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Cancer antigen 125 levels in patients with ascites

Asitli hastalarda KanserAntijen-125 değerleri

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Background/aims: *Cancer antigen 125 is a glycoprotein of 220 kDA molecular weight, that is released from coelomic epithelium during embryonic development. It has a low specificity, and high levels have been shown in many benign and malignant diseases. High correlation was detected between its level and ascites, especially in cirrhotic patients. In this study, we aimed to evaluate cancer antigen 125 levels in patients with ascites and determine the relationship between these levels and the amount of ascites.* ***Methods:*** *Fifty-eight patients (25 men, 33 women, mean age 54.34 years) with ascites, hospitalized in our clinic, were included in the study. The patients with ovarian cancer were not included. For all patients, physical examination and abdominal USG were done and blood samples for routine screening and cancer antigen 125 were obtained and studied on the same day.* ***Results:*** *Mean cancer antigen 125 levels in all patients were higher than normal. The highest levels were detected in patients with massive ascites and cirrhosis. With regard to diagnosis, the levels of cancer antigen 125 between groups were insignificant. According to USG results, there was a weakly positive but important correlation between groups. Although no correlation was present between cancer antigen 125 and ALT levels, a weak but positive correlation was present with AST levels.* ***Conclusion:*** *Our study showed that a correlation is present between cancer antigen 125 levels and the presence and amount of ascites. We also suggest that if cancer antigen 125 levels are above normal, the presence of ascites not detected by physical examination should be kept in mind.*

Keywords: Tumor markers, cancer antigen 125, ascites

Amaç: *Kanser Antijen 125 yaklaşık 220 kDA molekül ağırlığında, embryonik gelişim sırasında çölemik epitelden üretilen bir glikoproteindir. Spesifisitesi düşük bir belirteçtir ve pek çok benign ve malign olayda yüksekliği bildirilmiştir. Özellikle sirozda asit varlığı ile Kanser Antijen 125 arasında belirgin bir korelasyon saptanmıştır. Biz de bu çalışmamızda asitli hastalardaki Kanser Antijen 125 düzeylerini ve bu değerlerin asit miktarı ile olan ilişkisini belirlemeyi amaçladık.* ***Yöntem:*** *Çalışmaya 3. Dahiliye Kliniğinde Mart 2001-Mart 2002 tarihleri arasında yatmış olan 58 asitli hasta dahil edildi. 25'i erkek, 33'ü kadındı ve ortalama yaşları 54.34 yıl idi. Over malignitesi olanlar çalışmaya dahil edilmedi. Hastaların fizik muayeneleri, abdominal USG'si yapıldı, rutin tetkikleri ve kanser antijen 125 için kan örnekleri alındı ve bekletilmeden çalışıldı.* ***Bulgular:*** *Hastaların tümünde ortalama Kanser Antijen 125 düzeyi normalin üstünde saptandı. Sirozlu hastalarda ve masif asiti olanlarda en yüksek değerler saptandı. Kanser Antijen 125 değerlerinin tanılara göre gruplar arası farkı önemsiz saptandı. USG sonuçları ile kanser antijen 125 değerleri arasında pozitif yönde zayıf ama önemli bir ilişki saptandı. Transaminazlardan ALT ile belirgin bir korelasyon saptanmazken AST ile arasında pozitif fakat zayıf bir ilişki saptandı.* ***Sonuç:*** *Bu çalışmamızda asit mai varlığı ve miktarı ile Kanser Antijen 125 değerleri arasında bir ilişki olduğunu ve fizik muayene ile tespit edilemeyen asit varlığının bu belirtecin yüksekliği durumunda akla gelmesi gerektiğini ortaya koyduk.*

Anahtar kelimeler: Tümör markırları, kanser antigen 125, asit

INTRODUCTION

Cancer antigen 125 (CA 125) is a glycoprotein of 220 kDA molecular weight, that is derived from coelomic epithelium during embryonic development (1). It was first immunized with epithelial ovarian carcinoma cell series (OVCA 433) by Bast et al. in 1981 and defined as a monoclonal antibody by somatic hybridization with spleen cells of mice. It was then defined as OC-125 (2).

Kabawat et al. suggested that CA 125 expression is present in most ovarian epithelial tumors, but not in other types of tumors, by using immunohistochemical methods (1,3,4). Detection of CA 125 with radioimmunoassay method has been suggested in evaluating the follow-up of ovarian epithelial cancer, and in more than 80% of histologically proven ovarian cancer cases, increased CA 125 levels have been detected (4).

Cancer antigen 125 has a low specificity as a tumor marker. High levels were detected in many benign and malignant diseases, such as in lung,

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mammarian, and pancreatic cancers, gynecologic malignancies, hepatobiliary system malignancies, colorectal cancer, endometriosis, pelvic inflammatory disease, ovarian hyperstimulation syndrome, and liver cirrhosis (4-18).

In chronic liver diseases, especially liver cirrhosis, CA 125 levels are usually elevated. In acute and chronic hepatitis, this rate is 2-22%, and in cirrhosis 20-100% (7-11,19-23). A significant correlation has been detected between CA 125 levels and the presence of ascites in cirrhotic patients (10,24-26). In cirrhosis, higher CA 125 levels have been detected in patients with ascites than in those without, at rates of 83-100% and 20-38%, respectively (8,10,23). According to these results, it is suggested that a strong correlation is present between ascites and increased CA 125 levels, and that CA 125 can be used in detection of ascites.

In this study we aimed to evaluate both the CA 125 levels in different diseases and the probable relation between the high levels and the amount of ascites.

MATERIALS AND METHODS

Fifty-eight patients with ascites (25 male, 43.1%; 33 female, 56.9%) who were hospitalized in our clinic between March 2001 and March 2002 were included in this study (Table 1). The patients' ages were between 16-78 years; mean age was 54.34 years. Ovarian cancer patients were excluded from the study. Of 58 patients with ascites, 30 were liver cirrhosis (15 hepatitis B, 8 hepatitis C, 3 alcohol, and 4 cyryptogenic) (51.7%), 4 were peritoneal tuberculosis (6.9%), 9 were heart failure (15.5%) and 8 were malignancies other than ovarian cancer (13.8%). Seven patients were grouped as others (12.1%); 1 lupoid hepatitis, 2 portal venous thrombosis, 1 nephrotic syndrome, 1 pancreatitis, 1 endometriosis and 1 peritonitis (Table 2).

Table 1. Sex distribution of patients

	Number	%
Male	25	43.1
Female	33	56.9
Total	58	100

Table 2. Diagnosis of patient groups

	Number	%
Liver cirrhosis	30	51.7
Tuberculosis	4	6.9
Cancer	8	13.8
Heart failure	9	15.5
Others	7	12.1
Total	58	100

In the hospital, physical examination and abdominal ultrasonography (USG) were performed on all patients and venous blood samples were obtained for blood count, biochemistry, and CA 125 levels. The samples were studied on the same day. CA 125 levels were measured by immulyte OM-MA method. Normal range is between 1.9 U/ml -16.3 U/ml.

The amount of ascites was classified with regard to physical examination and USG findings into one of three groups: minimal ascites was defined as the amount that can be recognized only by USG around liver and between intestinal loops, but not by physical examination; medium ascites indicated an amount not causing distension in the abdomen, but with palpable liver and spleen easily visualized on USG; massive ascites indicated distension in the abdomen and visualization on USG. In our study, 7 patients (12.1%) had minimal, 14 (24.1%) medium, and 37 (63.8%) massive ascites (Table 3).

ANOVA test was used for evaluation of the significance of CA 125 levels in regard to the different groups according to diagnosis. Spearman's rank correlation analysis was used to determine the correlation between CA 125 levels and the amount of ascites and transaminases. A value of $p<0.005$ indicated significance. The variants were homogeneous according to Levene test. The levels were defined as mean +/- SD.

Table 3. Degree of ascites of patients

	Number	%
Minimum	7	12.1
Medium	14	24.1
Massive	37	63.8
Total	58	100

RESULTS

In all patients, mean CA 125 levels were above normal. Mean CA 125 levels and standard deviations in all groups are shown in Table 4. Mean levels were 324.1 U/ml in liver cirrhosis, 287.0 U/ml in tuberculosis, 222.85 U/ml in malignancies, 280.42 U/ml in heart failure and 271.0.U/ml in the "others" group. The mean for the total population was 294.39 U/ml (Table 4). The minimum and maximum levels of CA 125 in all groups are shown in Table 5. Remarkably, in two patients, despite massive ascites, CA 125 levels were detected as normal; one was heart failure, the other was ma-

Table 4. Cancer antigen (CA) 125 levels according to subgroups

Diagnosis	No	Mean CA125	SD	St. Error	95% Confidence lower level	95% Confidence higher level
Liver Cirrhosis	30	324.1033	176.8245	32.2836	258.0760	390.1307
Tbc	4	287.0	110.2028	55.1014	111.6427	462.3573
Cancer	8	222.850	193.7128	68.4878	60.9020	384.7980
Heart failure	9	280.4222	194.7707	64.9236	130.7082	430.1362
Others	7	271.0429	222.3747	84.0497	65.3805	476.7052
Total	58	294.3966	181.5747	23.8419	246.6539	342.1392

Tbc: tuberculosis

Table 5. Maximum and minimum levels of cancer antigen (CA) 125 in subgroups

Diagnosis	Min	Max
Liver Cirrhosis	23.40	500.0
Tbc	202.0	449.0
Cancer	15.30	500.0
Heart failure	13.40	500.0
Others	20.50	500.0
Total	13.40	500.0

lignancy. In 14 patients, CA 125 levels were above 500 U/ml. Of these, one had medium and the others had massive ascites. With regard to diagnosis, the levels of CA 125 between groups were insignificant (F=0.537, p=0.709). According to Levene test the variants were all homogeneous (L=1.627, p=0.181).

Table 6. Cancer antigen (CA) 125 levels according to amount of ascites

Amount	Min (U/ml)	Max (U/ml)	Mean (U/ml)
Minimum	30.70	429.0	160.37
Medium	20.50	500.0	266.21
Massive	13.40	500.0	330.41
Total	13.40	500.0	294.39

Mean CA 125 levels were 160.37 U/ml in the minimal ascites group, 266.21 U/ml in medium ascites group and 330.41 U/ml in the massive ascites group (Table 6). The variants were homogeneous(L=1.021, p=0.367). According to USG results there was a weakly positive but important correlation between groups (F=3.0, p=0.058) (Table 7).

Table 7. Correlation Between Cancer Antigen (CA) 125 Levels and USG

			USG	CA125
Spearman's rho	USG	correlation (r) Coefficient	1.000	0.299
		Sig. (2-tailed) (p)		0.023
		N	58	58
	CA125	Correlation Coefficient	0.299	1.000
		Sig. (2-tailed)	0.23	
		N	58	58

With regard to transaminases, no correlation was present between CA 125 and ALT levels (r=0.034, p=0.799), and a weak but positive correlation was present between AST and CA 125 levels (r=0.166, p=0.214) (Table 8).

Table 8. Relation between cancer antigen (CA) 125 levels and transaminases

		CA125	ALT	AST
CA125	Pearson Correlation	1.000	0.034	0.166
	Sig. (2-tailed)		0.799	0.214
	N	58	58	58
ALT	Pearson Correlation	0.034	1.000	0.542
	Sig. (2-tailed)	0.799		0.0001
	N	58	58	58
AST	Pearson Correlation	0.166	0.542	1.000
	Sig. (2-tailed)	0.214	0.000	0.0001
	N	58	58	58

DISCUSSION

Cancer antigen 125 as a tumor marker is widely used in diagnosis and follow-up of ovarian cancer. Its sensitivity is high but specificity is low. High levels of CA 125 can be detected in cirrhosis, peritonitis, pancreatitis, endometriosis, uterine leiomyomas, benign ovarian cysts, pelvic inflammatory disease (PID) and malignant ovarian tumors. The origin of CA 125 is defined as not only ovarian cells, but also peritoneal, pleural, pericardial and endometrial cells and benign ovarian cysts (27). In this study, we evaluated both CA 125 levels in patients with benign and malignant ascites and also the correlation between ascites amount and CA 125 levels.

In previous studies it was suggested that CA 125 had a highly negative predictive value in evaluating the amount of ascites (95.9%) (26). But it was also suggested as a sensitive quantitative marker for ascites (sensitivity: 83.3%, specificity: 86.3%) and its levels were shown to be correlated with ascites amount (26, 28). In our study a weakly positive but important relation was also detected between USG findings and CA 125 levels.

With regard to ascites amount, although mean CA 125 levels were lowest in minimal ascites and highest in massive ascites, no significant correlation was detected between groups. This result may be due to the small number of patients included in the study.

The exact origin of CA 125 in patients with ascites has not been defined yet, but there are three theories: Kabawat et al. detected CA 125 in all kinds of coelomic epithelium derived from the same origin as pericardium, pleura and mesothelial cells lining the peritoneum (1). Mezger et al. defined CA 125 as a strong immunohistochemical marker in mesothelial cell proliferation (29). It was suggested that CA 125 may be synthesized from peritoneal epithelial cells as a response to mechanic distress because of ascites, and then diffuse to serum (16, 17). This can explain the ascites in diseases other than cirrhosis, and also the increasing levels of CA 125 parallel to the amount of ascites.

Molina et al. suggested that CA 125 levels can increase as a result of metabolic problems of tumor markers in chronic liver disease even if there is no ascites (30).

In this study we evaluated the high levels of CA 125 in patients with ascites and as a result we suggest that there is a correlation between CA 125 levels and presence and amount of ascites. Furthermore, if cancer antigen 125 levels are above normal, the presence of ascites not detected by physical examination should be kept in mind.

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