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Research Article

The Relation of Atopy Status with Response to Treatment in Lung Cancer Patients

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Abstract: The Objective of the study was to identify atopy ratio among lung cancer patients and then compare the response to treatment of lung cancer between atopic and non-atopic groups. Between December 2004 and August 2006; two hundred and one patients, whom were hospitalized and diagnosed as lung cancer, were evaluated by clinical and demographic properties and skin prick test results related to gender, smoking status, cancer cell type-stage and status due to response to treatment. The mean age of lung cancer diagnosed patients was 61.9±0.7. According to histopathologic classification %85 had non-small cell lung cancer and %15 had small lung cancer. In the %13.4 of the patients there was at least one sensitivity to inhalant allergens which were used in skin prick testing. The results of skin prick test on behalf of gender, smoking status, lung cancer type and stage were not significant ($p>0.05$). One hundred and thirty-six patients, whom were treated with chemotherapy, were evaluated at the end of three months and there was not a significant difference between the responses to treatment according to skin prick test results. There was not a significant relation between skin prick test sensitivity to inhalant allergens which was used as a criteria to asses atopy and response to the treatment of lung cancer. The possible effect of having an atopic status on cancer prognosis could not be claimed.
Keywords: Atopy, lung cancer, skin prick test, response to treatment

INTRODUCTION

Lung Cancer was among the rarely seen diseases in the beginning of last century. By the increases of smoking habits worldwide, the incidence of lung cancer has risen and has become the mostly diagnosed cancer type [1].

Atopy term was firstly used by American immunologist Arthur Coca. Atopy word was created from the 'weirdness' in old Greek language. It was described to define weird conditions in which the different reactions against allergens form in the human body [2]. Recently it is considered that there may be relation between allergic condition and tumor genesis [3]. Despite the contrary results in different studies, it's figured that there may be opposite relation between allergy and cancer [4]. In distinct studies it was expressed that hyperstimulating of immune system may cause diverse results [5].

The effective treatment of lung cancer is still being investigated. The factors effecting the tumor response in the disease will certainly be guides in the evolution of treatment. In this context we aimed to determine the atopy ratio in the lung cancer patients and compare the treatment responses between atopic and non-atopic patient groups.

MATERIALS AND METHODS

Two hundred and one newly diagnosed and nontreated lung cancer patients in Chest Diseases and Surgery Center participated in this study between December 2004-August 2006 and they had been examined prospectively. All the patients were informed about the study and their permissions were taken. Also ethic council approval was taken for the study.

The histopathologic classification of the tumors were done by Chest Diseases and Surgery Center Pathologic Department according to the 2004 WHO/IASC classification. Staging was done with respect to international lung cancers classification accepted by AJCC in 1996 [6].

The atopic conditions and allergen spectrum were assessed by skin prick testing. The antihistaminic and tricyclic antidepressant drugs were ceased one and two weeks before the test. The age criteria was between 16 and 85 for participating in the study. Pregnancy and

having the dermatologic lesions hindering the skin prick testing were the causes of exclusion.

Allergen sensitivities were assessed by reactions formed against 18 common aeroallergens (Dermatophagoides pteronyssinus, Dermatophagoides farinae , Mel. D'arbres trees mixture, Peuplier populus alba, 5 Graminees, Plantain plantago lan., Oseille rumex acetosa, Cereales , Armoise Artemisia vulgaris, Aspergillus mix, Mucor, Penicillium mix, Cladosporium, Alternaria, Blatte Germanique Cockroach, P.S. chien dog hair, P.S chat cat fur, Feathers mix plumes) produced by Stallergenes (France) company. Histamine and tremoin was used for positive and negative control.

Allergenes were applied at least 2 cm far away from each other. The results were evaluated 15 minutes after the test application. When the negative control reacted, it was accepted as dermographism and these patients were excluded from the study and if the positive control reacted less than 3 mm, these patients were excluded from the study due to the ineffective histamine response. It was accepted as positive reaction if the erythamatous papule was at least 3 mm more than negative control in the region where the allergen had been applied.

The patients were classified as atopic and nonatopic ones with regard to skin prick testing results; radiological and clinical controls were done at the end of 3 months after the chemotherapy treatment. The patients were grouped as complete response, partial response, progression and exits according to the responses to the cancer treatments..

Statistical Study

The datas obtained from our study were evaluated by loading SPSS (Statistical Package for Social Sciences) program in the Windows XP environment. Nominal values n (%) and results were marked as mean (%95 CI) ± SH. Chi-square or Fisher's exact test were used to interpret the relation between skin prick test sensitivity and gender, smoking history, lung cancer cell type, staging in the small and nonsmall cell lung cancer, treatment response at the end of three months in the patients treated with chemotherapy. Statistical significance threshold was taken as $p<0,05$. The relation between skin prick test sensitivity in the study group and society was evaluated by Z test.

Signs

Two hundred and one newly diagnosed nontreated lung cancer patients were included to the study. According to the histopathologic classification; %85 (n=171) of the patients were non-small cell lung cancer (NSCLC), %15 (n=30) were small cell lung cancer (SCLC) . The ages of the patients were between 34 and 82, the mean age was 61,9±0,7. %94,5 (n=190) of the patients were male, %5,5 (n=11) were female. While %36,3 of NSCLC were (n=62) epidermoid carcinoma and %21,6 (n=37) were adenocarsinoma, in %42,1 of patients (n=72) cell differentiation couldn't be done. In terms of NSCLC %4,1 (n=7) of patients were determined as stage 1, %5,8 (n=10) stage 2, %40,9 (n=70) stage 3 and %49,1 (n=84) stage 4. In terms of SCLC %53,3 (n=16) of the patients were limited, %46,7 (n=14) of them were diffuse cancer. Demographic and clinic properties of subjects involving in the study were given in the Table 1.

Table 1. Demographical and clinical properties of study group

	NSCLC N=171	**SCLC N=30**	**P**
Age,mean±SE(year) (min.-max.)	62.2±0.8 (34-82)	60.3±2 (43-80)	NS
Gender, N (%)			
Female	11 (6.4)	-	
Male	160 (93.6)	30 (100)	
Smoking, mean±SE (min.-max.)	51.9±2.7 (1-200)	48.2±3.9 (20-100)	
Cell type, N (%)			
Epidermoid	62 (36.3)	-	
Adenocarsinoma	37 (21.6)	-	
Undifferentiated	72 (42.1)	-	
Stage, N (%)			
Stage 1	7 (4.1)	-	
Stage 2	10 (5.8)	-	
Stage 3	70 (40.9)	-	
Stage 4	84 (49.1)	-	
Stage, N (%)			
Limited	-	16 (53.3)	
Diffuse	-	14 (46.7)	

In %13,4 (n=27) of the subjects there was sensitivity against at least one inhaled allergen. %66,7 (n=18) of the subjects were monosensitized, %33,3 (n=9) were polisensitized. The sensitivities to house dust mite, blatella, mold, pollen and animal allergenes were %28,6 (n=12), %28,6 (n=12), %14,3 (n=6), %16,7 (n=7) and %11,8 (n=5) consequently. When the skin prick test sensitivity with inhalant allergens were compared according to gender, smoking, cancer cell type and stages, it hasn't been found significant (p>0.05) (Table 2).

Table 2: Distribution of skin prick test results according to groups

		Skin prick test		P
		Positive N (%)	**Negative N (%)**	
Gender	Female	2 (18.2)	9 (81.8)	NS
	Male	25(13.2)	165 (86.8)	
Smoking	Smoker	25(13.5)	160 (86.5)	NS
	Non smoker	2 (12.5)	14 (87.5)	
Cell type	SCLC (n=30)	4 (13.3)	26 (86.7)	NS
	NSCLC(n=171)	23 (13.5)	148 (86.5)	
SCLC Stage	Limited stage	2 (12.5)	14 (87.5)	NS
	Diffuse stage	2 (14.3)	12 (85.7)	
NSCLC Stage	Stage 1	2 (28.6)	5 (71.4)	NS
	Stage 2	4 (40.0)	6 (60.0)	
	Stage 3	7 (10.0)	63 (90.0)	
	Stage 4	10 (11.9)	74 (88.1)	

One hundred and thirty-six subjects who had been treated only with chemotherapy were evaluated according to the treatment responses three months after the beginning of treatment. In %25,7 (n=35) of the subjects there was complete response, in %48,5 (n=66) partial response, in %22,1 (n=30) progression. %3,7 (n=5) of the subjects died in the following period. Skin prick test sensitivity with inhalant allergens were not unlike for all groups, NSCLC and SCLC (p>0,05) (Table 3).

Table 3: Skin prick test sensitivity with inhaled allergenes according to treatment response in the groups treated by chemotherapy

		Skin prick test		P
		Positive N(%)	**Negative N(%)**	
Treated with Chemotherapy T:136	Partial-complete response	14 (13.9)	87 (86.1)	NS
	Progression & Death	4 (11.4)	31 (88.6)	
SCLC N:29	Partial-complete response	3 (11.5)	23 (88.5)	NS
	Progression & Death	1 (33.3)	2 (66.7)	
NSCLC N:107	Partial-complete response	11 (14.7)	64 (85.3)	NS
	Progression & Death	3 (9.4)	29 (90.6)	

DISCUSSION

The relationship between cancer and atopy has been a wondered concept especially in the last quarter century. The common result of many studies on this issue hasn't been met. Different results have brought possible different mechanisms. The possibility of protection of augmented immunity against cancer cells with the atopy has been potent among these mechanisms. On the contrary augmented immune activity in the atopic subjects has possibility to form the chronic inflammation and increase the cancer risk. These two opposite opinions are emphasized in diverse studies [7-9].

The cancers of different organs and discrete atopy criterias were used in the studies analyzing relationship between cancer and atopy. These are the important factors in the occurrence of contradictory results. One of the atopy criterias is skin prick tests. Skin prick tests were applied to 201 newly diagnosed and nontreated lung cancer patients in our study. Our main target was to compare the treatment response clinically and radiologically between the lung cancer patients having the atopy and not. Since the radiological follow-up couldn't be significant in the surgically treated subjects, the comparing was done in the ones accepted as inoperabl and then treated with chemotherapy. The relation between skin prick test positivity and response to chemotherapy treatment was found insignificant in only NSCLC and only SCLC subjects (p>0,05). When SCLC and NSCLC were evaluated together, relation between skin test positivity and response to chemotherapy treatment were also found insignificant (p>0,05). Besides the relation between skin prick test

results and gender, smoking, cancer type and cancer stages were found insignificant (p>0,05). Skin prick test positivity in cancer patients were found lower than the healthy people in population in previous studies [10-12]. Some reasons may be considered for this. First of all there may be supression of immunity due to the cancer effects [7]. This change in immunity may be limited to the local immune response in skin or may be systemic which can be demonstrated by decrease of IgE level. Burtin and friends showed decreased skin sensitivity against histamine injection in the lung cancer patients [12]. It was emphasized that there is less skin test positivity in lung cancer patients than healthy control group in another study investigating the relation between atopy and cancer [11].

Furthermore the second possible reason may be the smoking habit in lung cancer patients of our study. Indeed allergen specific IgE levels were low in the smokers in a study of Wang and friends [13].

Thirdly the mean age of patients included in our study was high and this may be one of the possibilities. Advanced age is one of the substantial causes of false negative score in skin prick tests [14]. In a study done by Niemeijer and friends, it was detected that the positivity of skin prick tests other than grass polens was diminishing by the age [15]. In another study done by Schwarzenbach and friends, it was shown that skin reactions against histamine was decreasing by the age [16]. This low atopy ratio in the lung cancers caused the diminished number of patients who had lung cancer and atopy in our study.

The relation between skin prick test sensitivity to inhalant allergen which is used to define atopy and response to lung cancer treatment was not significant in our study. In this way it was shown that possesion of atopy didn't have any favorable or unfavorable effect on cancer treatment. It was asserted that there was no need in the change of chemotherapy protocol for the lung cancer patients having atopy by this study. Due to the lack of cases and low atopy level in the lung cancer patients in our study, new large series of studies with many combined atopy criterias are needed to understand the effect of atopy on treatment response in lung cancer.

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