Role of laparoscopic surgery in the etiologic diagnosis of exsudative ascites: a prospective study of 90 cases

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SUMMARY

Purpose — Peritoneal tuberculosis and carcinomatosis are the most frequent etiologies of exsudative ascites and require rapid diagnosis and treatment.

The purpose of this study has been to evaluate the predictive value of clinical and complementary data for the etiologic diagnosis of exsudative ascites and to assess the results of laparoscopic surgery.

Material and methods — We report a prospective long-term study conducted over 10 years, having included all cases of exsudative ascites of unidentified etiology. We excluded patients with a history of anterior laparotomy and patients having a contraindication for laparoscopic surgery. Clinical signs, results of the cytochemical and bacteriological exam of the ascitic fluid and findings from radiological exams and endoscopic investigations were noted. Open laparoscopic exploration noted the macroscopic aspect and many peritoneal biopsies were obtained as well as a liver biopsy when possible. Statistical analysis was performed with SPSS10.0 software. The degree of statistical significance was set for P < 0.05.

Results — We included 90 cases of isolated exsudative ascites. There were 59 cases of tuberculosis and 31 of carcinomatosis. Mean patient age was 47 years with a sex ratio of 0.5. Bowel transit disorders were significantly in favor of a carcinomatosis (P = 0.04) but in both instances, the positive predictive value (PPV) of these two signs was weak, respectively 29% and 43%. Relative to chemical and cytologic study of ascitic fluid, hemorrhagic fluid, low white cell count, low lymphocyte differential and presence of atypical cells were significantly linked with the carcinomatosis (P = 0.01) but with a PPV < 85%. Radiological exams were not very contributive for the etiologic diagnosis. The laparoscopic peritoneal aspect was typical of tuberculosis in 90% of proved cases and in 29% of carcinomatosis cases, underlying the importance of peritoneal biopsies for histological study. Hepatic tuberculosis was associated with peritoneal localisation in 48% of cases. We had no surgical mortality and the morbidity was about 1%

Conclusion — Etiological diagnosis of exsudative ascites remains difficult to establish. Peritoneal biopsies under videolaparoscopy are currently the “gold standard” for diagnosis.

RÉSUMÉ

Place de la chirurgie laparoscopique dans le diagnostic étiologique des ascites exsudatives : à propos d’une étude prospective de 90 cas

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Les étiologies des ascites exsudatives sont dominées par la tuberculose péritonéale et la carcinose qui représentent des urgences thérapeutiques nécessitant une certitude diagnostique.

But — Étudier la valeur prédictive, respectivement des éléments cliniques et paracliniques, dans le diagnostic étiologique d’une ascite exsudative et évaluer les résultats de la cœlioscopie diagnostique.

Matériel et méthodes — Nous rapportons une étude prospective s’étalant sur 10 ans, ayant inclus toutes les ascites exsudatives isolées. Nous avons exclu les malades porteurs d’une cicatrice de laparotomie et les malades inopérables ou ayant une contre-indication à la chirurgie laparoscopique. Nous avons relevé les signes cliniques, les données de l’examen cytochimique et bactériologique du liquide d’ascite et les données des examens radiologiques et endoscopiques. L’exploration laparoscopique relevait l’aspect macroscopique ; des biopsies péritonéales étaient alors réalisées systématiquement ainsi qu’une biopsie hépatique dans la mesure du possible. L’étude statistique a utilisé le logiciel SPSS10.0. Le degré de significativité statistique a été fixé pour P < 0,05.

Résultats — Nous avons colligé 90 cas d’ascite exsudative isolée. Il s’agissait de 59 tuberculoses et 31 carcinoses. L’âge moyen des malades était de 47 ans avec un sex-ratio de 0,5. Sur le plan clinique, les troubles du transit étaient significativement en faveur d’une carcinose (P = 0,04), tandis que la fièvre et les sueurs nocturnes étaient en faveur de la tuberculose (P = 0,04), mais à chaque fois la valeur prédictive positive (VPP) de ces signes était faible respectivement de 29 % et 43 %. Concernant l’étude du liquide d’ascite, le caractère hémorragique, la faible cellularity, le faible taux de lymphocyte et la présence de cellules atypiques étaient significativement corrélés à la carcinose (P = 0,01) mais avec une VPP < 85 %. Les examens radiologiques étaient peu contributifs au diagnostic étiologique. L’aspect laparoscopique était typique de tuberculose dans 90 % des cas de tuberculose avérés et était retrouvé dans 29 % des cas de carcinose dénotant de l’importance des biopsies péritonéales. Les biopsies hépatiques avaient objectivé une hépatite granulomateuse associée à la tuberculose péritonéale dans 48 % des cas. La mortalité opératoire était nulle et la morbidité de 1 %.

Conclusion — Le diagnostic étiologique des ascites exsudatives reste difficile à établir. Les biopsies péritonéales sous cœlioscopie représentent à l’heure actuelle le « gold standard » pour le diagnostic.
Introduction

Peritoneal tuberculosis and carcinomatosis are the main causes of lymphocytic exsudative ascites, which requires rapid diagnosis to institute appropriate therapeutic management. The etiological diagnosis is a particularly difficult task due to the lack of specific clinical, radiographic, or biological signs and the fact that none of the proposed complementary tests have sufficient positive predictive value (PPV) for definitive diagnosis. Consequently, a histological sample from a peritoneal biopsy, ideally obtained laparoscopically, is required to establish the final etiologic diagnosis.

The purpose of this work was the study the predictive value of clinical data and complementary findings for the etiologic diagnosis of isolated exsudative ascites and to evaluate the results of diagnostic laparoscopy.

Material and methods

We report a prospective study conducted from 1996 through 2006 which included all cases of isolated exsudative ascites with an unidentified etiology. The etiologic work-up included a search for tuberculosis with a chest x-ray (lateral and anteroposterior views), search for Koch’s bacillus, direct examination of sputum, urine, gastric aspiration products, ascitic fluid, and a tuberculin interdermal reaction. A gynecology examination together with pelvic ultrasound was performed in all women with a search for an ovarian tumor. In the event of suspected peritoneal carcinomatosis, the work-up included an abdominal computed tomography (CT) scan and/or an exploratory laparoscopy in patients aged over 60 years and/or presenting signs of gastrointestinal involvement. Patients who had prior laparotomy and patients not eligible for surgery or with a contraindication for laparoscopic surgery were excluded from the study. We collected clinical data for all patients. An abdominal ultrasound was performed in all patients. A sample of ascitic fluid was obtained by puncture (with or without ultrasound guidance) for cytochemistry and bacteriological exams in all cases. A diagnostic laparoscopy was performed systematically under general anesthesia using the French position. The first 10-mm trocar was introduced via the umbilicus. Two other 5-mm trocars were required for biopsies taken from various positions depending on accessibility of the recessus of the peritoneal cavity. The gross aspect of the cavity was noted first. The aspect was considered "typical" of tuberculosis (TB) in the presence of millimetric white granulations of equivalent size scattered over the visceral and parietal peritoneum, associated with fibrin deposits, peritoneal congestion and agglutination of the intestinal loops. The aspect was noted "atypical" in the presence of irregular umbilicated retractile peritoneal nodules of variable size preferentially located on the diaphragm or in the pelvis with a non-inflammatory peritoneum. Several peritoneal biopsies were taken, particularly including granulations. A liver biopsy was also performed when possible (in many patients the right hypochondrium was inaccessible due to adherences). For the statistical analysis, data were processed with SPSS10.0 software. Fisher’s test was used to compare means and Student’s t test for percentages. The level of significance was set at 0.05.

Results

We collected 90 cases of isolated exsudative ascites explored laparoscopically. There were 59 cases with a final diagnosis of peritoneal TB and 31 of histologically-proven carcinomatosis (peritoneal biopsy specimens). Mean patient age was 47±15 years; the sex ratio was 0.5. There was no difference by age or gender between patients with TB and carcinomatosis (P= 0.6 and 0.4 respectively). Functional impairment, abdominal pain, poor general status (defined by asthenia, anorexia and weight loss greater than 5% of usual weight), fever, and abdominal distension were not found to be contributive to the etiologic diagnosis (Table I). Bowel transit disorders were found in 29% of patients with carcinomatosis and in 12% of those with TB. The difference was significant (P=0.04). Signs of tuberculous impregnation (nighttime sweating and fever) were significantly more frequent in patients with a diagnosis of TB (73%) than those with carcinomatosis (51%) (P=0.04). However, the positive predictive values of these two signs were low, respectively 29% and 43%. Examination of the ascitic fluid (Table II) revealed that a hemorrhagic fluid with low white cell counts (< 400 WC/ml), a low lymphocyte differential (< 60%), and the presence of atypical cells was statistically significantly correlated with carcinomatosis (P=0.01). The positive predictive values of these elements for the diagnosis of carcinomatosis were, respectively: 90%, 72%, 68% and 82%. On the contrary, a yellowish fluid with a high white cell count > 400 WC/ml, devoid of atypical cells and with a high lymphocyte differential was in favor of TB, with a statistically significant difference for each element (P=0.01) and positive predictive values of, respectively: 72%, 78%, 81% and 78%. Koch’s bacillus was never identified at the direct examination of ascitic fluid.

The abdominal ultrasound was not contributive to the etiologic diagnosis since none of the following elements were found to be correlated with either diagnosis: visualization of nodules (10% in TB vs 19% in carcinomatosis, P=0.6), partitioned ascites (25% vs 16%, P=0.3), abundance of the ascitic fluid (P=0.3). The pelvic ultrasound was normal in all patients. The chest x-ray, per}

Table I – Functional signs observed in patients with peritoneal tuberculosis and carcinomatosis (P < 0.05 considered significant).

<table>
<thead>
<tr>
<th>Sign</th>
<th>Tuberculosis</th>
<th>Carcinomatosis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>49%</td>
<td>48%</td>
<td>0.94</td>
</tr>
<tr>
<td>Fever</td>
<td>47%</td>
<td>29%</td>
<td>0.09</td>
</tr>
<tr>
<td>Poor general status</td>
<td>66%</td>
<td>77%</td>
<td>0.26</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>73%</td>
<td>84%</td>
<td>0.2</td>
</tr>
<tr>
<td>Transit disorders</td>
<td>12%</td>
<td>29%</td>
<td>0.04</td>
</tr>
<tr>
<td>Fever and nighttime sweating</td>
<td>73%</td>
<td>51%</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table II – Characteristic features of ascitic fluid in peritoneal tuberculosis and carcinomatosis (P < 0.05 considered significant).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Tuberculosis</th>
<th>Carcinomatosis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspect</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yellowish</td>
<td>98%</td>
<td>71%</td>
<td>0.01</td>
</tr>
<tr>
<td>hemorrhagic</td>
<td>10%</td>
<td>29%</td>
<td>0.01</td>
</tr>
<tr>
<td>Cell count (WC/mm3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;400 WC/mm3</td>
<td>10%</td>
<td>51%</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;400 WC/mm3</td>
<td>90%</td>
<td>49%</td>
<td>0.01</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;60%</td>
<td>96%</td>
<td>48%</td>
<td>0.01</td>
</tr>
<tr>
<td>&lt;60%</td>
<td>8.5%</td>
<td>35%</td>
<td>0.01</td>
</tr>
<tr>
<td>Atypical cells</td>
<td>6%</td>
<td>58%</td>
<td>0.01</td>
</tr>
</tbody>
</table>
formed systematically, visualized fluid in the cul-de-sac in five patients. The tuberculosis reaction was positive in 22% of patients with peritoneal TB with a low PPV (48%). Search for Koch’s bacillus in sputum samples was positive in only six patients (10% of patients with peritoneal TB). Upper gastrointestinal endoscopy, performed in 48 patients, was normal in all. A colonoscopy was performed in eleven patients with transit disorders and was normal in all. A CT scan was obtained in eleven patients whose abdominal ultrasonic visualization suggested intestinal loops and confirmed the presence of agglutinated loops with no identifiable tumor.

The gross aspect of the abdominal cavity at laparoscopy was typical of TB in 90% of patients with confirmed TB and in 29% of those with carcinomatosis (P=0.002). The PPV of this aspect in favor of TB was 85%. The PPV of the atypical aspect in favor of carcinomatosis was 78%. Among the 59 patients with peritoneal TB, 33 had a liver biopsy.

Among the 90 laparoscopic explorations, one conversion was necessary (1.1%) because of a fibro-adhesive form of tuberculosis hindering access to the peritoneal cavity. There were no operative deaths. There was one minor postoperative complication due to discharge of the ascitic fluid via the umbilical portal which resolved with local care.

Pathology examination of the biopsy specimens confirmed the diagnosis of peritoneal tuberculosis in 58 patients (98%) and carcinomatosis in 31 (100%). In one patient, the biopsies were negative and the diagnosis was established on the basis of the highly suggestive clinical presentation and the typical per laparoscopic aspect. In addition, culture of the ascitic fluid was positive two months later. In the patients with peritoneal tuberculosis, concomitant hepatic involvement (granulomatous hepatitis) was noted in 48% of patients. A four-drug regimen was instituted at histological confirmation of TB. The results of the ascitic fluid culture were available on average 55 days later and were positive in only 32% of patients. Search for a primary tumor was initiated in patients with carcinomatosis and identified an ovarian tumor in 20 patients, a pancreatic localization in four and a peritoneal localization in seven. These patients were 21 women (63%) and 12 men (37%). Among the women with carcinomatosis, 95% had a primary ovarian tumor.

**Discussion**

In Tunisia, tuberculosis and carcinomatosis are the leading etiologies of exudative ascites. Tuberculosis is an endemic disease in Tunisia with an estimated prevalence of 20.1 cases/100000 inhabitants according to the Tunisian healthcare database published in 2006. Incidence has risen in western countries during the last decade due to population migrations and immunodepression related to alcoholic cirrhosis or HIV infection [1]. Peritoneal TB raises significant diagnostic difficulties due to the poor predictive value of complementary tests and the low rate of positive bacteriological samples, with about 3% of positive results on direct examinations and a delay of more than two months for culture results which are positive in less than 35% of cases [2]. The diagnosis of carcinomatosis is equally difficult to establish in patients with a primary ovarian tumor where the differential diagnosis with peritoneal TB is a difficult task. The physical examination is poorly contributive and imaging, particularly the CT scan, cannot visualize partitioned ascites with fascial thickening, leading to the risk of misdiagnosis of tuberculosis [3]. It is also known that the tumor marker CA125 can be elevated in patients with peritoneal TB. This tumor marker has even been used by some authors to replace peritoneal biopsy since the risk of a typical aspect of TB being a false positive can reach up to 29%, as observed in this series. Thus the histological examination of peritoneal biopsies is the only way to establish a safe definitive diagnosis. Certain complementary explorations available in Tunisia have been reported for the diagnostic approach to peritoneal tuberculosis. Lactate dehydrogenase (LDH) assay in the ascitic fluid has a sensitivity of 90% but poor sensitivity (14%) [10]. The serum ascites albumin gradient (SAAG) can be suggestive of TB when it is less than 11g/L with a sensitivity of 100% but with low specificity [7]. Adenosine deaminase assay has good sensitivity and specificity for the diagnosis of TB with a PPV of 96% for a value greater than 30IU [11]. Polymerase chain reaction (PCR) and ligase chain reaction (LCR) are costly methods with still uncertain results [1, 12, 13].

Chow et al [14] have proposed optimizing bacteriological tests by using a radiometric detection system (BACTEC) which reduces the time required for bacteriological results to 15 days. Ultracentrifugation of one liter of ascitic fluid instead of 50 ml can also improve the rate of positive results up to 83% [2].

All of these often costly methods cannot replace pathological examination of laparoscopic peritoneal biopsies where the rate was close to 98% in our series. This rate is much higher than reported in series with results obtained with peritoneoscopy with local anesthesia [6-8, 15]. The fact that results are better with laparoscopy can be explained, at least in part, by the better visual exposure and also by the quality of the biopsy material obtained with laparoscopy. Laparoscopy is thus the method of choice with nearly zero mortality and very low morbidity, but is nevertheless a surgical operation with the real inherent risks of anesthesia and surgery. The question is thus whether certain diagnosis can be obtained with non-surgical histology biopsy specimens. With this problem in mind, we obtained per laparoscopic hepatic biopsies which demonstrated a rate of associated granulomatous hepatitis of about 48%. It remains to be proven with a randomized prospective study that surgical liver biopsy provides the same diagnostic yield as percutaneous biopsy, in which case laparoscopy might be avoided in 48% of patients with probable tuberculous ascites by simple percutaneous liver biopsy. Another alternative to surgery has been proposed by Vardareli et al who suggest that percutaneous biopsies of the peritoneum under radiographic guidance can provide very promising results [16].

**Conclusion**

The etiologic diagnosis of exudative ascites remains a difficult challenge despite the availability of a wide range of often complex and costly complementary exams. At the present time, the gold standard is to obtain laparoscopic peritoneal biopsies to establish the histological diagnosis. Percutaneous biopsy of the liver or the peritoneum is in the research phase and may in the near future provide a way of avoiding laparoscopic surgery.

**REFERENCES**


