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RESEARCH ARTICLE

CCL18 as immunomarker in patients with lung carcinoma

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Abstract

In current study fifty two patients suffering from lung cancer disease were admitted to the Oncology Unit of Al-Sadder Medical City /Al-Najaf Al-Ashraf during the period from January till August 2014. All lung cancer patients were diagnosed by specialist physician. Patients with lung carcinoma (n=52) were divided in two categories male (n=29) and female (n=23) and both male and female groups were subdivided into four categories according to types of lung cancer and stage of disease. By types, they were subdivided into four groups: squamous cell carcinoma, adenocarcinoma, large cell carcinoma and small cell carcinoma. By stage male and female groups they were subdivided into four groups stageI, stageII, stageIII and stage IV**.**, the result CCL18 of has shown significant increase ($p<0.05$) in squamous cell carcinoma than other types of lung cancer. In the current study serum levels of CCL18 shown in early stage is lower than in late stage in lung carcinoma patients

INTRODUCTION

Lung cancer determined as the most important malignant carcinoma because of its increased incidence and elevated prevalence. Lung cancer (pulmonary carcinoma) could be described as uncontrolled cell growth within the lung tissues, without treatment abnormal growth is spreading successfully by metastasis process into other part of the body .When the cancer begins in the lung, it is identified as primary lung cancers. Small cell lung carcinoma (SCLC) and non-small cell lung carcinoma(NSCLC) are the two types of pulmonary carcinoma , NSCLC can be divided in to three subtypes are adenocarcinoma (AD), squamous-cell carcinoma(SCC) and large-cell carcinoma(LCC). (Jemal *et al*., 2005; Horn *et al*., 2012).

Lung cancer is connected with highly mutations rates and research for immune system potential role versus lung cancer is ongoing .The interactions within the tumor microenvironment between tumor-infiltrating immune cells and tumor cells have been shown the effect of the immune response in NSCLC (Ho MY, *et al* ., 2011; Lawrence, *et al*., 2013).

The capacity of tumor to induce an immune response called a cancer immunogenicity. When the rate of mutations increased tumor immunogenicity increased too .Greatly change occurs in tumor antigen, leading to these antigens which are able to trigger the immune response (Chen et al., 2012; Chen and Mellman ,2013).

CCL18 is a cytokine part from the family of chemokine known as CC, C-C motif or Chemokine ligand 18, possibly known as macrophage inflammatory protein-4 , macrophage activation alternative connected with CC chemokine-1, dendritic cell -chemokine 1,Pulmonary and activated of chemokine regulation and DC-derived CC chemokine 1,The innate immune system by their antigen-presenting cells can produced CCL-18 such as monocytes, macrophages and dendritic cells generate this a 7.8-kDa chemokine(Ferrara *etal*.,2008;Bellinghausen

etal.,2012;Schraufstatter etal.,2012).This C-C motif acquired from fetal lung of human and reveal that elevated level in lung together with it is inducible expression in some lines of human cell led to appointment as Pulmonary and activated of chemokine regulation, also this chemokine encoding a polypeptide of 89 amino acids by an open-reading frame, in this way the submitted NH2-terminal hydrophobic signal sequence can cleavage and produce a mature protein consist of sixty nine amino acids lacking a site of putative N-glycosylation (Wells *et al.*,1997;Schutyser *et al*.,2005;Frauenschuh *et al*.,2007).

CCL18 has main role is the lymphocytes homing and DC to micro anatomical places of the lymphoid secondary organs and in the lymphoid structures organization under physiological situations wherefore this chemokine to be both characteristics inducible-inflammatory and a constitutive-homeostatic, CCL18 can mediate native T cells attraction toward the completely matured and DC could be help in a primary immune response mounting this occur in sever inflammation, the cells that produce of this chemokines also can be attract native B cells to the edge of the T cell zones to effector Th2 cells and to bring them in closer vicinity of potential antigen(Kuscher,2008;Baay *et al*.,2011).

Materials and Methods

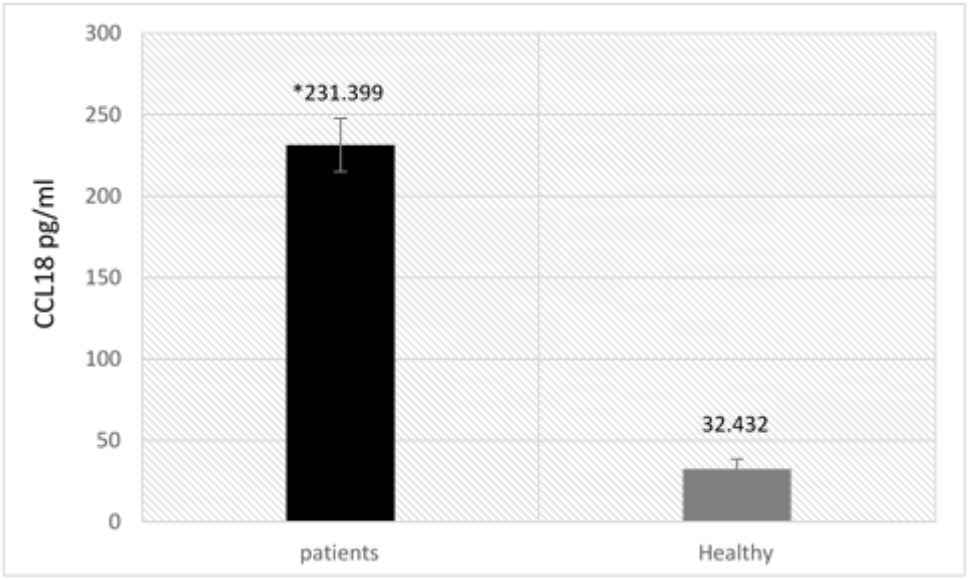
Serum CCL18 Estimation

This assay is executed with specific kit for test, supplied by (US Biological, life Sciences.).

Result:

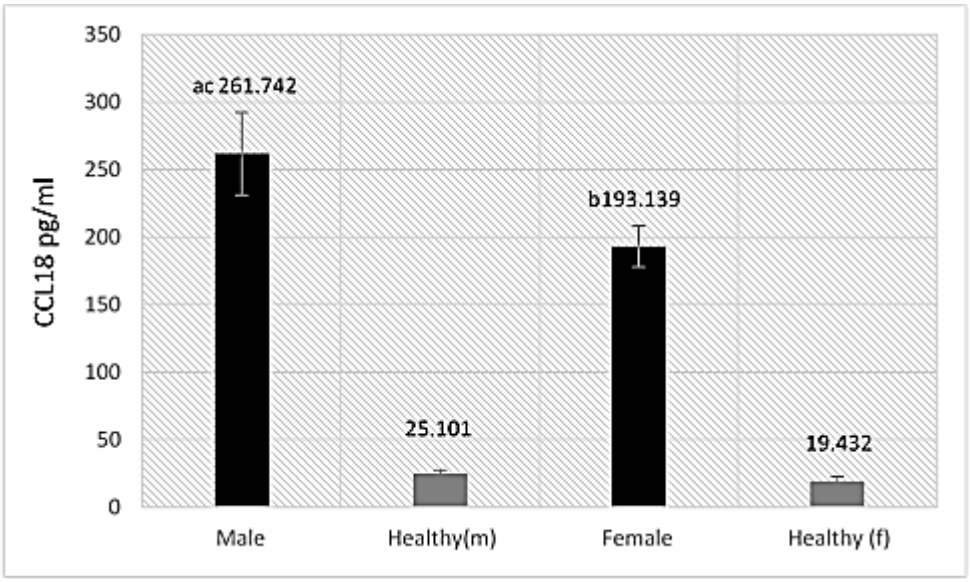
The result in figure (1) explained significant increase ($p<0.05$) serum concentration 0f CCL18 in lung cancer patients group (231.399± 42.427 pg/ml) as compare with healthy group (32.432± 32.241 pg/ml).

Whereas the result in figure (2) also showed significant increase ($p<0.05$) serum concentration of CCL18 in lung cancer patients male group (261.742± 30.599 pg/ml) compared with male healthy group (25.101±2.101 pg/ml) and female group (193.139± 15.403 pg/ml) as compared with female healthy group (19.432± 3.224 pg/ml).



*Statistically significant differences ($P < 0.05$) between patients, healthy group.

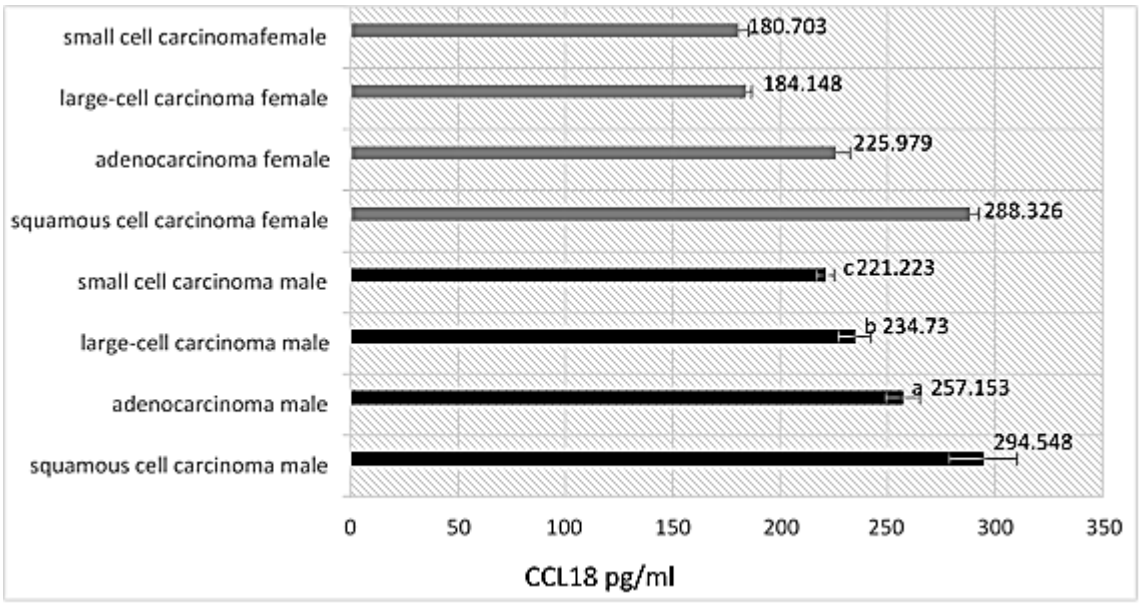
Figure (1): Serum level of CCL18 in lung cancer patient's comparison with healthy group.



(a) Statistically significant differences (P < 0.05) between male, healthy group.
(b) Statistically significant differences (P < 0.05) between female, healthy group.
(ac) Statistically significant differences (P < 0.05) between male, female group.

Figure (2): Serum level of CCL18 in lung cancer patient's male group and female group comparison with healthy group.

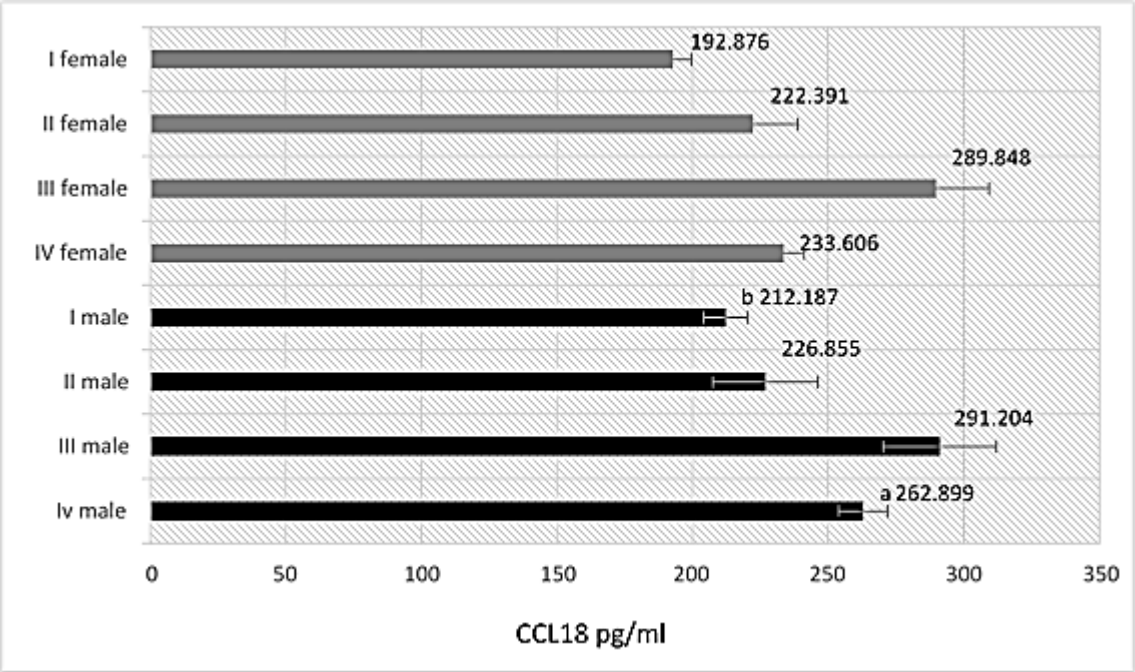
Figure (3) shown the result of CCL18 value that in significant increase ($p<0.05$) of female serum CCL18 concentration squamous cell carcinoma, adenocarcinoma, large-cell carcinoma and small cell carcinoma (288.326±4.279 225.979±6.589, 184.148±2.528,180.703±4.638) pg/ml , also significant increase ($p<0.05$) of male serum CCL18 concentration in squamous cell carcinoma, adenocarcinoma, large-cell carcinoma and small cell carcinoma (294.548±15.785, 257.153±7.911,234.73±7.578, 221.223±3.942) pg/ml. Also Significant increase ($p<0.05$) in CCL18 serum concentration between type of lung cancer in male and female.



(a) Statistically significant differences (P < 0.05) between adenocarcinoma male and adenocarcinoma
(b) female (b) Statistically significant differences (P < 0.05) between large-cell carcinoma male and large-cell carcinoma female. (c) Statistically significant differences (P < 0.05) between small cell carcinoma male and small cell carcinoma female.

Figure (3): Serum level of CCL18 in lung cancer patient's male group and female group comparison with types of lung cancer.

Figure (4) explained the result of CCL18 value in serum of female group have significant increase ($p<0.05$) with stage I, stage II, stage III and stage Iv of disease (192.876±6.676, 222.391±16.491, 289.848±19.593, 233.606 ,233.606±7.592) pg/ml , the result of serum concentration of CCL18 shown significant increase ($p<0.05$) with stage I, stage II, stage III and stage Iv of disease (212.187±7.942,226.855±19.362,291.204±20.856,262.899± 8.989) pg/ml, as well significant increase ($p<0.05$) between stage of disease in female and stage of disease in male .



(a) Statistically significant differences ($P < 0.05$) between I male and I female.
(b) Statistically significant differences ($P < 0.05$) between IV male and IV female.
Figure (4): Serum level of CCL18 in lung cancer patients (male and female) and stage of disease.

Discussion:

Plones *et al* ., (2012) and Prasse (2009) both are suggested that by the activated immune cells CC-chemokine ligand 18 (CCL18) is expressed which have an important role in lung carcinoma. The CC-Chemokine CCL18 named ‘‘pulmonary and activation-regulated chemokine’’ is expressed forcefully in patients lungs but expressed less in other lymphatic tissue such as thymus or lymph nodes. Healthy serum of subjects constantly level of CCL18 while it is increased in several malign and benign tumor such as lung fibrosis, leukemia and atopic dermatitis, Also CCL18 can assist tumor cells to avoid the immune surveillance.

Expression of CCL18 was reported in areas of more severe lung inflammation that lungs from patients with subacute/chronic strongly overexpress CCL18 compared with normal lung parenchyma. The expression of this chemokine was more abundant through the subacute state of the disease, which is characterized CCL18 expression and affected by severe inflammation, there was a strong correlation between the levels of CCL18 in the lungs and the percentage of lymphocytes (Pardo *et al* ., 2001).

The serum concentrations of CCL18 in this study are highly elevated in squamous cell carcinoma and show significant difference among lung cancer types shown in figure (3). The result agrees with Plones *et al* ., (2012) who refer to CCL18 in squamous cell carcinoma elevated more than other lung carcinoma types.

In the current study serum levels of CCL18 shown in early stage is lower than in late stage in lung carcinoma patients. Figure (4) means that CCL18 elevated in late stage. These results agrees with Plönes *et al* .(2012) who refer to the measured data of CCL18 in lung carcinoma patients correlated with tumor stage ,histology and clinical parameter reported that found differed significantly between early and late stage of disease, whereas levels of this cytokine elevated with cancer stage progress gradually, that serum CCL18 concentrations correlate with tumor volumes. Therefore who refers to significant correlation between CCL18 serum concentration and volume of tumor .

CONCLUSIONS:

The elevation of serum CCL18 was a risk modulator in lung cancer because it contributes in the escaping of the tumor from immune surveillance.

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