The Spectrum of Tuberculous Peritonitis*

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From 1966 to 1973, a total of 30 cases of tuberculous peritonitis were seen in Seattle-King County. Abdominal pain, swelling, and constitutional symptoms were the most frequent initial complaints. Radiographic abnormalities consistent with tuberculosis were present in 25 cases, and pulmonary disease was proven in ten. An initial tuberculin test with intermediate-strength purified protein derivative of tuberculin was negative in 19 of 27 patients. Six of 13 initial nonreactors still had negative reactions on repeat testing, and four appeared to be anergic when retested one to four months later. Ascites was present in 67 percent (20) of the 30 patients, and laparotomy was used most frequently to establish the diagnosis. Diagnosis was particularly difficult in 13 alcoholics, in whom the disease was usually unsuspected, the findings in the ascitic fluid were uncharacteristic, and negative tuberculin reactions were frequent. Peritoneal tuberculosis was a contributory cause of death in five cases. Three of these patients, who were also alcoholics, went undiagnosed and untreated. Two patients died of unrelated causes. Twenty-three have done well, and 19 have completed chemotherapy.

Because of variability and nonspecificity in clinical presentation, tuberculous peritonitis often has been overlooked in the differential diagnosis of abdominal disease. Moreover, confirmation of the infection may prove difficult, especially if there is undue delay in obtaining appropriate histopathologic specimens and material for culture. These statements particularly apply to the alcoholic patient, in whom tuberculous peritonitis frequently occurs. Ascites in this setting is often erroneously assumed to be due to cirrhosis, and frequently tuberculosis is not considered in the differential diagnosis. The comprehensive review by Burack and Hollister pointed out that among 20 alcoholic patients with tuberculous peritonitis, the diagnosis was unsuspected antemortem in 11 patients.

The failure to establish an antemortem diagnosis and to institute appropriate treatment in an alcoholic patient seen by one of us prompted this retrospective study. Tuberculous peritonitis is reviewed, with particular reference to the alcoholic patient, in terms of clinical presentation, diagnostic evaluation, and response to treatment.

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Criteria for Selection of Patients

A review was conducted of the hospital and outpatient records of all patients diagnosed as having tuberculous peritonitis at the hospitals affiliated with the University of Washington and at the Seattle-King County Tuberculosis Clinic during the seven-year period from 1966 to 1973.

The diagnosis of peritoneal tuberculosis was established in 25 patients by a positive culture of Mycobacterium tuberculosis from the ascitic fluid or peritoneal tissue or by the demonstration of caseous or noncaseous peritoneal granulomas containing acid-fast bacilli, or both. Caseating granulomas alone, without demonstrable acid-fast bacilli in the microscopic sections of peritoneal tubercles, were recovered from three patients, all of whom showed a response to chemotherapy. Two patients, both of whom exhibited exudative ascites, were included on the basis of finding caseating granulomas containing acid-fast bacilli in specimens from a pleural biopsy and from a liver biopsy, respectively. These 30 patients comprise the subject of our review. The number of additional patients who may have had tuberculous peritonitis that was not diagnosed or was missed by the review is unknown.

Results

Demographic Data

Of the 30 patients, 16 were male and 14 were female patients. The mean age of the entire group, similar for both sexes, was 50 years (range, 12 to 81 years). Seventeen patients (57 percent) were nonwhite; of these, six were black, five were American Indian, two were Filipinos, two were Samoans, and two were Chinese. By comparison, 75 percent of all new patients with tuberculosis in Seattle-King County are white.
Nineteen patients had a significant underlying illness. Thirteen were chronic alcoholics, five of whom had confirmed Laennec’s cirrhosis. Renal failure, silicosis, myelofibrosis, congestive heart failure, mental retardation, and schizophrenia were the underlying diseases in the remaining six patients. Eight individuals were aware of recent or remote exposure to a person with active pulmonary tuberculosis.

Clinical Manifestations

The initial symptoms and signs in our 30 patients are shown in the following tabulation listing the numbers of patients (numbers within parentheses are percentages):

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>18 (60)</td>
</tr>
<tr>
<td>Abdominal swelling</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Fever and chills</td>
<td>15 (50)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>15 (50)</td>
</tr>
<tr>
<td>Loss of weight</td>
<td>14 (47)</td>
</tr>
<tr>
<td>Constipation or diarrhea</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Respiratory symptoms</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Night sweats</td>
<td>5 (17)</td>
</tr>
<tr>
<td>Malaise</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Elevation of temperature</td>
<td>27 (90)</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>23 (77)</td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>12 (40)</td>
</tr>
<tr>
<td>Chronic illness or wasting</td>
<td>10 (33)</td>
</tr>
<tr>
<td>Hepatic or splenic enlargement</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Abnormal auscultatory finding in chest</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

Abdominal pain and abdominal swelling, the most common complaints, were seen in 60 percent (18) and 53 percent (16) of the 30 patients, respectively. Constitutional symptoms of fever, chills, anorexia, and weight loss were cited by about half of the patients. The average duration of symptoms prior to admission of the 30 patients was slightly less than three months, with a range of two weeks to 13 months. Initial symptoms did not differ between the alcoholic and the nonalcoholic patients.

Temperatures were recorded in 29 patients. All exhibited fever (oral temperature above 37.2°C [99°F]) at some time during the course of their illness, but in two patients, this developed only following laparotomy. Fever was most often of low grade. Ten of the 30 patients were described as chronically ill or wasted in appearance, and seven of these ten were alcoholics. Twenty-three percent (seven) of the 30 patients had abnormal auscultatory findings of the chest, suggestive of consolidation or effusion. Abdominal distention was noted at the time of admission in 23 patients, and 20 were thought to have ascites. Among alcoholic patients the abdomen was often described as “drum-like” or tense. The abdomen was described as “doughy” in only one patient, and a palpable abdominal mass was noted in one other, a woman with an enlarged uterine salpinx. Six of the nine patients with hepatic or splenic enlargement (or both) were alcoholics. Abdominal tenderness was present in 12 patients. In nine, this was generalized, but in three others the pain was more pronounced in the right side of the abdomen or flank.

Thirteen of the 30 patients initially had an extraperitoneal focus of active infection with M tuberculosis which was proven bacteriologically (ten pulmonary or pleural, five pelvic, and one each of liver, rib, and the central nervous system). None of the patients had evidence of pericardial, bone marrow, or renal involvement with tuberculosis.

Laboratory Studies

Twenty-seven patients had tuberculin tests with intermediate-strength purified protein derivative of tuberculin (PPD) applied near the time of admission (Table 1). Negative reactions were recorded in 19 (70 percent), including four patients with a previously positive test with intermediate-strength PPD. Four of seven individuals then tested with second-strength PPD also failed to react. Of the 13 patients with initially negative reactions to intermediate-strength PPD who underwent retesting one week to 12 months later (mean, 11 weeks), seven subsequently reacted to intermediate-strength PPD. All seven had been receiving antituberculosis therapy for periods ranging from one week to five months (mean, nine weeks). Six individuals continued to exhibit a negative reaction to intermediate-strength PPD. Two of the six reacted to second-strength PPD; but four (including three alcoholics)

<table>
<thead>
<tr>
<th>Reagent and Reaction</th>
<th>Initial Test</th>
<th>Repeat Test**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermediate-strength PPD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not done</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Positive reaction</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Negative reaction</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>Second-strength PPD**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not done</td>
<td>12</td>
<td>2†</td>
</tr>
<tr>
<td>Positive reaction</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Negative reaction</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

*Table values are numbers of patients.
**Performed only in patients with negative reaction to intermediate-strength PPD.
†Although not retested with second-strength PPD, these two patients reacted to antigens of Candida, Trichophyton, and mumps.

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appeared to be anergic, failing to react to cutaneous testing antigens for mumps, Trichophyton, or Candida, as well as to tuberculin.

Absence of cutaneous reactivity to tuberculin early in the course of hospitalization was observed more frequently in the alcoholic patients (11/12), compared with the nonalcoholic (7/15), but this difference was not statistically significant (0.05 > P < 0.10, Yates' correction).

Samples of ascitic fluid were always yellow and either clear or cloudy in appearance. Although several traumatic taps produced an amber-colored fluid, no true bloody return was encountered. There was no significant difference in the total or differential white blood cell (WBC) counts between alcoholic and nonalcoholic patients (Table 2). Although mononuclear cells usually predominated, in four individuals (including three alcoholics), polymorphonuclear leukocytes were more than 50 percent of the differential count. The protein content of the ascitic fluid from alcoholic patients was significantly less (P < 0.01) than that of nonalcoholic subjects. Five of eight specimens of ascitic fluid, all from alcoholics, could be considered a transudate on the basis of a protein content below 3.0 gm/100 ml. In four, the protein level ranged from 0.8 to 2.4 gm/100 ml, while simultaneously determined serum levels of albumin were less than 3.0 gm/100 ml in each instance. Fifty percent of the specimens of ascitic fluid that were cultured grew M. tuberculosis. The amount of fluid submitted to the laboratory for culture rarely exceeded 200 ml.

Chest x-ray films were abnormal in 25 of 30 patients. A pulmonary parenchymal abnormality or pleural effusion (diagnostic standard III, A 1 or 2) was present in the chest x-ray films of all 25 patients. Of these 25 patients, ten had positive bacteriologic findings, as previously noted. The protein content of the pleural fluid was more than 4.0 gm/100 ml in four or five cases. Cell counts of the fluid ranged from 140 to 3,700 WBC/cu mm, and mononuclear cells accounted for more than 80 percent of the differential count in all five patients.

On examination with a barium enema, four of 15 patients had abnormal results, which led to surgical intervention and the subsequent diagnosis of tuberculous peritonitis. In three, this consisted of compression of the sigmoid colon or deviation secondary to a tuberculous uterine salpinx, and in one other patient the abnormality was a polyp in the middle portion of the sigmoid colon.

Routine laboratory studies, including the complete blood cell count and urinalysis, were not helpful in making the diagnosis. Westergren's determinations of sedimentation rates were consistently elevated, ranging from 21 to 138 mm/hr (mean, 58 mm/hr). Deranged values on tests of hepatic function (levels of alkaline phosphatase, bilirubin, and serum glutamic-oxaloacetic transaminase and prothrombin time) were limited to the 13 alcoholic patients, 11 of whom showed abnormalities in three or more of these tests.

Confirmation of Diagnosis

Tuberculous peritonitis was suspected in only four patients at the time of admission to the hospital. An average of 31 days (range, 2 to 150 days) elapsed before a presumptive diagnosis was established and antituberculosis therapy was begun in 27 patients. Suspicion of the diagnosis was frequently strengthened by findings from chest x-ray films. Visualization of the peritoneal cavity was the most common method employed to confirm the diagnosis, as shown by the following tabulation listing the methods of confirming the diagnosis and the number of patients (numbers within parentheses are percentages):

Peritoneal tissue diagnosis 23 (77)
Laparotomy 16
Peritoneoscopy 4
Autopsy 2
Needle biopsy 1
Liver biopsy 1 (3)

Table 2—Examination of Ascitic Fluid in Alcoholic and Nonalcoholic Patients with Tuberculous Peritonitis*

<table>
<thead>
<tr>
<th></th>
<th>Alcoholic</th>
<th>Nonalcoholic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBCs/cu mm</strong></td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td><strong>Polymorphonuclear leukocytes, percent</strong></td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td><strong>Protein level, gm/100 ml</strong></td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td><strong>Smear for acid-fast bacilli</strong></td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td><strong>Culture of fluid for acid-fast bacilli</strong></td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>

*Results are means; numbers within parentheses are ranges.
**P < 0.01 by Student's t-test.
Grossly, tubercles or nodular implants (or both) were universally present, covering the peritoneum, mesentery, omentum, or the serosa of the bowel. A diffuse inflammatory process with multiple adhesions involving the omentum, mesentery, or bowel was rarely seen. In two patients, tuberculous peritoneal implants were discovered only at postmortem examination. In another patient the diagnosis was established by peritoneal biopsy via Cope’s needle; and in two other individuals with exudative ascites, the diagnosis was made by a pleural biopsy and by a liver biopsy, respectively. Histopathologic studies confirmed the diagnosis in 25 individuals. This included three patients who responded to chemotherapy and who had typical findings of tuberculous peritonitis at laparotomy, but whose histologic sections revealed caseating granuloma without acid-fast bacilli and whose cultures were negative or not done. Culture of ascitic fluid alone established the diagnosis in the remaining five patients, four of whom were alcoholics. Two of the latter died without receiving antituberculosis therapy.

**Treatment and Follow-Up**

Twenty-seven patients received antituberculosis therapy. The maximum duration of follow-up among treated patients was 6.8 years, and the minimum was one month (mean, 34 months). Twenty-three of 24 patients discharged from the hospital have done well. One patient died of bacterial pneumonia 30 months after completing chemotherapy. Nineteen patients completed a full course of chemotherapy. Of these, 15 received triple-drug regimens (isoniazid, streptomycin, and p-amino salicylic acid, ethambutol, or rifampin), and four were treated with two antituberculosis drugs (isoniazid and p-amino salicylic acid or ethambutol). Tuberculous peritonitis was a contributory cause of death in five patients (17 percent). These included two individuals (one an alcoholic) who died while receiving chemotherapy and three patients (all alcoholics) who died while undiagnosed and untreated. They had been hospitalized a total of 28, 44, and 55 days, respectively, prior to their deaths. Eleven patients were given corticosteroids in an uncontrolled fashion at the discretion of the physician in charge. No conclusions regarding effectiveness can be made because of inadequate controls and duration of follow-up.

**Discussion**

Since pleuropulmonary involvement was a common finding in the patients with tuberculous peritonitis reported from Iran, Borhanmanesh and associates suggested that peritoneal tuberculosis likely results from hematogenous dissemination from a pulmonary focus. Conversely, radiographic abnormalities have been an uncommon finding in some series, which had led others to accept the hypothesis that tuberculous peritonitis is due to the activation of a long latent tuberculous focus in the peritoneum. Both concepts appear to be valid. The pulmonary abnormalities in our patients suggest the possibility of hematogenous spread from re-crudescent pulmonary lesions, or simultaneous reactivation may have occurred at several sites. The nearly equal number of female and male patients who had tuberculous peritonitis in Seattle during the period of time studied is in contrast to the male: female ratio of 2:1 expected in pulmonary tuberculosis. A similar sex incidence of patients with tuberculous peritonitis has been reported by others.

It seems likely that in some female patients, following hematogenous dissemination of tuberculosis from the chest to the pelvis, contiguous spread of infection from the pelvic organs to the peritoneum may result.

Five of our 14 female patients did have concomitant genital tuberculosis. Other female patients, like male patients, develop peritoneal tuberculosis from hematogenous dissemination of organisms from a pulmonary focus or from a latent peritoneal focus. The prevalence of nonwhite patients among those who develop peritoneal tuberculosis has been noted in several other reports and may, in part, reflect the lower socioeconomic status of these ethnic groups.

Other than overwhelming disease, the reason for apparent nonreactivity to tuberculin in some patients was not obvious. This phenomenon has been noted in previous studies from this country, while patients reported from India and Iran and also from Chicago have had positive reactions to tuberculin. Obviously, when interpreting cutaneous tuberculosis tests as recorded in charts, one has to consider several factors which might account for negative results. The available records were not always adequate in providing the type of information necessary to assess the validity of testing products and methods. Improper application, the use of cutaneous testing with tuberculin that has not been stabilized with polysorbate (Tween) (employed in nine of 19 nonreactors), inaccurate interpretation of results, immunosuppressive drugs, some infections and vaccines, and, finally, true anergy have been noted in persons with active tuberculosis and negative tuberculin skin tests. Recent studies indicate that lymphocytic function is at least partially intact in some anergic and relatively anergic (negative reaction to intermediate-strength PPD but posi-
tive reaction to second-strength PPD) patients with pulmonary and disseminated tuberculosis; however, in others, lymphocyte function may be profoundly, although temporarily, depressed. In individuals with peritoneal disease who fail to react to intermediate-strength PPD, a test for lymphocyte transformation might prove a beneficial diagnostic aid.

Rapid diagnosis and treatment are essential in the management of patients with tuberculous peritonitis. In this study, laparotomy was the most common procedure used to obtain tissue for histologic examination. Some centers have recommended that in patients with ascites, biopsy with a Cope needle or peritoneoscopic examination should be considered before laparotomy. False-negative results may occur with blind biopsy, but complications from both techniques in experienced hands are uncommon; however, fatal hemorrhage in an alcoholic patient has been reported. Careful examination of histopathologic sections is required. In three of our patients, the diagnosis was established only when new sections of the original blocks of tissue were cut. In one, multiple noncaseating granulomas were found, several of which contained acid-fast bacilli, a finding previously reported. In addition to the previously mentioned diagnostic techniques, endometrial curettage might be considered in female patients when pelvic disease is concomitantly suspected. Although percutaneous liver biopsy provided the diagnosis in one patient, this technique has not been considered a rewarding procedure. Likewise, biopsy and culture of the bone marrow were not helpful. Examination of the ascitic fluid in most cases proved useful in suggesting or confirming the suspicion of tuberculous infection; however, the fluid was not always an exudate. The low protein content of the ascitic fluid in alcoholic cirrhotic patients with tuberculous peritonitis has been previously noted. In the alcoholic, low levels of protein in the ascitic fluid associated with a depressed serum level of albumin does not rule out the diagnosis of tuberculosis. In order to increase the possibility of growing M. tuberculosis from the ascitic fluid, it has been suggested that at least 1 L of fluid be submitted to the laboratory for culture. Although this maneuver was not carried out in our patients, M. tuberculosis was grown from 50 percent of the patients in whom ascitic fluid was cultured. Studies with radiographic dyes were generally unrewarding, except in female patients with concomitant pelvic and peritoneal infection.

More than 90 percent of the patients in this and other recent reports have had documented fever which did not remit without treatment; however, the fever present in all of the alcoholic patients was not a particularly useful diagnostic clue, since it is commonly observed in hospitalized patients with alcoholic hepatic disease alone. Burack and Hollister have suggested that the presence of fever, abdominal pain and tenderness other than in the right upper quadrant of an alcoholic patient with cirrhosis, and of ascites should raise the suspicion of coexisting intra-abdominal disease, including tuberculosis. Three of our alcoholic patients who had these findings died without correct diagnosis or treatment. Clearly, the single most important aid in diagnosing peritoneal tuberculosis in the alcoholic patient remains a high index of suspicion.

References


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III International Symposium on Infectious Diseases

The III International Symposium, in honor of Dr. Saul Krugman, will be held in Guadalajara, Mexico, October 31-November 2, sponsored by the Universidad Autonoma de Guadalajara and the Asociacion Mexicana de Infectologia. For information, contact: Educacion Continuada UAG, Montevideo 3331, Acueducto Providencia, Guadalajara, Jalisco, Mexico.

Annual Scientific Meeting, American Society of Cytology

The 25th Annual Scientific Meeting of the American Society of Cytology will be held at the Sheraton Centre, Toronto, Ontario, November 1-5. For information, contact Warren R. Lang, M.D., Health Sciences Center, 130 South Ninth Street, Philadelphia 19107.

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