PROTEIN C LEVELS IN PATIENTS WITH MALIGNANCIES

Kanserli hastalarda protein C seviyeleri

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Summary: *Protein C is a vitamin-K-dependent plasma glycoprotein that inhibits coagulation by selectively inactivating the active forms of factor V and factor VIII. In 20 patients with malignancies and 10 healthy subjects, protein C levels were measured. Protein C levels in patients with malignancies (94.4 ± 19.4) were significantly lower than those in the control group (105.7 ± 11.71) (P < 0.05). In 10 patients with lung cancer, protein C levels (91.3 ± 12.13) were lower than those in the control group (P < 0.05). However there was no significant difference in plasma protein C levels between the other patients with malignancies (97.5 ± 25) and the control group(P > 0.05). These findings indicate that protein C deficiencies may occur in patients with lung cancer.*

Key Words: *Protein C, Malignancy.*

Özet: *Protein C, selektif olarak aktif faktör V ve faktör VIII'i inaktive ederek koagülasyonu inhibe eden, K vitamininie bağımlı bir plazma glikoproteinidir. 20 kanserli hasta ve 10 sağlıklı kontrolde, protein C seviyeleri (94.4 ± 19.4), kontrol gurubundan (105.7 ± 11.71) anlamlı derecede düşük bulundu (P < 0.05). Akciğer kanserli 10 hasta ile (91.3 ± 12.13) ile kontrol gurubu, arasında, protein C seviyeleri yönünden anlamlı bir fark bulunamadı (P > 0.05). Bu bulgular, akciğer kanserli hastalarda protein C eksikliği olabileceğini göstermektedir.*

Anahtar Kelimeler: *Protein C, Kanser*

Protein C is synthesized in the liver (7). It is the zymogen of vitamin K dependent serine protease involved in blood coagulation (3,7). In the absence of protein C, the inactivation of activated factor V and factor VIII is impared and the fibrinolytic capacity of the circulating blood is impared (9). These conditions promote excessive fibrin formation and thus constitute a risk factor for thrombosis (2,4).

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Patients with an inherited deficiency of protein C have been recognized in both heterozygous and homozygous states (9,10). Acquired protein C deficiency has been described in liver disease (which causes decreased synthesis), consumptive coagulation processes such as disseminated intravascular coagulation, sepsis, the postoperative state, and the adult respiratory distress syndrome (5, 6, 8,10). In this study we planned to determine the changes in plasma levels of protein C in patients with malignancies.

METHODS

We analysed samples from 20 patients with malignancy (10 patients with lung cancer, 10

other patients with malignancies); and 10 healthy persons as control group.The patients with liver disease and the recently operated were not included. Blood samples were collected into 0.1 vol 3.8 % sodium citrate, resulting with 9/1 ratio of blood/anticoagulant and centrifuged at 3000 r/min. for 20 min. to prepare platelet poor plasma. Pooled normal platelet-poor plasma was obtained from 10 healthy donors. All plasma was stored at 20°C for up to 3 weeks until use. Protein C antigen levels were determined by Enzyme Lynked Immuno-Sorbent Assay (ELISA) (Asserachrom protein C Kit) (1). Statistical calculations were made between patients and controls by Mann-Whitney U test. Significance was assigned to P values lower than 0.05. The results are expressed as mean ± standard deviation.

RESULTS

Ten healthy subjects, 6 women and 4 men (aged 24-34 years, mean 30.5 years) were assumed to represent a normal control population. In controls, there were no significant differences in plasma protein C concentrations between age and sex. (mean 105.7 ± 11.71 ; data not shown). Protein C levels were also measured in group with malignancies (mean 94.4±19.4). This group consisted of 20 patients (2 women and 18 men; aged 32-83 years; mean 55.6 years) (Table I).

Table I. Age, sex and protein C concentrations of patients

No	Age/Sex	Diagnosis	Protein C %
1.MB	60/M	LC	96
2.FÖ	48/M	LC	75
3.AB	48/M	LC	85
4.HÖ	60/M	LC	94
5.HBT	58/M	LC	98
6.SŞ	48/M	LC	95
7.MŞ	53/M	LC	105
8.MA	62/M	LC	110
9.AY	60/M	LC	80
10.AD	60/M	LC	75
11.SK	32/M	ML	105
12.SA	57/M	LaC	135
13.BG	65/M	HD	95
14.SY	53/F	MM	108
15.KD	60/M	ML	90
16.MS	63/M	HD	100
17.KÇ	55/F	BC	35
18.TY	28/M	HD	103
19.GA	83/M	PC	104
20.MG	58/M	ML	100

LC:Lung Cancer, ML: Malign Lymphoma, HD: Hodgkin Disease
MM: Multipl Myeloma, LaC: Larinx Cancer, BC: Breast Cancer, PC:Prostate Cancer

Protein C concentrations in patients with malignancies were significantly lower than in controls. (U= 142 ; $p < 0.05$). Furthermore, ten of the patients with malignancies were lung cancer. (10 men; aged 48-60 years; mean 56 years). Protein C levels in patients with lung cancer (mean 91.3 ± 12.13) were found to be significantly lower than in controls(U= 82 ; $P < 0.05$) (Table II).

Protein C levels of the other patients with malignancies (2 women and 8 men; aged 32-83 years; mean 55.4 years) were compared to the levels in controls. The difference was not statistically significant ($P > 0.05$). Protein C levels in patients with lung cancer were

Table II. Protein C levels of patients and controls.

	n	Mean Protein C Levels (%)	SD	% with low protein C levels	P value
Normal Subjects	10	105.7 (95-135)	11.71	--	--
All patients with malignancies	20	94.4 (35-135)	19.4	35	< 0.05
Patients with lung cancer	10	91.3 (75-110)	12.13	50	< 0.05
Other patients with malignancies	10	97.5 (90-135)	25	20	Not significant

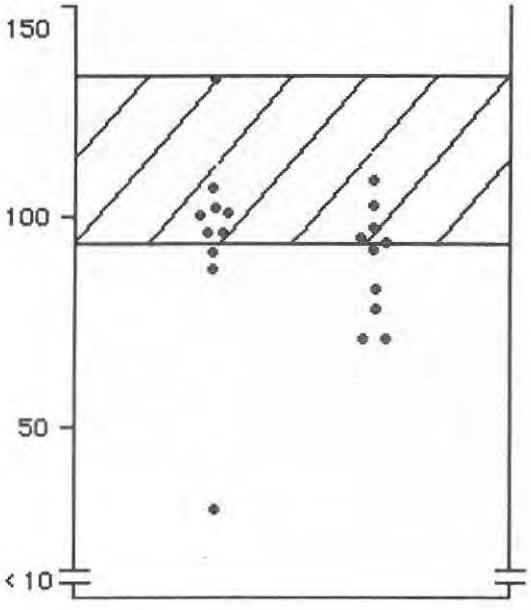

Fig 1. Protein C in patients with lung cancer (LC) and other patients with malignancies (OPM).Shaded area: normal range of protein C in healthy subjects. For differences between the patients with lung cancer and control group p<0.05.

significantly lower than the other patients with malignancies (U= 79; P < 0.05) (Fig 1).

DISCUSSION

Patients with an inherited deficiency of protein C have been recognized in both heterozygous and homozygous states (9,10). Thrombosis of the deep venous system is associated with pulmonary embolism in approximately 50 % of these patients.

Acquired protein C deficiency has been described in liver disease (which causes decreased synthesis), consumptive coagulation processes such as disseminated intravascular coagulation, sepsis, postoperative state, adult respiratory distress syndrome, and in terminal renal failure and during hemodialysis (5,6,10). But in one study, it was suggested that levels of protein C were not low in patients with terminal renal failure before and after hemodialysis (6). Previous studies suggested that levels of protein C were low in postoperative patients with malignancies (8). Low postoperative protein C levels might be explained by a latent disseminated intravascular coagulation state present before operation. However, low postoperative levels were also found in patients without cancer

undergoing relatively minor abdominal operations, such as appendicectomy and hernia repair (8).

In this study, we found that levels of protein C were significantly low in preoperative patients with lung cancer than in controls. However there was no significant difference between the other patients with malignancies and controls. In patients with lung cancer, low protein C concentrations might be explained by a latent DIC state (8). In one patient with breast cancer, protein C level was very low (%35). However, there was no history of thromboembolic attack in this patient. Our findings showed that there might be acquired defects in patients with lung cancer.

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