

Diagnosis of abdominal tuberculosis: Experience from 11 cases and review of the literature

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Abstract

AIM: To analyze the experience within our hospital and to review the literature so as to establish the best means of diagnosis of abdominal tuberculosis.

METHODS: The records of 11 patients (4 males, 7 females, mean age 39 years, range 18-65 years) diagnosed with abdominal tuberculosis in Harran University Hospital between January 1996 and October 2003 were analyzed retrospectively and the literature was reviewed.

RESULTS: Ascites was present in all cases. Other common findings were weight loss (81%), weakness (81%), abdominal mass (72%), abdominal pain (72%), abdominal distension (63%), anorexia (45%) and night sweat (36%). The average hemoglobin was 8.2 g/dL and the average ESR was 50 mm/h (range 30-125). Elevated levels of cancer antigen CA-125 were determined in four patients. Abdominal ultrasound showed abnormalities in all cases: ascites in all, tuboovarian mass in five, omental thickening in 3, and enlarged lymph nodes (mesenteric, para-aortic) in 2. CT scans showed ascites in all, pelvic mass in 5, retroperitoneal lymphadenopathy in 4, mesenteric stranding in 4, omental stranding in 3, bowel wall thickening in 2 and mesenteric lymphadenopathy in 2. Only one patient had a chest radiograph suggestive of a new TB lesion. Two had a positive family history of pulmonary TB. None had acid-fast bacilli (AFB) in the sputum and the tuberculin test was positive in only two. Laparotomy was performed in 6 cases, laparoscopy in 4 and ultrasound-guided fine needle aspiration in 2. In those patients subjected to operation, the findings were multiple diffuse involvement of the visceral and parietal peritoneum, white 'miliary nodules' or plaques, enlarged lymph nodes, ascites, 'violin string' fibrinous strands, and omental thickening. Biopsy specimens showed granulomas, while ascitic fluid showed numerous lymphocytes. Both were negative for acid-fast bacilli by staining. PCR of ascitic fluid was positive for *Mycobacterium tuberculosis* (*M. tuberculosis*) in all cases.

CONCLUSION: Abdominal TB should be considered in all cases with ascites. Our experience suggests that PCR of ascitic fluid obtained by ultrasound-guided fine needle aspiration is a reliable method for its diagnosis and should at least be attempted before surgical intervention.

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INTRODUCTION

Tuberculosis (TB) causes some 3 million deaths per year world wide and is increasing in incidence in developed, and developing countries. Abdominal TB, which may involve the gastrointestinal tract, peritoneum, lymph nodes or solid viscera, constitutes up to 12% of extrapulmonary TB and 1-3% of the total^[1,2]. The disease can mimic many conditions, including inflammatory bowel disease, malignancy and other infectious diseases^[3]. Diagnosis is therefore often delayed. This may not only result in mortality but also in unnecessary surgery. We therefore set out to establish the most useful diagnostic procedure(s) in the light of our experience and reports in the literature.

MATERIALS AND METHODS

A retrospective study of the files of patients admitted to Harran University Hospital from January 1996 to October 2003 was carried out. Cases of abdominal TB were identified and data on age, sex, clinical presentation, diagnostic investigations, treatment and outcome were abstracted.

RESULTS

Eleven patients, none of whom were immunocompromised, were diagnosed with abdominal TB during the period (Table 1). Nine cases had peritoneal TB, while the remaining two had TB of the colon. The median age was 39 years (range 18-65) and the ratio of males and females was 4:7.

The mean duration of symptoms was 14 wk (range 1-32 wk). Ascites was present in all cases, while 9 (81%) showed weight loss, 9 (81%) weakness, 8 (72%) abdominal mass, 8 (72%) abdominal pain, 7 (63%) abdominal distension, 5 (45%) anorexia and 4 (36%) night sweat.

The average hemoglobin was 8.2 g/dL and the average ESR was 50 mm/h (range 30-125). Levels of cancer antigen CA-125 were elevated in four patients.

Abdominal ultrasound (US) was carried out on all patients and abnormal findings were noted in all: ascites in all, tuboovarian mass in five, omental thickening in three, and enlarged lymph nodes (mesenteric, para-aortic) in two.

All patients also had computed tomography (CT) scans, with results consistent with US (Table 2).

At this stage, diagnoses of peritoneal carcinomatosis, colon cancer, Chron's disease and ovarian cancer were considered. Laparotomy was performed in the first six cases and the diagnosis of abdominal TB was made intraoperatively based on macroscopic findings, including multiple diffuse involvement of the visceral and parietal peritoneum, white 'miliary nodules' or plaques, enlarged lymph nodes, ascites, 'violin string' fibrinous strands and omental thickening, and confirmed by microscopic examination of biopsies of lymph nodes and peritoneal nodules and by positive polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* (*M. tuberculosis*) on ascitic fluid taken during the procedure. Smears of ascitic fluid showed numerous lymphocytes but no acid-fast bacilli.

Laparoscopy was used in the examination of the next three cases. Biopsies were again taken and examined microscopically and confirmation of the diagnosis was made by PCR on ascitic fluid.

Table 1 Details of patients with abdominal tuberculosis

Case No.	Sex	Age (yr)	Clinical findings	Intervention	Diagnosis
1	M	38	Ascites, colonic obstruction, weight loss, weakness, abdominal distension, anorexia, retroperitoneal lymphadenopathy, bowel wall thickening	Laparotomy	Colon TB
2	F	26	Ascites, elevated CA-125 ($\times 4$), abdominal mass, weight loss, weakness, abdominal pain, anorexia	Laparotomy	Peritoneal TB
3	M	40	Ascites, abdominal mass, enlarged lymph nodes, weight loss, weakness, abdominal pain, abdominal distension, anorexia, bowel wall thickening	Laparotomy	Colon TB
4	F	54	Ascites, elevated CA-125 ($\times 3$), abdominal mass, weakness, abdominal pain, abdominal distension, night sweats	Laparotomy	Peritoneal TB
5	M	44	Ascites, omental thickening, enlarged lymph nodes, weakness, abdominal pain, anorexia	Laparotomy	Peritoneal TB
6	F	42	Ascites, tuboovarian mass, elevated CA-125 ($\times 4$), weight loss, weakness, abdominal pain, night sweats	Laparotomy	Peritoneal TB
7	M	65	Ascites, abdominal mass, weight loss, weakness, abdominal pain, abdominal distension	Laparoscopy	Peritoneal TB
8	F	51	Ascites, tuboovarian mass, positive family history of pulmonary TB, weight loss, weakness	Laparoscopy	Peritoneal TB
9	F	18	Ascites, elevated CA-125 ($\times 4$), tuboovarian mass, weight loss, weakness, abdominal distension	Laparoscopy	Peritoneal TB
10	F	20	Ascites, omental thickening, weight loss, abdominal pain, abdominal distension, anorexia, night sweats, retroperitoneal lymphadenopathy	Fine needle aspiration	Peritoneal TB
11	F	40	Ascites, abdominal mass, positive family history of pulmonary TB, omental thickening, weight loss, abdominal pain, abdominal distension, night sweats	Fine needle aspiration	Peritoneal TB

Table 2 CT scan characteristics of patients with abdominal tuberculosis

CT findings	No. of patients (%)
Ascites	11 (100)
Pelvic mass	5 (45)
Retroperitoneal lymphadenopathy	4 (36)
Mesenteric stranding	4 (36)
Omental stranding	3 (27)
Bowel wall thickening	2 (18)
Mesenteric lymphadenopathy	2 (18)

Because of this experience, the Radiology Department was alerted to the necessity of including abdominal TB in the differential diagnosis and the final two patients in the series were spared surgical intervention, the diagnosis was confirmed by PCR of ascitic fluid obtained by US-guided fine needle aspiration.

Only one patient had a chest radiograph suggestive of a new TB lesion. Two had a positive family history of pulmonary TB. None had acid-fast bacilli (AFB) in the sputum and the tuberculin test was positive in only two.

All patients were started on quadruple antituberculous therapy comprising rifampicin (10 mg/kg-d), isoniazid (5 mg/kg-d), ethambutol (15 mg/kg-d) and pyrazinamide (30 mg/kg-d) for two months and then maintained on rifampicin and isoniazid for 9-12 mo. Response was good in all patients. The mean follow-up time was 24 mo (range 19-38 mo).

DISCUSSION

In accord with other reports^[4,5], our 'typical' patient was a middle-aged female. Signs and symptoms observed were generally in line with those of other reports except that the percentage of our patients showing weight loss was the highest for any series. Fever was the most common finding (73%) in the series reported by Muneef *et al.*^[6], but our results agree with most other studies in reporting about half this incidence. The

most consistent finding, in our study and in the literature, was the presence of ascites, although Muneef *et al.*^[6] again differed in finding ascites present in only 61% of their patients.

Presence of TB at other sites or a patient with a family history of TB may be helpful in suggesting the diagnosis, but this occurs in somewhat less than 30% of patients. This may indicate that the majority of cases had primary lesions were acquired through the gastrointestinal tract. Given the preponderance of females affected, it may also be that some cases in females are acquired genitally (though not necessarily sexually). TB skin tests were positive in only about a quarter of patients in most reports but Demir *et al.*^[7] obtained a positive result in all their 26 patients.

Although US^[8] and CT scanning^[9] have been claimed to give definitive diagnoses, this was not the case in our series or in the other cases surveyed. Both US and CT were abnormal in all cases in most reports (though in only 80% of CT scans in the series reported by Muneef *et al.*^[6]) but findings were largely non-specific.

The great majority of reported cases were, like the first six cases in our series, diagnosed at laparotomy after they were initially misdiagnosed as tumors or carcinomas^[4-6,10-17]. In female patients, misdiagnosis was made even more likely by the raised levels of CA-125 that were apparently universally observed and the fact that an elevated level of CA-125 has been recognized as a marker of non-mucinous epithelial ovarian carcinomas^[13-17]. In the light of this finding, Thakur *et al.*^[13] went so far as to suggest that high serum CA-125 should always raise a suspicion of TB. However, the finding has not so far been validated in males.

Diagnosis at laparotomy was made largely by histology of frozen or paraffin-embedded sections, which typically revealed epithelioid granulomas with central caseous necrosis, although Muneef *et al.*^[6] reported 68% of peritoneal biopsies were positive by smear/culture. Zaidi and Conner^[12] performed PCR for *M. tuberculosis* on paraffin-embedded tissues.

With increasing experience, laparoscopy has become the diagnostic procedure of choice, both in our hospital and in the literature^[18-24]. Again, in most cases histology was the main confirmatory method, smear and culture were largely unhelpful.

PCR was used to confirm the diagnosis in two cases^[21,22].

Laparoscopy is, however, invasive and expensive, but was associated with an overall incidence of major complications in up to 5.7% of patients^[25]. Because of this, several investigators looked at abdominal paracentesis as a diagnostic method. Ascitic fluid in abdominal tuberculosis is exudative, usually containing 500 to 2000 cells. Lymphocytes typically predominate, although in some cases polymorphonuclear leukocytes were more abundant early in the process. Acid-fast stains were usually negative. Though culture might eventually be positive in up to a third of cases^[6], the time taken for growth (usually 6 wk) was too long to be useful in diagnosis.

The use of PCR to detect *M. tuberculosis* in abdominal tuberculosis was reported by Moatter *et al.*^[26]. In their study, as in most later ones^[12,21-23], DNA was extracted from tissues. They found that an IS6110 primer was detected in only 60% of specimens and another primer was necessary to detect the other 40%. Schwake *et al.*^[23] obtained a negative result in the two cases they tested, perhaps because they only used a single primer.

In all eleven patients presented here, PCR analyses for *M. tuberculosis* complex on ascitic fluid were positive. Protopoulos *et al.*^[24] (single case) and Tzoanopoulos^[27] (3 patients) also successfully used PCR of ascitic fluid to obtain a diagnosis.

In the light of our accumulated experience, we would suggest that PCR of ascitic fluid obtained by US-guided fine needle aspiration is now the investigation of choice for patients with the described clinical and radiological presentations and should at least be attempted before surgical intervention. Our final two patients were diagnosed by this means. If the result was negative, diagnostic laparoscopy or, if this was not feasible, laparotomy should be performed.

Ascitic fluid adenosine deaminase (ADA) activity has been proposed as a useful diagnostic test for abdominal TB. In countries with a high incidence of TB and in high risk patients, measurement of ADA in ascitic fluid might be a useful screening test^[28]. However, in populations with a low prevalence of TB and a high prevalence of cirrhosis, ascitic fluid ADA activity has been good in accuracy but poor in sensitivity and imperfect in specificity^[29].

In the reports reviewed, there was only one recorded death due to TB in patients with abdominal tuberculosis receiving anti-TB therapy (most commonly, a four drug regimen for several mo) and that was in a patient with extensive involvement of other organs^[6]. The prognosis was therefore good if the condition was promptly diagnosed and treated, though the emergence of multi-resistant strains might alter this picture.

In conclusion, abdominal TB should be considered in the differential diagnosis of abdominopelvic masses, ascites or elevated CA-125. PCR for *M. tuberculosis* complex is a non-invasive method which can provide the diagnosis in most cases. If this test is negative and a high index of clinical suspicion remains, laparoscopy or, if this is not feasible, laparotomy should be performed.

REFERENCES

- Farer LS, Lowell AM, Meador MP. Extrapulmonary tuberculosis in the United States. *Am J Epidemiol* 1979; **109**: 5-15
- Sheer TA, Coyle WJ. Gastrointestinal tuberculosis. *Curr Gastroenterol Rep* 2003; **5**: 273-278
- Jadvar H, Mindelzun RE, Olcott EW, Levitt DB. Still the great mimicker: abdominal tuberculosis. *Am J Roentgenol* 1997; **168**: 1455-1460
- Zhang Z, Shi X, Li J. Abdominal tuberculosis misdiagnosed as tumor. *Zhonghua Jiehe He Huxi Zazhi* 2001; **24**: 400-403
- Bilgin T, Karabay A, Dolar E, Develioglu OH. Peritoneal tuberculosis with pelvic abdominal mass, ascites and elevated CA 125 mimicking advanced ovarian carcinoma: a series of 10 cases. *Int J Gynecol Cancer* 2001; **11**: 290-294
- Muneef MA, Memish Z, Mahmoud SA, Sadoon SA, Bannatyne R, Khan Y. Tuberculosis in the belly: a review of forty-six cases involving the gastrointestinal tract and peritoneum. *Scand J Gastroenterol* 2001; **36**: 528-532
- Demir K, Okten A, Kaymakoglu S, Dincer D, Besisik F, Cevikbas U, Ozdil S, Bostas G, Mungan Z, Cakaloglu Y. Tuberculous peritonitis-reports of 26 cases, detailing diagnostic and therapeutic problems. *Eur J Gastroenterol Hepatol* 2001; **13**: 581-585
- Malik A, Saxena NC. Ultrasound in abdominal tuberculosis. *Abdom Imaging* 2003; **28**: 574-579
- Sinan T, Sheikh M, Ramadan S, Sahwney S, Behbehani A. CT features in abdominal tuberculosis: 20 years experience. *BMC Medical Imaging* 2002; **2**: 3-16
- Ozalp S, Yalcin OT, Tanir HM, Kabukcuoglu S, Akcay A. Pelvic tuberculosis mimicking signs of abdominopelvic malignancy. *Gynecol Obstet Invest* 2001; **52**: 71-72
- Mahdavi A, Malviya VK, Herschman BR. Peritoneal tuberculosis disguised as ovarian cancer: an emerging clinical challenge. *Gynecol Oncol* 2002; **84**: 167-170
- Zaidi SN, Conner M. Disseminated peritoneal tuberculosis mimicking metastatic ovarian cancer. *South Med J* 2001; **94**: 1212-1214
- Thakur V, Mukherjee U, Kumar K. Elevated serum cancer antigen 125 levels in advanced abdominal tuberculosis. *Med Oncol* 2001; **18**: 289-291
- Barutcu O, Erel HE, Saygili E, Yildirim T, Torun D. Abdominopelvic tuberculosis simulating disseminated ovarian carcinoma with elevated CA-125 level: report of two cases. *Abdom Imaging* 2002; **27**: 465-470
- Lantheaume S, Soler S, Issartel B, Isch JF, Lacassin F, Rougier Y, Tabaste JL. Peritoneal tuberculosis simulating advanced ovarian carcinoma: a case report. *Gynecol Obstet Fertil* 2003; **31**: 624-626
- Piura B, Rabinovich A, Leron E, Yanai-Inbar I, Mazor M. Peritoneal tuberculosis-an uncommon disease that may deceive the gynecologist. *Eur J Obstet Gynecol Reprod Biol* 2003; **110**: 230-234
- Panoskaltis TA, Moore DA, Haidopoulos DA, McIndoe AG. Tuberculous peritonitis: part of the differential diagnosis in ovarian cancer. *Am J Obstet Gynecol* 2000; **182**: 740-742
- Piura B, Rabinovich A, Leron E, Yanai-Inbar I, Mazor M. Peritoneal tuberculosis mimicking ovarian carcinoma with ascites and elevated serum CA-125: case report and review of literature. *Eur J Gynaecol Oncol* 2002; **23**: 120-122
- Rai S, Thomas WM. Diagnosis of abdominal tuberculosis: the importance of laparoscopy. *J R Soc Med* 2003; **96**: 586-588
- Wu JF, Li HJ, Ni YH, Yu SC, Chang MH. Tuberculous peritonitis mimicking peritonitis carcinomatosa: a case report. *Eur J Pediatr* 2003; **162**: 853-855
- Lal N, Soto-Wright V. Peritoneal tuberculosis: diagnostic options. *Infect Dis Obstet Gynecol* 1999; **7**: 244-247
- Bouma BJ, Tytgat KM, Schipper HG, Kager PA. Be aware of abdominal tuberculosis. *Neth J Med* 1997; **51**: 119-122
- Schwake L, von Herbay A, Junghanss T, Stremmel W, Mueller M. Peritoneal tuberculosis with negative polymerase chain reaction results: report of two cases. *Scand J Gastroenterol* 2003; **38**: 221-224
- Protopoulos A, Milingos S, Diakomanolis E, Elsheikh A, Protogerou A, Mavrommatis K, Michalas S. Miliary tuberculous peritonitis mimicking advanced ovarian cancer. *Gynecol Obstet Invest* 2003; **56**: 89-92
- Martin JR, Whitted R, Latchaw GA, Yebara S. Complications of operative and diagnostic laparoscopy: a retrospective study. *Obstet Gynecol* 2001; **97**: S20
- Moatter T, Mirza S, Siddiqui MS, Soomro IN. Detection of Mycobacterium tuberculosis in paraffin embedded intestinal tissue specimens by polymerase chain reaction: characterization of IS6110 element negative strains. *J Pak Med Assoc* 1998; **48**: 174-178
- Tzoanopoulos D, Mimidis K, Giaglis S, Ritis K, Kartalis G. The usefulness of PCR amplification of the IS6110 insertion element of *M. tuberculosis* complex in ascitic fluid of patients with peritoneal tuberculosis. *Eur J Intern Med* 2003; **14**: 367-371
- Voigt MD, Kalvaria I, Trey C, Berman P, Lombard C, Kirsch RE. Diagnostic value of ascites adenosine deaminase in tuberculous peritonitis. *Lancet* 1989; **1**: 751-754
- Hillebrand DJ, Runyon BA, Yasminah WG, Rynders GP. Ascitic fluid adenosine deaminase insensitivity in detecting tuberculous peritonitis in the United States. *Hepatology* 1996; **24**: 1408-1412