

Original Research Article

The diagnostics significance of serum cancer antigen-125 in abdominal tuberculosis

Anil Kumar^{1*}, Shiv S. Paswan², Bindey Kumar³, Pragati Raj⁴, Sunita⁵

¹Department of General Surgery, All India Institute of Medical Sciences, Patna, Bihar, India

²Department of General Surgery, All India Institute of Medical Sciences, Bhubaneswar, Odisha, India

³Department of Paediatric Surgery, ⁴Intern, ⁵MBBS Student, All India Institute of Medical Sciences, Patna, Bihar, India

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*Correspondence:

Dr. Anil Kumar,

E-mail: dranil4@gmail.com

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ABSTRACT

Background: Various serum markers have been shown to be helpful in diagnosing tubercular infection, but none has been proven to be specific. The present study was undertaken to ascertain the role of serum cancer antigen (CA) -125 in diagnosing and monitoring therapeutic response in abdominal tuberculosis.

Methods: Fifty diagnosed cases of abdominal tuberculosis and equal number of controls were included in the study. All the patients underwent clinical, radiological and hematological examination. Twenty-two patients had acute presentation and underwent laparotomy and twenty-eight patients had a chronic presentation and were managed conservatively. Biopsy was taken in all patients undergoing laparotomy. Serial measurement of serum levels of CA-125 were done at 0, 3 and 6 months in all the patients.

Results: The CA-125 levels were significantly higher in tuberculosis patients than in control group (PPV 95.74% at 0 month). It was also observed that the levels correlated significantly with the disease activity (sensitivity 90 percent, specificity 96 percent) and return to normal level with the treatment given. It was shown that sensitivity reduced to 12 percent and 6 percent at 3 months and 6 months respectively after completion of treatment. The specificity however remained unchanged.

Conclusions: The measurement of CA-125 may be a valuable parameter in diagnosing and determination of disease activity in abdominal tuberculosis.

Keywords: Abdominal, CA-125, Koch's, Tuberculosis

INTRODUCTION

Abdominal tuberculosis remains a common disease in Indian subcontinent and constitutes 2% of all cases of tuberculosis.¹ Up to 11 percent of cases of small intestinal obstruction and 5.7 percent of cases of intestinal perforation are due to intestinal tuberculosis.^{2,3} The incidence of abdominal tuberculosis continues to rise due to increased incidence of HIV.⁴ The clinical condition usually mimics inflammatory diseases such as crohn's disease or malignancies, which are becoming more

prevalent, so the diagnosis is always doubtful.⁴ The diagnosis of the abdominal tuberculosis is mainly based on clinical grounds and contrast studies. Definitive diagnosis still depends on finding characteristic of granulomas in biopsy which however are not available in every case. Further, follow up of infection activity and response to therapy is not easy to evaluate. Different biochemical parameters have been proposed as helpful tool for this purpose including various markers of cellular activity, acute phase reactants and enzymes.⁵ The tumour marker CA-125 has been proposed as a useful diagnostic

tool for tuberculosis.¹ CA-125 usually raised in malignant condition but may be raised in pulmonary and extra pulmonary tuberculosis also.⁵ The present study was undertaken to ascertain the efficacy of CA-125 in diagnosing abdominal tuberculosis, monitoring the disease activity and its response to therapy.

METHODS

The study was performed at tertiary referral hospital over a three-year period from 2013 to 2016. Fifty patients with clinically suspected abdominal tuberculosis were enrolled in study after obtaining written consent (group 1). Fifty healthy volunteers akin the patient population were also included in the study (group 2) and considered as controls. The mean age was 29.4 years and 27.8 years with a male to female ratio of 1.3:1 and 1.5:1 in group 1 and group 2 respectively. The patients were further sub classified into two groups depending on clinical presentation. Acutely presenting patients of group A, had either acute intestinal obstruction or bowel perforation with peritonitis was 22 in number (A1). Patients with chronic symptoms of group A presented with either recurrent episodes of intestinal obstruction or ascites was 28 in number (A2).

All patients underwent routine haematological investigations, skiagraphy of chest and abdomen along with ultrasound of abdomen. Significant features in chest x-ray (hilar lymphadenopathy with or without calcification and pleural effusion) and abdominal x-ray (dilated bowel loops with thickened walls and/or free fluid with internal septations) were present in 81.8 and 54.5% respectively. This was followed by urgent exploratory laparotomy. Biopsy was obtained in all patients who underwent laparotomy (n=22) and was positive in 21 patients. Tissue biopsy showing Granuloma with central caseation necrosis was taken as diagnostic for tuberculosis.

The patient group with chronic presentation (group B), in addition to baseline investigation mentioned above also underwent barium contrast studies, abdominal Contrast enhanced computed tomography scans and ascitic fluid examination, wherever indicated. CT scans of the abdomen (done in 27 cases) and barium contrast studies (done in 17 patients) were suggestive of tuberculosis in 96 percent and 61 percent of cases respectively. Ultrasonography/CT guided Fine Needle Aspiration Cytology (FNAC) was also done in 18 patients of this subgroup and was positive in 15 patients. Both the groups received antitubercular treatment as per current recommendations.

Levels of CA-125 were measured with an enzyme immuno assay method (EIA) in all patients, at presentations (0 month), 3 months and 6 months respectively. A value of >35IU/ml was taken as positive.

Fifty healthy volunteers with no features of abdominal tuberculosis also underwent serum CA-125 assay at 0 month. Statistical analysis was carried out by using paired t-test, ROC Curve and Goldman test for calculating sensitivity, specificity, positive and negative predictive values. Statistical analysis was performed with the SPSS software package (version 11.0; SPSS Inc, Chicago, IL).

RESULTS

A total of 50 patients were included in the study. The most common presentations in the study group were acute and sub-acute intestinal obstruction. The most common symptoms were abdominal pain (82%), vomiting (72%) and fever (70%). CA-125 levels were positive (>35IU/ml) in 45 patients (90%) at 0 month with values ranging from 158IU/ml to 1326IU/ml (average 613.38IU/ml). The values remained high in 6 patients (12%) at 3 months of treatment and in 4 patients (8%) after 6 months of anti-tubercular therapy. Among 50 patients, 46 improved clinically after anti tubercular treatment on reassessment at 3 and 6 months. Two patients failed to show improvement, one patient died after 8 months of treatment and one patient was lost to follow up after 6 months. Two patients who failed the primary therapy were started on second line of therapy and improved subsequently.

Table 1: Levels of CA-125 among cases and controls at zero month.

Group	No.	Mean	SD	SE	95%confidence interval
1	50	613.38	347.2	49.11	514.68-712.08
2	50	13.62	17.78	2.51	8.57-18.68
Combined	100	313.50	388.1	38.82	236.39-390.53
Difference		599.75		49.17	502.16-697.35

P<0.001

Table 2: Difference in ca-125 levels at zero and three months.

Variable	No.	Mean	SD	SE	95%confidence interval
CA-0	50	613.38	347.29	49.11	514.68-712.08
CA-3	50	78.918	207.07	29.29	20.07-137.77
		534.46	321.61	45.48	443.06-625.86

CA-0: CA-125 at zero months; CA-3: CA-125 at three months

Table 3: Difference in Ca-125 levels at zero and six months.

Variable	No.	Mean	SD	SE	95%confidence interval
CA-0	50	61.31	347.28	49.11	514.68-712.07
CA-6	50	70.758	240.95	34.07	2.279-139.24
difference		542.62	346.74	49.03	444.07-641.06

CA-0: CA-125 at zero months; CA-3: CA-125 at three months

Table 4: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for serum CA-125 in diagnosis of abdominal tuberculosis at 0, 3 and 6 months.

Stage of assessment	0 month	3 months	6 months
Sensitivity	90%	12%	8%
Specificity	96%	96%	96%
PPV	95.74%	75%	66.67%
NPV	95.57%	52.17%	51.06%

Of the controls, two had a positive CA-125 assay with levels of 88 and 96IU/ml respectively and were further investigated for alternative diagnosis. The levels were not raised in other healthy subjects. Using the paired t-test, the difference in the levels of CA-125 among the cases and control groups at 0 month was found to be statistically significant ($p < 0.001$) (Table 1). The difference in CA-125 levels among cases at 0 and 3 months and 0 and 6 months were also statistically significant (Table 2,3). Thus, the test was found to have a high sensitivity and specificity when the disease was active (90% and 96% at 0 month). The sensitivity decreased with initiation of anti-tubercular therapy (Table 4), however no decrease in specificity was observed during the study time period. High serum CA-125 levels were also found in patients with tuberculous ascites in whom bacteriological studies of ascetic fluid were negative.

DISCUSSION

Despite the widespread impression worldwide that abdominal tuberculosis is rare today, the disease continues to appear regularly in the Indian subcontinent. It constitutes the third most common etiological factor for ascites after cirrhosis and malignancy and is also among the most frequent causes of extra pulmonary tuberculosis.⁶ The onset of disease is usually insidious although presentation as an acute abdomen is well known. The symptoms are usually abdominal distension, weight loss, abdominal pain and fever.⁷ The disease can be difficult to diagnose in some instances even with the combined approach including clinical, radiological as well as invasive technique.⁸ The definitive diagnosis is dependent on histopathological finding of characteristic granulomas which however is not available in all cases. Culture of acid fast bacilli also requires large amount of ascitic fluid and with a limited success.⁹ Use of polymerase chain reaction for detection of mycobacterium is not possible widely because of high cost as well unavailability in the developing countries.

CA-125 is a glycoprotein oncofetal antigen that is secreted by different coelomic epithelium. Increased serum levels of CA-125 have been reported in various malignant and benign conditions and also in 1-2 percent of healthy individuals.¹⁰ The benign conditions associated with increased levels of CA-125 are cardiac failure,

pulmonary disease, cirrhosis and in patient with previous history of surgery.¹¹ Elevated levels of CA-125 have also been reported in other non-malignant conditions like pelvic inflammatory disease, endometriosis, peritoneal dialysis, pancreatitis and autoimmune diseases.¹²⁻¹⁴ Uzunkoy et al observed elevated levels in four patients out of eleven cases of abdominal tuberculosis in their study.¹⁵ WU JF et al also reported increased CA-125 levels in a thirteen year old girl with tuberculous peritonitis mimicking peritonitis carcinomatosis.¹⁶ Two patients out of four women with peritoneal tuberculosis mimicking ovarian malignancy also presented with elevated CA-125 in another report.¹⁷ Thakur et al also suggested that a high CA-125 in patients with abdominopelvic mass with or without ascites should raise a suspicion of tuberculosis.¹⁸

Serum CA-125 level was high in a case of tuberculous peritonitis accompanied with active pulmonary tuberculosis in which acid fast bacilli were detected in ascites.¹⁹ In the present study 46 patients out of a total of 50 had elevated serum CA-125 levels at 0 months thus affirming to the observations in other studies.²⁰⁻²⁴ Several studies have also observed a close correlation between the normalization of CA-125 levels with the response to anti-tuberculous therapy.^{25,26} Author on present study also found a steady decline in the elevated CA-125 levels coupled with clinical improvement after initiation of antitubercular therapy. The association was also statistically significant. Most of the studies in the literature have been done on peritoneal tuberculosis and to the best of our knowledge none has been done on the other forms of abdominal tuberculosis.

In the present study we also found elevated levels of CA-125 in other forms of abdominal tuberculosis like intestinal obstruction secondary to hypertrophic tuberculosis and mesenteric lymphadenitis. Though the levels were moderately high in obstructive cases, they were minimally raised in mesenteric lymphadenitis. Very high levels were found in ascites and peritonitis cases.

CONCLUSION

The present study suggests that CA-125 may be a valuable parameter in diagnosing and determination of disease activity. However, as its levels are also known to increase in other benign and malignant conditions the test seem more applicable in monitoring of disease activity and its response to therapy.

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