• CLINICAL RESEARCH •

A clinical dilemma: abdominal tuberculosis

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Abstract

AIM: To evaluate the clinical, radiological and microbiological properties of abdominal tuberculosis (TB) and to discuss methods needed to get the diagnosis.

METHODS: Thirty-one patients diagnosed as abdominal TB between March 1998 and December 2001 at the Gastroenterology Department of Kartal State Hospital, Istanbul, Turkey were evaluated prospectively. Complete physical examination, medical and family history, blood count erythrocyte sedimentation rate, routine biochemical tests, Mantoux skin test, chest X-ray and abdominal ultrasonography (USG) were performed in all cases, whereas microbiological examination of ascites, upper gastrointestinal endoscopy, colonoscopy or barium enema, abdominal tomography, mediastinoscopy, laparoscopy or laparotomy were done when needed.

RESULTS: The median age of patients (14 females,17 males) was 34.2 years (range 15-65 years). The most frequent symptoms were abdominal pain and weight loss. Eleven patients had active pulmonary TB. The most common abdominal USG findings were ascites and hepatomegaly. Ascitic fluid analysis performed in 13 patients was found to be exudative and acid resistant bacilli were present in smear and cultured only in one patient with BacTec (3.2 %). Upper gastrointestinal endoscopy yielded nonspecific findings in 16 patients. Colonoscopy performed in 20 patients showed ulcers in 9 (45 %), nodules in 2 (10 %) and, stricture, polypoid lesions, granulomatous findings in terminal ileum and rectal fistula each in one patient (5 %). Laparoscopy on 4 patients showed dilated bowel loops, thickening in the mesentery, multiple ulcers and tubercles on the peritoneum. Patients with abdominal TB were divided into three groups according to the type of involvement. Fifteen patients (48 %) had intestinal TB, 11 patients (35.2 %) had tuberculous peritonitis and 5 (16.8 %) tuberculous lymphadenitis. The diagnosis of abdominal TB was confirmed microbiologically in 5 (16 %) and histo-pathologically in 19 patients (60.8 %). The remaining nine patients (28.8 %) had been diagnosed by a positive response to antituberculous treatment.

CONCLUSION: Neither clinical signs, laboratory, radiological and endoscopic methods nor bacteriological and histopathological findings provide a gold standard by themselves in the diagnosis of abdominal TB. However, an algorithm of these diagnostic methods leads to considerably higher precision in the diagnosis of this insidious disease which primarily necessitate a clinical awareness of this serious health problem.

INTRODUCTION

Tuberculosis (TB) was a prevalent infection even in Ancient Greek and Egypt. The disease could be taken under control only after the advent of antimicrobial therapy in 1946. However, it has started to resurge worldwide in the last 10 years, due to HIV epidemic and to primary resistance to first-line drugs. One-third of the world population is under the risk of acquiring TB according to WHO and more than 30 million deaths had been expected due to TB in the nineties especially in Africa and Asia[1]. Not surprisingly, there is also an increase in the percentage of patients with atypical presentations and atypical extra-pulmonary forms of TB. Extra-pulmonary organ involvement of TB is estimated as 10-15 % of patients not infected with HIV whereas the frequency is about 50-70 % in patients infected with HIV[2].

Abdominal TB is one of the most prevalent forms of extra-pulmonary disease. Gastrointestinal involvement had been reported to be 55-90 % in patients with active pulmonary TB before the advent of specific anti-TB treatment. But it was regressed to 25 % after the development of specific drugs[3]. The abdominal form of TB has an insidious course like any other chronic infectious disease without any specific laboratory, radiological or clinical findings. Due to this non-specificity there are great difficulties in its diagnosis. Various methods of investigation had been reported as the gold standard of diagnosis in earlier studies; however there are great difficulties in clinical practice. As a result, the diagnosis of abdominal TB is still a challenge to the physician. In the present prospective study, we analyzed the clinical, laboratory, radiologic, endoscopic and microbiological features of abdominal TB patients in order to evaluate the diagnostic value of various methods and to define the correct tool of diagnosis.

MATERIALS AND METHODS

Thirty-one patients were diagnosed as abdominal TB in Gastroenterology Department of Kartal State Hospital-Istanbul, between March 1998 and December 2001. On admission, every patient had a complete physical examination, medical and family history, blood count and erythrocyte sedimentation rate (ESR), routine biochemical tests, Mantoux skin test, chest X-ray and abdominal ultrasonography (USG). After these basic investigations, an algoritm of diagnostic evaluation was applied according to the presence of certain symptoms, namely, ascites, upper gastrointestinal symptoms, chronic or bloody diarrhea, change in bowel habits, malabsorption, and additional suspicious lesions in other body parts. If present, ascites was taken for direct examination and culture for Mycobacterium tuberculosis. Patients complaining of dyspepsia, abdominal pain, vomiting, upper gastrointestinal bleeding or gastric

distention had an upper gastrointestinal endoscopy. 3 to 4 gastric biopsies were routinely taken from corpus and antrum during the endoscopy and the specimens were investigated for mycobacterium tuberculosis or the presence of granulomas. If the patient had symptoms suggestive of intestinal TB like chronic diarrhea, bloody stools or change in bowel habit, stool was examined for bacilli and culture for mycobacterium tuberculosis was done. Then, colonoscopy, or in patients with problems of performing colonoscopy, barium enema was performed. Eight to ten biopsies were taken for histopathologic and microbiological examinations if any lesions were found present during colonoscopy. Signs of small bowel involvement like malabsorption were evaluated with small bowel series. Any abnormality of abdominal organs, lymph nodes, mesentery and peritoneum seen on abdominal USG examination was evaluated by abdominal CT. Otherwise routine abdominal CT was not done. If necessary for any additional suspected lesions, mediastinoscopy, laparoscopy or laparotomy was also performed. In the presence of any pathological findings, multiple biopsies were taken and sent for bacteriological and histopathological investigations. A microbiological diagnosis was attempted in all cases. However, in some of the patients where no microbiological diagnosis could be met despite every effort, the histopathological finding of typical caseating granulomas was accepted as a definite evidence of TB. In patients where none of the diagnosis was available and clinical suspicion of abdominal TB was high, a therapeutic trial of anti-TB treatment with four agents (Rifampicin, Ethambutol, Isoniazid and Morphozinamide) was started, and response to treatment was evaluated after three months.

We treated all patients with the standard four-drug regimens (streptomycin or ethambutol, rifampin, pyrazinamide, isoniazid) for 9 months and the patients were reevaluated again at the end of this time. If there was no resolution of symptoms and Mycobacterium tuberculosis was still present in any specimen, an additional 9-months of treatment was given.

RESULTS

Thirty-one patients with abdominal TB (14 females, 17 males) with a median age of 34.2 years (range 15-65 years) were diagnosed in 5 years. A past medical history of pulmonary TB was obtained in 6 patients (19.2 %) and of bone TB in 2 patients (6.4 %). There was a family history of TB (in the first-degree relatives of index patient) in 8 (25.6 %). The mean duration of symptoms showed great variation among the patients (range l month-11 years).

The presenting symptoms and signs were summarized in Table 1. Abdominal pain and weight loss appeared to be the most frequent symptoms among these.

Laboratory investigations revealed anemia in 22 (70.4 %), elevated ESR in 20 (64 %), and hypoalbuminaemia in 15 (48 %) patients as the most prominent features. Other findings were leucocytosis in 2 (6.4 %), positive CRP in 5 (16 %), elevated transaminases in 7 patients (22.4 %). Of these 7 patients, 2 were chronic HBV carriers, 1 was immune to HBV and 1 was anti-HCV positive. In 4 patients (12.8 %), all laboratory examinations were within normal limits.

Mantoux skin test was found positive in 6 (19.2 %) of the patients. There was ascites in 13 (41.6 %). Ascitic fluid analysis performed in those patients was found to be exudative in character and only in one patient acid-fast bacilli (ARB) were present in smear and cultured only in one patient with BacTec (3.2 %).

In 11 patients (35.2 %), chest X-ray showed lesions compatible with active pulmonary TB, like fibrocavitary lesions, effusions, or lymphadenopathies. Thorax CT was carried out on these patients and lung lesions such as pleural

involvement, lymphadenopathy or nodular infiltration were present in all of them. Thorax CT did not provide additional data in comparison to chest X-ray.

Abdominal USG was performed on all patients except in five because of technical problems due to recent operations. USG findings of 26 patients were summarized in Table 2. Abdominal CT was performed on 22 of these patients who presented with abnormal findings in USG. Ascites in 8 (36.3 %), thickening of mesentery in 5 (22.7 %), abdominal lymphadenopathy in 3 (13.6 %), omental pathology in 3 (13.6 %) and lymphadenopathy in liver hilum, cholelithiasis, destruction in sacral bone, ovary cyst and splenomegaly each for one (4.5 %) occasions had been observed as the most important CT findings among these patients. Only 3 patients (13.6 %) presented with completely normal CT examination.

Table 1 Presenting symptoms (*may be more than one in each patient*) and signs and their frequency in patients (*n*=32)

Symptoms and signs	Number of patients	Percentage (%)
Abdominal pain	16	51.2
Weight loss	16	51.2
Ascites	12	38.4
Diarrhea	10	32
Cough and sputum	6	19.2
Vomiting and nausea	5	16
Fever	4	12.8
Perforation	3	9.6
Bone pain	2	6.4
Night sweats	2	6.4
Urinary symptoms	1	3.2
Mass in the lower quadrant	1	3.2
Cervical pain	1	3.2
Evisseration following laparotomy	1	3.2
Incidental	1	3.2
Operation because of brid ileus	1	3.2

Table 2 Abdominal ultrasonographic findings (*may be more than one in each patient*) and their frequency in the patients (*n*=26)

Abdominal USG findings	Number of patients	Percentage (%)
Normal	4	17.2
Ascites	14	53.2
Hepatomegaly	4	17.2
Thickening	3	11.4
Atrophic	2	7.6
Abdominal	2	7.6
Hepatosteatosis	2	7.6
Splenomegaly	1	3.8
Pericardial	1	3.8
LAP	1	3.8
Calcifications	1	3.8

Small bowel follow-up was done on seven patients and the bowel was significantly shortened due to extensive resection because of perforation in one of them. Barium enema was performed on two, and there was irregularity and ulcers in the bowel wall of one patient' s.

Upper gastrointestinal endoscopy was performed in 17 patients and showed nonspecific findings in 16. In every case, gastric biopsies were taken but no acid- resistant bacilli (ARB) or granulomas were identified in tissue sections.

Colonoscopy was performed in 20 patients. There was no abnormality in 8 patients (40 %). Ulcers in 9 (45 %), nodules in 2 (10 %) and, stricture, polypoid lesions, granulomatous

findings in terminal ileum and rectal fistula each in one (5 %), occasions were found in these patients.

Laparoscopy was performed on 4 patients and there were positive findings in all of them. Dilated bowel loops, thickening in the mesentery, multiple ulcers and tubercles on the peritoneum, each for once, were observed in these patients. Peritoneal biopsies confirmed the diagnosis of tuberculosis in three of these patients. In the fourth patient, a peritoneal biopsy could not be taken because of high bleeding risk due to a very long prothrombin time.

Mediastinoscopy in one patient, and fine needle aspiration biopsy of the lymphadenopathy in liver hilum in another one were performed to confirm the diagnosis. In only 2 patients of the whole series, the diagnosis was clarified by biopsies taken in an operation under general anesthesia (one was operated because of bulging cervical disc and the other because of intestinal obstruction).

Patients with abdominal TB were divided into three groups according to the type of involvement. 15 patients (48 %) had intestinal TB, 11 patients (35.2 %) tuberculous peritonitis and 5 (16.8 %) tuberculous lymphadenitis.

It wase able to confirm the diagnosis of abdominal tuberculosis microbiologically in 5 patients (16 %). Two of these patients were diagnosed by positive ARB smears of sputum, 1 with ARB in enterocutaneous fistula discharge, 1 with ARB in ascitic fluid, and 1 with ARB in biopsy material. Two patients were found positive in BacTec, but none of these patients had positive culture on Löwenstein medium. Nineteen patients (60.8 %) were diagnosed histopathologically and the diagnosis in the remaining nine patients (28.8 %) have been reached by a positive response to antituberculous treatment. In 2 patients, there were both, histopathologic and microbiologic diagnosis of tuberculosis.

Twenty-eight patients were symptom-free after 9 months of treatment. Furthermore, no pathological findings were observed in the next follow-up visits after six months. In the remaining 3 patients, the disease had a complicated course and although antituberculous treatment with four agents (streptomycin or ethambutol, rifampin, pyrazinamide, isoniazid) was begun, mammarian abscess developed in one of them, osteomyelitis and enterocutaneous fistula in the second patient, and incisional enterocutaneous fistula in the last patient.

DISCUSSION

Abdominal TB is again on the rise all over the world with the resurgence of multidrug resistant TB and with AIDS pandemic. It is also an increasing health problem because of the immigrants from underdeveloped countries where it is more common. However, this topic is still restricted within a few paragraphs in the textbooks and the current knowledge of abdominal TB has to be updated. Sensitivity of various methods have already been speculated in previous studies without any serious conclusion. In the present study we aimed to investigate the relative reliability of these tools in the diagnosis of abdominal TB which has an exceptionally insidious course. As shown in the present study, the clinical and laboratory features of abdominal TB are nonspecific and lead to the suspicion of only a chronic infectious disease.

Three diagnostic stages have been evaluated in the diagnosis of abdominal TB. The first two stages, clinical evaluation of the patient and the radiologic examination, give indirect evidence of the disease. The third stage includes the invasive techniques to achieve direct evidence. However, the diagnosis of TB has its own difficulties that these evidences generally come out to be relatively direct in practice.

The vague character of symptoms has been previously defined in many studies[4,5] and the radiographic presentation of this disease which frequently mimics many other conditions

has already been described[6,7]. The combination of mesenteric thickening of 15 mm with associated mesenteric lymphadenopathy has been stated as a prominent sonographic finding in abdominal TB[8,9] which could not be confirmed in our study. We found rather nonspecific findings in abdominal ultrasonography such as ascites and hepatomegaly. However, CT features of abdominal TB have been reported to be of value in the diagnosis[10] and the ability to differentiate TB peritonitis from malignant diseases of the peritoneum could be increased by combining some CT findings[11]. The same is true for this study; we had a positive finding in 88 % of the patients in abdominal CT. The results obtained on CT scans are comparable to USG findings in the literature[4]. Thus abdominal CT findings appear to provide more objective data about the disease than other radiological methods.

The invasive diagnostic tools have the very real advantage of examining the lesion itself either macroscopically or microscopically. However, even these direct methods have their own drawbacks in clinical practice.

Colonoscopic findings of abdominal TB are problematic because of segmentary involvement of the disease[12] and because of low yield of granulomas as a result of submucosal disease. In a study of Singh and associates[13], granulomas were seen in 44 % of the patients, and 19 % of them had caseation. We could find colonoscopic abnormalities in 60 % of the patients and confirm TB histopathologically. However, colonoscopy is still mandatory to obtain tissue for culturing the agent which is very important for the diagnosis of intestinalTB.

The sensitivity of endoscopic biopsy ranges between 30 and 80 % and Bhargawa et al[14] suggested obtaining 8 to 10 biopsies for histology and 3 to 4 specimens for culture.

In patients with palpable abdominal masses, direct fine needle aspiration cytology can also be applied[5]. This method is not feasible in any of our patients because we could not palpate these masses in any of them.

Laparoscopic pattern and biopsies obtained from the peritoneum have been reported to be more helpful and that this finding could be used even for treating patients with abdominal TB without any histopathologic or bacteriologic confirmation[15]. In the present study, laparoscopy was performed in 4 patients and confirmed the diagnosis histopathologically in 3 and macroscopically in one patient. Thus, it appeared to be a highly sensitive diagnostic tool in all selected patients. In a study of Lisehora et al[16], even mini laparotomy was reported as the most sensitive and specific diagnostic procedure in abdominal TB.

The diagnosis of abdominal TB classically requires microbiological and culture confirmation of mycobacterium tuberculosis, whereas, the diagnosis can be established histopathologically in many studies[4,15]. Also in the current study, the diagnosis could be reached histopathologically in 60.8 % of the patients. If the isolation of Mycobacterium tuberculosis is accepted as "sine qua non" for this infectious disease according to the postulates of Koch, histopathological diagnosis can not be regarded as standard. However, microbiological isolation of the agent is very rare for patients with abdominal TB. It has remained under 50 % in all the reported series. Isolation of bacilli in endoscopic biopsy materials has been postulated as even to be zero[12,13]. It is known that Mycobacterium tuberculosis can be occasionally isolated in stool of persons with healthy conditions. Therefore special decontamination techniques and BacTec technology must be used for culture of this agent[17]. Interestingly, we could not be able to confirm the existence of Mycobacterium tuberculosis in any of our patients using Löwenstein medium that was said to be the ideal culture medium for this bacterium. Even in patients who were ARB positive in direct smear, culture in Löwenstein was not positive; but we had culture positivity in

two patients with BacTec technique. In a case report of Anand and associates[17], PCR was used on endoscopic biopsy specimens obtained from a patient with chronic diarrhea and the result was found positive.

The isolation of Mycobacterium tuberculosis with BacTec or PCR are promising methods for the future but even these methods appear to be far from ideal since it is not enough for the treatment of the disease because of the lack of culture. We think that we have to refine our isolation procedures for the bacterium and in every case of extrapulmonary TB, not only histopathological but also microbiological confirmation should still be sought in order to break the vicious circle of multidrug resistancy.

A past history of pulmonary TB or a family history of TB is quite frequent in patients with abdominal TB[19] which is also the case in our study. It is known that patients with multidrug resistant organisms acquire the organisms through multiple ineffective courses of treatment with various drugs[20]. Thus, it can be concluded that most of the cases with abdominal TB have a primary resistance to conventional chemotherapy.

The isolation of mycobacterium tuberculosis is also essential for susceptibility tests which are now performed on every patient with pulmonary TB because of the high incidence of multidrug resistance (it has increased from 2 % to 9 % in the past three decades)[20].

Based upon our clinical observation with abdominal TB, we can stress on these patient with high resistance because of the long course of the disease and because of frequency of complications. If a better way of isolating the organism cannot be found and if the resistance cannot be detected before starting with the antituberculous treatment, the increase of new TB cases will be inevitable. The problem of mutant strains could also be expected in the future. It is known that two different mutant strains can coexist in the same patient which further complicates the resistance problem. Although the molecular fingerprinting of mycobacterium tuberculosis may help to solve these problems in some extent[21], these facts should be taken into consideration for future directions in the diagnosis and treatment of abdominal TB.

CONCLUSION

Neither clinical signs, laboratory, radiological and endoscopic methods nor bacteriological and histopathological findings provide a gold standard by themselves in the diagnosis of abdominal TB. However, an algorithm of these diagnostic methods leads to considerably higher precision in the diagnosis of this insidious disease which primarily necessitate a clinical awareness of this serious health problem.

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