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Original Article

A Clinical Study on Active Pulmonary Tuberculosis Using Cancer Antigen-125 as a Diagnostic and Prognostic Tool

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Abstract

Background: Cancer antigen-125 (CA-125) is produced by coelomic epithelium. Its levels are increased in malignant diseases, like ovarian cancer but also in other medical conditions, such as pulmonary and extra-pulmonary tuberculosis (PTB). TB is usually diagnosed using conventional methods such as smear microscopy, culture, and chest radiography. The other methods used are the detection of immunological response and the search for biochemical markers. CA-125 was evaluated mainly in patients with extra-PTB.

Aim of the Study: This study aims to use CA-125 in differentiating PTB from other pulmonary infections; also to determine its value as an indicator of response to antituberculous drugs.

Materials and Methods: Group A consisted of 42 patients with active PTB, Group B consisted of 23 patients with extra-PTB, and Group C consisted of 21 healthy volunteers. CA-125 levels were estimated in all the groups. It was reassayed 4 months after antituberculous medication in Group A.

Observations and Results: The CA-125 values of Group A were higher at significant levels than the other groups. The sensitivity and specificity of CA-125 were found to be 79.34% and 91.30%, respectively, at a 34.6 U/ml cutoff point.

Conclusions: CA-125 was a useful tool in differentiating PTB from extra-PTB. It was also useful in assessing the response to antituberculous drugs in patients.

Key words: Cancer antigen-125, Malignancy and immunological response, Tuberculosis

INTRODUCTION

Even today, tuberculosis (TB) represents an important health problem worldwide that was declared by the World Health Organization to be global emergency;[1] the most common form of clinical form of presentation with TB is pulmonary type. 95% of TB cases reported from developing countries.[2] It is estimated that 12 million patients are coinfected with HIV and mycobacterium TB, with the majority living in Africa and Southeast Asia.[3] Microscopic examination and demonstration of acid-fast stained sputum smears is the most useful diagnostic method. If it is positive, the initiation of TB therapy and respiratory isolation could be started immediately. However, in few patients, positive acid-fast bacillus in sputum samples may be negative or respiratory specimens may not be available, and other methods have to be used to establish the diagnosis of TB. In addition to microbiological molecular diagnostic tests, certain biochemical parameters are being used as helpful tools for this purpose, including various markers of cellular activity, acute phase reactants, and enzymes.[4-8] Cancer antigen-125 (CA-125) tumor marker also was proposed as a useful diagnostic tool for TB. CA-125 serum concentrations are known to rise in some benign and malignant diseases.[9,10] High serum levels of CA-125 are reported in patients with pulmonary and extra-pulmonary TB (PTB), including pleural, peritoneal, pelvic, miliary, and intra-abdominal TB. However, the diagnostic value of CA-125 to help differentiate PTB from other pulmonary infections has been poorly studied.[11-13] CA-125 antigen or carbohydrate antigen-125 is a high-molecular-weight glycoprotein (200 KDa) which was identified on the surface

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of the ovarian carcinoma cell line OVCA 433 by Bast *et al.*,[14] in 1981. High levels of CA-125 have been reported in patients with pulmonary and extra-PTB, including pleural, peritoneal, pelvic, miliary, and intra-abdominal disease.[11-13] The present study was conducted to assess the specificity and accuracy of serum CA-125 levels in differentiating PTB and non-PTB; to use its levels as prognostic tool to know the effect of antituberculous chemotherapy.

Institution of Study

This study was conducted at Kannur Medical College, Anjarakandy, Kannur.

Period of Study

This study was from May 2010 to –April 2013.

MATERIALS AND METHODS

A total of 86 subjects were included in the present study. They were divided as Group A consisted of 42 patients with active PTB, Group B consisted of 23 patients with extra-PTB, and Group C consisted of 21 healthy volunteers. An ethical committee clearance was obtained before commencing the study. An ethical committee cleared consent form was used to collect the data.

Inclusion Criteria

1. Patients aged above 18 years were included in all groups
2. Patients with active PTB were included in Group A
3. Patients with non-PTB diseases were included in the Group B
4. Healthy subjects were taken as control
5. Patients with typical symptoms of TB such as cough, expectoration, fever, chills, evening rise in temperature, night sweating, loss of weight, and appetite were included.

Exclusion Criteria

1. Patients non-TB lung diseases were excluded.
2. Patients with acute pyrexia of unknown origin were excluded.
3. Patients with COPD were excluded.
4. Patients with rheumatic fever or carditis were excluded.
5. Patients with malignancies, cirrhosis of liver, renal diseases, and gynecological tumors were excluded.
6. Patients with heart failure (left-sided heart failure) were excluded.

All the patients in Group A (42 patients) were elicited about their illness and symptoms of TB. All the patients were subjected to TC, DC, ESR, and Mantoux test, sputum for AFB, X-ray chest, and serum CA-125 levels. All patients in Group A received antituberculous drugs in the form of 2 months of intensive therapy of rifampicin, isoniazide, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazide. After 2 months of treatment, sputum smears were repeated and conversion into sputum smear-negative occurred in all patients. Radiological signs of PTB were noted in the data. In Group B, patients (23 patients) with non-PTB were included. Patients in this group were those who had cervical TH lymphadenitis, TB osteomyelitis, and renal TB and dermatological TB diseases. All the patients in this group were negative for sputum AFB staining. All patients in group A received antituberculous drugs in the form of 2 months of intensive therapy of rifampicin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazid. After 2 months of treatment, serum CA-125 levels were estimated. Group C subjects were healthy individuals without respiratory symptoms or TB symptoms. They also were subjected to all the tests on special consent. 5 ml of venous blood was drawn from each subject. Blood samples were left to clot for 15–20 min at 37°C, and then centrifuged at 3000 rpm for 20 min. Expressed serum was frozen at 40°C till the time of CA-125 assay. The results were automatically calculated by the instruments and the concentrations were expressed in U/ml. Another assessment of serum CA-125 was detected among Group (A) only after 4 months of antituberculous drugs. All the data collected were analyzed using standard statistical methods; $P < 0.05$ was taken as significant.

OBSERVATIONS AND RESULTS

In the Group A 42 patients, there were 28 males and 14 female patients. The age group was between 20 and 60 years with a mean age of 38.42 ± 2.68 years. In the Group B 23 patients, there were 15 males and 08 female patients. The age group was between 20 and 60 years with a mean age of 36.35 ± 3.47 years. In the Group C 21 patients, there were 11 males and 10 female patients. The age group was between 20 and 60 years with a mean age of 39.10 ± 2.68 years [Table 1]. The data are not significant in regards with the formation of groups ($P = 0.601$) but significant in regards with the mean age ($P = 0.041$), [Table 1].

The mean CA-125 levels in Group A were 91.6 U/ml, in Group B, it was 61.4 U/ml, and in Group C, it was 12.6 U/ml. The CA-125 levels were significant.

Table 1: The gender incidence and age incidence (*n*=A-42, B-23, C-21)

Gender	Group A	Group B	Group C	*P* value
Male	28	14	11	0.601
Female	15	08	10	-
Mean age	38.42±2.68	36.35±3.47	39.10±2.68	0.041

CA-125: Cancer antigen-125

Higher among Group A compared to normal subjects in Group C ($P = 0.006$) [Table 2]. The CA-125 values are compared between Groups B and C and found to be significant ($P = 0.028$). Similarly, the CA-125 values compared between A and B groups were not significant ($P = 0.061$) ($P < 0.05$).

Serum CA-125 levels were reassayed after 4 months of antituberculous treatment among Groups A and B patients. CA-125 levels were significantly lower after treatment than before in Group A patients; it was 32.7 U/ml, and in Group B, it was 27.4 U/ml with $P = 0.008$ [Table 3].

The radiological signs before and after treatment in Group A patients were correlated with the C-125 levels and found that there was statistical significance with $P = 0.042$ [Table 4].

The sensitivity and specificity of CA-125 values in the diagnosis and as a tool of prognostic assessor in the study were calculated from the data and found to be 81.4% and 95%, respectively.

DISCUSSION

CA-125 levels in the serum as a tumor marker although used in the diagnosis and assessing the prognosis of ovarian and other malignant tumors in the literature, later, it was found to be useful in diagnosing the benign conditions also. It was reported in literature that serum CA-125 levels were higher than normal in patients with pulmonary and extra-PTB and that serum CA-125 level may be a useful marker for discriminating between patients with active TB and those with inactive disease.[6,13,15] In the present study, serum CA-125 levels were significantly higher in Group A patients with active PTB when compared to healthy subjects as well as Group B patients with non-PTB and healthy subjects of Group C [Table 2]. The mean CA-125 values in a study by Yilmaz *et al.*[15] among patients with PTB were ([109.7] 86.9 U/ml), while it was ([118.46] 248.41 U/ml) in Ozsahin *et al.* study;[16] which are closer to the values in the present study (91.6 U/ml). On the other hand, Kim *et al.* study[17] showed a lower mean value of CA-125 in patients with active PTB ([54.5] 22.4). The difference may be due to the different methods of diagnosis used for tuberculous; they depended on sputum culture while in this study sputum examination of acid-fast bacillus was used. The authors Ronay *et al.*[18] determined that CA-125 was immunohistochemically localized and sharply demarcated around tubercular granuloma with peritoneal TB; they concluded that the inflammatory mesothelial cell proliferation was the source for secretion of CA-125 in patients with TB. In the present study, there was a significant positive correlation between serum CA-125 levels and incidence of positive radiological signs of PTB [Table 4]. Similar results are in agreement with those reported by Kanagarajan *et al.*,[19] who found that levels of CA-125 being highest in cavitary PTB and in miliary TB. Kim *et al.*[17] also found that CA-125 levels appeared to be highest in patients with cavitary rather than nodular type and this may reflect the level or extent of the infection. In the present study, there was an insignificant correlation of age and sex to CA-125 among the entire studied Table 1. The sensitivity and specificity of CA-125 values in the diagnosis and as a tool of prognostic assessor in the study were calculated from the data and found to be 81.4% and 95%, respectively.

Table 2: The serum CA-125 levels in the three Groups A-C (*n*=A-42, B-23, C-21)

Observation	Group A	Group B	Group C	*P* value
Mean serum CA-125	91.6 U/ml	61.4 U/ml	12.6 U/ml	0.006

CA-125: Cancer antigen-125

Table 3: The mean serum CA-125 levels before and after treatment (*n*=A-42, B-23)

Mean serum CA-125	Group A	Group B	*P* value
Before treatment	91.6 U/ml	61.4 U/ml	
After treatment	32.7 U/ml	27.4 U/ml	0.008

CA-125: Cancer antigen-125

Table 4: Correlation between radiological signs and CA-125 levels in Group A patients (*n*=42)

Observations	Before treatment	After treatment	*P* value
Radiological signs positive	43	04	
Mean serum CA-125 levels	91.6 U/ml	32.7 U/ml	0.042

CA-125: Cancer antigen-125

REFERENCES

1. World Health Organization. Global Tuberculosis Control: Surveillance, Planning, and Financing. WHO Report No. WHO/HTM/TB: 331. Geneva: WHO; 2004.
2. World Health Organization. Groups at Risk: WHO Report on the Tuberculosis Epidemic 1996. Geneva, Switzerland: World Health Organization; 1996.
3. Barnes PF, Lakey DL, Burman WJ. Tuberculosis in patients with HIV infection Infect. Dis Clin North Am 2002;16:107-26.
4. Ameglio F, Giannarelli D, Cordiali-Fei P, Pietravalle M, Alemanno L, Paone G, *et al.* Use of discriminant analysis to assess disease activity in pulmonary tuberculosis with a panel of specific and nonspecific serum markers. Am J Clin Pathol 1994;101:719-25.
5. Hosp M, Elliott AM, Raynes JG, Mwinga AG, Luo N, Zangerle R, *et al.* Neopterin, beta 2-microglobulin, and acute phase proteins in HIV-1-seropositive and -seronegative zambian patients with tuberculosis. Lung 1997;175:265-75.
6. Aoki Y, Katoh O, Nakanishi Y, Kuroki S, Yamada H. A comparison study of IFN-gamma, ADA, and CA125 as the diagnostic parameters in tuberculous pleuritis. Respir Med 1994;88:139-43.

7. Taha RA, Kotsimbos TC, Song YL, Menzies D, Hamid Q. IFN-gamma and IL-12 are increased in active compared with inactive tuberculosis. Am J Respir Crit Care Med 1997;155:1135-9.
8. Verbon A, Juffermans N, Van Deventer SJ, Speelman P, Van Deutekom H, Van Der Poll T, *et al.* Serum concentrations of cytokines in patients with active tuberculosis (TB) and after treatment. Clin Exp Immunol 1999;115:110-3.
9. Hunter VJ, Weinberg JB, Haney AF, Soper JT, Lavin P, Metsch L, *et al.* CA 125 in peritoneal fluid and serum from patients with benign gynecologic conditions and ovarian cancer. Gynecol Oncol 1990;36:161-5.
10. Buamah P. Benign conditions associated with raised serum CA-125 concentration. J Surg Oncol 2000;75:264-5.
11. Yoshimura T, Okamura H. Peritoneal tuberculosis with elevated serum CA 125 levels: A case report. Gynecol Oncol 1987;28:342-4.
12. Candocia SA, Locker GY. Elevated serum CA 125 secondary to tuberculous peritonitis. Cancer 1993;72:2016-8.
13. Simsek H, Savas MC, Kadayifci A, Tatar G. Elevated serum CA 125 concentration in patients with tuberculous peritonitis: A case-control study. Am J Gastroenterol 1997;92:1174-6.
14. Bast RC Jr, Xu FJ, Yu YH, Barnhill S, Zhang Z, Mills GB, *et al.* CA 125: The past and the future. Int J Biol Markers 1998;13:179-87.
15. Yilmaz A, Ece F, Bayramgürler B, Akkaya E, Baran R. The value of ca 125 in the evaluation of tuberculosis activity. Respir Med 2001;95:666-9.
16. Ozsahin SL, Turgut B, Nur N, Dogan OT, Erselcan T, Berk S, *et al.* Validity of the CA125 level in the differential diagnosis of pulmonary tuberculosis. Jpn J Infect Dis 2008;61:68-9.
17. Kim HS, Choi HY, Lee M, Suh DH, Kim K, No JH, *et al.* Systemic inflammatory response markers and CA-125 levels in ovarian clear cell carcinoma: A Two center cohort study. Cancer Res Treat 2016;48:250-8.
18. Ronay G, Jäger W, Tulusan AH. Immunohistochemical and serologic detection of ca-125 in patients with peritoneal tuberculosis and ascites. Geburtshilfe Frauenheilkd 1989;49:61-3.
19. Williams KJ, Rupanagadi V, Jalliard M, Gandy G, Gupta K, KrishmanIs P. CA-125 a reliable serum marker for diagnosis of tuberculosis? Chest 2005;128:141S.

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