

# Tuberculous peritonitis in an Internal Medicine ward

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### Abstract

The authors reviewed the four tuberculous peritonitis cases admitted to the District Hospital of Santo Tirso medical ward from 1994 to 1995.

They studied patients distribution by age and gender, their previous contacts with tuberculosis, the coexistent diseases, the most relevant clinical data, additional tests, the treatment and

global results.

They discussed the present relevance of extrapulmonary tuberculosis, the reasons for their high prevalence and the procedures to improve diagnosis.

Key words: tuberculous peritonitis, extrapulmonary tuberculosis, deaminase-adenosine.

### Introduction

Tuberculosis became again a severe Public Health problem. In Portugal, where the infection has always been prevalent, we have a rate of 55.6 new cases per year per one hundred thousand inhabitants.<sup>1</sup> In Santo Tirso County (according to data supplied by the local STDR (Tuberculosis and Respiratory Disease Service), 85 new patients were registered by one hundred thousand inhabitants, in the years covered by the study.

Alongside the increase in the total number of cases of tuberculosis, we have also seen an increasing prevalence of extrapulmonary forms.<sup>2</sup> The peritoneal location of the disease, although rare in the developed countries, is relatively common elsewhere: 2% to 4%.<sup>3</sup> This location is always secondary, resulting from the hematogenous dissemination of a primary focus, generally pulmonary, with secondary implants in the peritoneal cavity, where they remain dormant and can reactivate years after the first infection. Also, in rare cases, they may be the result of dissemination from adjacent foci, in the intestines or genitals.<sup>4</sup> However,

in more than 80% of cases, there are no other manifestations of the disease, particularly pulmonary.<sup>5,6</sup>

Tuberculous peritonitis, known since Antiquity, was described for the first time in the last century. Later, in 1932, Crohn identified the regional enteritis of granulomatous bowel diseases, which at that time were globally considered to be forms of tuberculosis. In the 1950s and 1970s, major series were published, like those of Burack and Singh, or more recently, those of A. Salvador and Sherman.<sup>5,6,7,8</sup> These authors describe the four forms of presentation of the disease: ascitic, fibro-adhesive, nodular, and caseating. The first form, and the most common one, occurs in young people without other morbid manifestations, making diagnosis difficult due to the gradual increase in abdominal volume. It can also complicate chronic debilitating diseases, generally in the elderly.

As the disease progresses, the fibrin content in the fluid increases, forming adhesions and septae that can lead to intestinal obstruction. This fibro-adhesive stage is sometimes only discovered during laparotomy. The nodular form is characterized by the confluence of granulomas forming pseudo-tumoral masses that can become caseified, leading to the last, and rarest form of presentation: caseating. The pockets of caseum can communicate between themselves or open fistulae to nearby organs.

Clinically, the most frequent symptoms are fever, distension and abdominal pain, anorexia, slight weight loss, and in some cases, intestinal symptoms. The condition can continue for several weeks, and can be suddenly aggravated, simulating an acute abdominal pain, leading to laparotomy.<sup>9</sup>

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Received for publication on 17th October 1996

Of the subsidiary exams, the main one is the ascetic fluid test. An exudate is almost always revealed, with pleocytosis, at the cost of an elevation in the lymphocyte count.<sup>7</sup> The adenosine deaminase enzyme (A.D.A.) is generally high, presenting specificity and sensitivity over 97% when the titer is 40 U/L or above.<sup>10</sup> The productivity of the ascitic fluid culture for *Mycobacterium tuberculosis* (M. T.) is low, and peritoneal biopsy is the most adequate means of diagnosis.<sup>11</sup> This should be carried out during the laparoscopic exam which, as it enables visualization of the serosa, provides suggestive data in 85% to 90% of cases, on identification of the classic granulomas and inflammatory thickening of the peritoneum. Blind percutaneous biopsy with a Cope needle, the usual procedure before the advent of laparoscopy, although it has similar rate of complications, is less profitable and has been practically abandoned nowadays.<sup>6</sup>

### Material and methods

The authors carried out a retrospective, descriptive, non-observational study of cases of tuberculous peritonitis admitted to the Internal Medicine Service of Santo Tirso District Hospital in the years 1994 and 1995. The processes of four patients with this diagnosis were obtained from the hospital records, and a protocol was designed for the data collection.

The diagnostic categories of the disease were defined as follows: 1) positive ascetic fluid culture for M. T.; 2) presence of caseating granulomas or MT in the peritoneal biopsy tissue or positive culture up to six weeks; 3) peritoneal exudate (proteins > 2.5 g./dL) with lymphocytosis > 60% e A.D.A. > 40 U/L, which responded unequivocally to anti-bacillary treatment.

### Clinical cases

During the period covered by the study, four patients were admitted, all female, Caucasian, born and residing in the Santo Tirso County, aged 25, 32, 54 and 81 years, henceforth referred to as cases 1 to 4, respectively. None had a previous history of tuberculosis.

#### Case 1

Patient with a history of fever and abdominal distension, with three months of evolution. Two days before hospitalization, the patient suffered nausea, constipation and abdominal pain, followed by vomiting of food. She had fever, dehydration, and tachycardia, with violent pain on palpation of the abdomen. Nor-

mochromic normocytic anaemia with 10.6 g./dL of hemoglobin, neutrophilic leukocytosis, and ESR 70 mm in the 1<sup>st</sup> hour. Mantoux at 2 units of 25 mm. The peritoneal lavage carried out by the surgeon in the Emergency Service revealed sero-haematic fluid, and laparotomy was performed. The peritoneum was thickened and irregular, with numerous granulomas and mesenteric ganglions, and integrity of the ileum-caecal and adnexal region. The histological exam revealed caseating granulomas and reactive adenitis.

#### Case 2

Patient whose spouse has been undergoing treatment for tuberculosis for 5 months. One month before admission, she suffered onset of fever, general symptoms and abdominal distension. She came to the hospital with suspected pregnancy, increased abdominal volume and secondary amenorrhoea, and ascites was also detected. The gynecological exam was normal. The hemogram was normal. ESR 45 mm in the 1<sup>st</sup> hour. Mantoux at 2 units of 15 mm. The ascetic fluid test revealed an exudate, rich in lymphocytes, with very high A.D.A. and C.A - 125, without neoplastic cells (Table 1). C.A.T. scan of the pelvis ruled out genital neof ormation. Having ruled out other diagnostic hypotheses, namely, neoplasia, the epidemiological context associated with this clinical condition led to the start of specific therapy.

#### Case 3

Patient with alcohol-induced cirrhosis, with previous hospitalizations due to ascites, jaundice, alterations in state of consciousness and hemorrhagic manifestations. She was readmitted due to fever, and an increase in ascites and jaundice, with five weeks of evolution. Macrocytic anaemia of 8.9 g./dL hemoglobin, ESR 24 mm in the 1<sup>st</sup> hour, Mantoux at 2 and 10 negative units. Other causes of fever were excluded, with microbiological and imaging exams. The ascitic fluid proved to be a transudate, rich in lymphocytes, sterile, without neoplastic cells, and with high, persistent A.D.A.. The impossibility of performing laparoscopy in sufficient time in the units that habitually support us, and the deterioration of the clinical situation, led to a percutaneous biopsy of the peritoneum, which enabled the diagnosis (Table 1).

#### Case 4

Patient with long-lasting inoperable valvular cardio-

TABLE I

|                               | Case 1               | Case 2        | Case 3               | Case 4                          |
|-------------------------------|----------------------|---------------|----------------------|---------------------------------|
| Prot.(g/dL) (liq. / serum)    | 5.3 / 5.5            | 6.9 / 7.5     | 2.2 / 6.5            | 4.2 / 6.7                       |
| LDH ( U/L ) (liq. / serum)    | 1062 / 380           | 433 / 349     | 97 / 141             | 946 / 285                       |
| Glucose mg / dL               | 88                   | 84            | 88                   | 98                              |
| Cell count / % of lymphocytes | 2300 / 47%           | 5900 / 92%    | 660 / 73%            | 700 / 80%                       |
| A.D.A. (U /L)                 | 140                  | 100           | 86                   | 12                              |
| Z.N./Lowenstein               | neg. neg.            | neg./ neg.    | neg. / posit.        | neg. neg.                       |
| Histological exam             | Caseating granulomas | Not performed | Caseating granulomas | Lymphocyte infiltrate ZN posit. |

myopathy, with cardiac insufficiency (C.I.) class 4 on the NYHA scale, fibrillate, almost always without anasarca, with various hospitalizations, during which collections of pleural and pericardial fluid were taken. No aetiology other than cardiac pathology was ever attributed to the patient. One month prior to admission, ascites and fever were detected for the first time, as well as all signs of decomposition of C.I. She presented normochromic, normocytic anaemia of 10.6 g./dL hemoglobin, ESR of 76 mm in the 1<sup>st</sup> hour and for the first time, a Mantoux at 2 units of 20 mm. Ultrasound of the abdomen revealed only signs of portal hypertension and ectasia of the suprahepatic veins and cava inferior, without pathological alterations of the pelvis. Examination of the ascetic fluid revealed an exudate with pleocytosis at the cost of lymphocytes (Table 1), which led us to propose a hypothesis of tuberculosis, performing percutaneous biopsy of the peritoneum which enabled the diagnosis.

In all the patients, chest x-ray ruled out active tuberculosis lesions. The microbiology of the expectoration (in at least 3 samples) of the urine was negative on direct and culture examination. The gynecological exam, ultrasound and pelvic CAT were also normal. No intestinal studies were performed, as the only patient who reported symptoms was laparatomized. The serology for HIV 1 and 2 was negative in all the patients.

Treatment with four drugs was initiated in the hospital: isoniazid, rifampicin, pyrazinamide and ethambutol or streptomycin. Prednisolone was associated (0.5 mg./ kg. of weight) in cases 1 and 2. All the patients were then referred to the STDR (Tuberculosis and Respiratory Disease Service), where they completed the 9 to 12 months treatment. The

patient with C.I. died at 4 months of treatment, due to circulatory failure.

### Discussion

Unlike other forms of presentation of tuberculosis, the increased prevalence of which has been related to HIV infection, peritoneal tuberculosis has maintained a relatively stable prevalence, with only a slight increase, related to the proportional increase in all the extrapulmonary forms observed. In Santo Tirso, the worsening of socio-economic conditions, associated with the widespread endemic of the disease, may explain the cases found. Although the literature reports a higher incidence of females, related to possible genital foci, this could not be confirmed in our patients: the gynecological examination, pelvic ultrasound and, in case 2, CAT scan, and the cytological and microbiological study of the vaginal exudate were normal. Also, the ruling out of other sites of the disease (pulmonary and renal) with radiological and microbiological exams was negative, which is in accordance with the 80% of exclusive peritoneal sites described in the literature. The differential diagnosis depends on the symptoms reported by the patient. Thus, in case 1, initially approached by surgery, given the suspicion of acute abdominal pain, the differential diagnosis was made with appendicitis, intestinal occlusion by Crohn's disease, adnexal processes, and ectopic pregnancy. The latter two were ruled out by the gynecological exam and ultrasound, and laparotomy was therefore carried out. The macroscopic appearance of the serosa and the absence of intestinal lesions suggested the diagnosis, which was confirmed by findings of the ascites fluid tests, and by the histological exam. In case 2, gynecological neoplasias were the main concern,

given that the problems detected were amenorrhoea, ascites and high C.A. - 125. However, the investigation carried out for this purpose was negative. The characteristics of the ascetic fluid, in a patient whose spouse had tuberculosis, led to the start of therapy. We also see, in the literature, an increase in tumor marker C.A. - 125 in this pathology,<sup>12</sup> also serving as a biological marker of the evolution. This was also the case here, normalizing at the end of 1 month of treatment. We also demonstrated the disappearance of the ascites in the ultrasound.

The difficulties were greater in patients in whom a probable cause of ascites was already known: Hepatic cirrhosis in case 3, decompensated C.I. in case 4. However, Burack, in the 1950s, and more recently, Alvarez, demonstrated that these pathologies, because they can cause major ascites, are rarely the cause of abdominal pain or fever, and another aetiology should be comprehensively sought. In these cases, even in the presence of a transudate, we should not ignore investigation of the cause of the fever or worsening of the underlying pathology. Currently, the productivity of microbiological exams is still low. However, we have other methods of diagnosis that are extremely sensitive, such as A.D.A levels, which when higher than 33 U/L, (regardless of their serum value) are considered sufficient for the start of therapy in hospitals where access to laparoscopy is often impossible.<sup>11</sup>

In these hospitals, once a coagulopathy has been ruled out, which would contraindicate invasive manoeuvres, and confirming the existence of free fluid in the abdominal cavity, with no masses being felt on palpation, percutaneous biopsy can be performed with a Cope needle. In these conditions, the complications are slightly higher than for paracentesis.<sup>6</sup> We took this attitude in latter 2 cases, given the poor general state of the patients which was progressively worsening, and because we were unable to obtain a laparoscopy in sufficient time. We achieved satisfactory results, without complications.

Research of the antigen 60 in the extrapulmonary forms of tuberculosis has been the object of intense investigation, often with contradictory reports.<sup>13,14</sup> Although considered a useful exam, it is not conclusive in this form of presentation of the disease.

Magnetic resonance imaging cannot yet be considered a routine exam, because it is very costly, and does not provide relevant information compared with that obtained from conventional imaging exams.

Recently, studies were carried out to determine the role of determining the ascetic fluid levels of  $\gamma$ -interferon. This is a cytokine produced by the CD4 lymphocytes which stimulates the macrophages. With sensitivity and specificity close to 100% (higher than A.D.A.) when at values higher than 3 U/L, its use in the clinical practice is difficult, as it involves handling of radioisotopes and is around 85 times clearer than the determination of A.D.A. It is, therefore, reserved for investigation.<sup>10</sup>

In conclusion, peritoneal tuberculosis exists, and is relatively common. All cases of ascites should be included in the differential diagnosis. Even when aetiology is presumed, it should still be borne in mind, so that the diagnosis is not made too late. ■

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