosis underwent abdominal ultrasonography. All of the patients with focal splenic lesions that were detected by ultrasonography (n = 20) were compared with an equivalent random group with no splenic involvement. All the patients were male intravenous drug users. The most
frequent symptoms, physical findings, and laboratory data are shown in table 1. The numbers of patients in each group, with a given diagnosis, based on microbiological criteria, were as follows: disseminated tuberculosis, 15 case patients vs. 14 control patients; pulmonary tuberculosis, 4 vs. 5; and nodal involvement, 1 vs. 1.

Among case patients, the mean size (± SE) of the spleen, as measured by ultrasonography, was 134 ± 5 mm. Ultrasonographic follow-up studies were done for 13 of these patients. The splenic focal lesions disappeared with medical treatment in 10 of these patients and decreased in size and number in one patient 2.5 months later. For another patient, a repeated ultrasonogram was obtained 20 days after the first ultrasonogram was obtained, and the findings were similar. For the last patient, a clear increase in the number of splenic lesions was detected after 32 days. No tuberculosis-related deaths occurred during the 3 months after the diagnosis.

For patients in the control group, the mean size (± SE) of the spleen was 136 ± 5 mm. Ultrasonographic follow-up studies were done for six of these patients; no focal splenic lesions were found. During the 3 months following diagnosis, only one death, which was not related to tuberculosis, occurred.

When we compared the study and control groups on the basis of the parameters shown in table 1, we did not find any significant differences. The clinical patterns for both groups were similar; the median survival was 21 months (25th and 75th percentiles, 9 months and 26 months, respectively) for case patients and 16 months (25th and 75th percentiles, 9 months and 17 months, respectively) for control patients ($P = .18$, logrank test). Statistically significant differences were detected only when the CD4$^+$ cell counts were compared: the median CD4$^+$ cell count for case patients was 54/mm$^3$ (25th and 75th percentiles, 14/mm$^3$ and 96/mm$^3$, respectively), and that for control patients was 92/mm$^3$ (25th and 75th percentiles, 64/mm$^3$ and 110/mm$^3$, respectively).

**Discussion**

The incidence of tuberculosis in Spanish penitentiaries was high (2,283 cases per 100,000 inmates) in 1993–1994 [23]; this incidence is ~40 times higher than that in the general Spanish population [24]. Despite the limitations inherent in our study (i.e., the retrospective design and the peculiar population, which consisted entirely of male prison inmates, all of whom were intravenous drug users), we found that splenic tuberculosis might be less uncommon than previously thought. The characteristic splenic lesions of mycobacteriosis are small, multiple, and rounded and appear hypoechoic on an ultrasonogram (figure 1) and hypodense on a CT scan [22, 25]. Other medical conditions that might cause splenic lesions should be ruled out.

In a review of the recent literature, we found that 31 HIV-infected patients with splenic tuberculosis have been described [6–18], and another 29 have been included in general series [21, 22]. The diagnosis was definite in only 10 cases (splenic biopsy was performed by means of percutaneous fine-needle aspiration or at necropsy or surgery); the diagnosis was highly probable in the remaining cases. The tuberculous splenic abscesses in these cases were present predominantly in the setting of disseminated tuberculosis diagnosed by strict microbiologi-
Table 1. Symptoms, physical findings, and laboratory data for patients with tuberculosis, with and without splenic involvement.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Splenic involvement (n = 20)</th>
<th>No splenic involvement (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and physical findings*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever, chills</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Anorexia, weight loss</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Cough</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Liver enlargement</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Palpable lymph nodes</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Ascites</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Splenic enlargement</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Laboratory data*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin concentration (g/dL)</td>
<td>10.1 ± 0.3</td>
<td>10.9 ± 0.5</td>
</tr>
<tr>
<td>WBC count (×10^3/mm^3)</td>
<td>3.56 ± 0.5</td>
<td>4.62 ± 0.62</td>
</tr>
<tr>
<td>Neutrophil count (×10^3/mm^3)</td>
<td>2.72 ± 0.46</td>
<td>3.46 ± 0.62</td>
</tr>
<tr>
<td>Lymphocyte count (×10^3/mm^3)</td>
<td>584 ± 55</td>
<td>797 ± 139</td>
</tr>
<tr>
<td>Median CD4⁺ lymphocyte count (×10^3/mm^3)</td>
<td>54³</td>
<td>92³</td>
</tr>
<tr>
<td>CD8⁺ lymphocyte count (×10^3/mm^3)</td>
<td>304 ± 61</td>
<td>372 ± 43</td>
</tr>
<tr>
<td>Median lactate dehydrogenase (U/L)</td>
<td>231¹</td>
<td>226²</td>
</tr>
</tbody>
</table>

* Data are number of patients.
³ Twenty-fifth vs. 75th percentiles: 14/mm^3 vs. 96/mm^3, respectively, and 64/mm^3 vs. 110/mm^3, respectively.
⁴ P < .05.
² Twenty-fifth vs. 75th percentiles: 164 U/L vs. 301 U/L, respectively, and 172 U/L vs. 304 U/L, respectively.

Although both groups were severely immunocompromised when tuberculosis was diagnosed, those with splenic involvement had significantly lower CD4⁺ cell counts than those without splenic involvement (median CD4⁺ cell count, 54/mm^3 vs. 92/mm^3; P < .05). Six of 10 previously described patients with splenic involvement had CD4⁺ cell counts of <100/mm^3 (range, 20–284/mm^3) [7, 8, 11, 14, 16–18]. Jones et al. [26] found that extrapulmonary tuberculosis and mycobacteremia occurred more frequently in severely immunocompromised patients (mean CD4⁺ cell count, <100/mm^3), and it is possible that the splenic involvement became more frequent as the immunosuppression increased. Future well-designed studies may verify this theory.

Follow-up ultrasonography, which was performed for 13 patients between 20 days and 22 months after tuberculosis was diagnosed, confirmed the disappearance of the splenic lesions in 10 patients after specific therapy was instituted. The clinical outcome with medical treatment was favorable for both groups of patients. Splenic tuberculosis has been successfully treated with specific antimycobacterial drugs, and few of the previously described patients (8 [26%] of 31) required splenectomy [7, 8, 11, 12, 14, 17, 18]. Most investigators consider antituberculous drugs to be the first choice in the treatment of splenic tuberculosis and reserve splenectomy for complicated cases that do not respond initially [8]. In the present study, the clinical outcome with medical therapy was favorable for 19 patients. No tuberculosis-related deaths occurred, and ultrasonographic evidence of resolution was obtained for 77% (10 of 13) patients who underwent ultrasonography during the follow-up period. Splenectomy was not necessary in any of the cases.

We conclude that splenic tuberculosis in HIV-infected patients is not uncommon in certain clinical settings and in special populations. It occurs in more-severely immunocompromised patients and can be easily detected by ultrasonography and other imaging techniques. Splenic involvement does not generally imply a poor prognosis, the clinical response to drug therapy is usually favorable, and splenectomy is rarely necessary.

Acknowledgments

The authors are indebted to Dr. Federico Pulido (Hospital 12 de Octubre, Madrid), for statistical support and constructive comments; to Dr. Santiago Moreno (Hospital General Universitario Gregorio Marañón, Madrid) for constructive comments; to Marta R. Mahou and Dr. Luis Rico (Fundación Jiménez Díaz, Clínica Nuestra Señora de la Concepción, Madrid) for their help with English syntax; and to Dr. Margarita R. Mahou (Hospital General Universitario Gregorio Marañón, Madrid) and Dr. Pedro Mera (Hospital General Penitenciario, Madrid) for technical support.

References

11. Lozano F, Gómez-Mateos J, López-Cortés L, García-Bragado F. Tubercu-
losis splenic abscesses in patients with the acquired immune deficiency
J. Splenic tuberculosis in patients with AIDS. Rev Infect Dis 1991; 13:
1069–71.
13. De Marco O, Nasfi A, Bacques O, Gamerman H. Abcès splénique tuber-
culeux chez un malade avec une sérologie VIH positive [letter]. La
in patients positive for human immunodeficiency virus: report of two
de Mon M. Abscesos espléneos por Mycobacterium tuberculosis en
pacientes con síndrome de inmunodeficiencia adquirida. Gastroenterol
por Mycobacterium tuberculosis en el SIDA. Enferm Infecc Microbiol
17. Fuertes Martín A, Santana García S, Martín-Sánchez MJ, Jiménez-López
A. Abscesos espléneos tuberculosis en pacientes con sida: dos nuevos
avium and multidrug-resistant Mycobacterium tuberculosis dissemin-
ated mixed infection in a patient with the acquired immunodeficiency
19. Klatt EC, Meyer PR. Pathology of the spleen in the acquired immuno-
S. Tuberculosis en población penitenciaria: estudio de 138 casos. Med
21. Fee MJ, Oo MM, Gabayan AE, Radin DR, Barnes PF. Abdominal tubercu-
losis in patients infected with the human immunodeficiency virus. Clin
Infect Dis 1995; 20:938–44.
of the liver and spleen in AIDS: detection with 5-MHz sonography.
of tuberculosis in a large prison population. Am J Respir Crit Care Med
24. de March Ayuela P. Situación actual de la tuberculosis en España. Med
25. Radin DR. Intraabdominal Mycobacterium tuberculosis vs Mycobacterium
avium-intracellulare infections in patients with AIDS: distinction based
PF. Relationship of the manifestations of tuberculosis to CD4 cell counts
in patients with human immunodeficiency virus infection. Am Rev Re-