492. Bronchoalveolar lavage and biomarkers in diffuse parenchymal lung disease

P4761
Overexpression of matrix metalloproteinase-7 (MMP-7) in bronchoalveolar lavage fluid (BALF) of IPF and lung cancer patients
Katerina Samara1,2, Ioannis Giannarakis1,2, Ismini Papanikoalou2, Irini Lambiri1, Nikos Siafakas1, Katerina Antoniou1,2. 1Thoracic Medicine, Medical School, University of Crete, Heraklion, Greece; 2Laboratory of Molecular and Cellular Biology, Medical School, University of Crete, Heraklion, Greece

It is long recognised that lung cancer has an increased frequency in idiopathic...
Expression profiling of Th17 cell activators revealed elevation of STAT-3 in progression, migratory behaviour and metastasis potential. The over-expression of these markers could be predictive of tumor diagnosis, and the elevation of these molecular markers in sarcoid BAL cells was irrespective of clinical phenotype. The increased expression of MMP-7 in both m-RNA and protein level may suggest a common link between these lethal pulmonary diseases. Our aim was to standardize process for culturing cells from small volumes of diagnostic bronchoalveolar lavage (BAL) fluid samples and to characterize the immune response in fibroblasts and myofibroblasts. The decreased immune surveillance in smokers lower airways in general, increased risk of local carcinogenesis. The investigation of MMPs was performed in sarcoid BAL cells from 77 sarcoidosis patients (S) and 20 control subjects (C); MMP2, MMP7, MMP9, TIMP1 and TIMP2 mRNA expression levels were measured in BALF by real time RT-PCR. MMP7 protein levels were measured in BALF supernatants using ELISA kit. The expression of MMPs may suggest a common link between sarcoidosis and lung cancer while did not show significant difference at the mRNA level in comparison to controls. MMP7 protein levels (pg/ml) were significantly higher in both NSCLC and IPF populations compared to controls (NSCLC: 24.69±4.18, IPF: 18.8±2.11, C=9.76±1.92, p=0.032, IPFpC=0.005). Increased expression of MMP-7 in both m-RNA and protein level may suggest a common link between these lethal disorders. Given that our population was newly diagnosed, the over-expression of these markers could be predictive of tumor progression, migratory behaviour and metastasis potential.

Fibrocytes are detected in bronchoalveolar lavage (BAL) fluid in idiopathic pulmonary fibrosis (IPF), raising questions regarding the similarity of IPF and lung cancer. Matrix metalloproteinases regulate remodelling of the extracellular matrix, an important function for pathological processes such as angiogenesis, tissue repair and tumor invasion. Our aim was to assess the expression of this pathway in BALF samples of lung cancer patients and compare with IFP patients to examine possible pathogenic links between these two lethal pulmonary diseases. We prospectively studied 23 newly diagnosed patients, with non small cell lung cancer (NSCLC), 10 IPF patients and 10 healthy controls (C). MMP2, MMP7, MMP9, TIMP1 and TIMP2 mRNA expression levels were measured in BALF by real time RT-PCR. MMP7 protein levels were measured in BALF supernatants using ELISA kit.

mRNA expression of MMPs 2,7,9 and TIMP1 was significantly increased in lung cancer compared to controls (p<0.05). The IPF population showed decreased expression of the aforementioned MMPs in comparison with lung cancer while did not show significant difference at the mRNA level in comparison to controls. MMP7 protein levels (pg/ml) were significantly higher in both NSCLC and IPF populations compared to controls (NSCLC: 24.69±4.18, IPF: 18.8±2.11, C=9.76±1.92, p=0.032, IPFpC=0.005). Increased expression of MMP-7 in both m-RNA and protein level may suggest a common link between these lethal disorders. Given that our population was newly diagnosed, the over-expression of these markers could be predictive of tumor progression, migratory behaviour and metastasis potential.

Sarcoidosis is a Th1/Th17 multisystem inflammatory disorder of unknown aetiology. Although Th17 cells have been implicated in sarcoidosis and its progression, there is limited information about the molecules involved in the Th17 immune response in sarcoidosis and its phenotypes. We investigated, mRNA expression of Th17 pathway activators (IL-6, IL-23, IL-21, 23, TGFbeta, RORC, STAT3) together with the cytokines produced by Th17 cells (IL-17A, IL-17F, IL-22) by quantitative RT-PCR in bronchoalveolar (BAL) cells from 77 sarcoidosis patients (S) and 20 control subjects (C); subanalysis was performed in sarcoid phenotypes. Of studied Th17 activators, IL-6 (mean S: 0.37±0.04, p=0.0001), IL-23 (0.02±0.001, p=0.001), IL-22 (0.06±0.02, p=0.001), TGFbeta (0.86±0.51, p=0.002) and RORC (1.0±0.002) were up-regulated in sarcoidosis, compared to controls. Expression of Th17 cytokines did not differ between sarcoidosis and controls (p>0.05). The expression profiling in remitting (n=27) and progressing (n=40) sarcoidosis, as assessed by the disease outcome after 2 years, revealed elevation of STAT-3 in progressing sarcoidosis (p=0.01).

In conclusion, increased expression of Th17 activators (IL-6, IL-23, IL-21, 23, TGF-beta, RORC) was observed in sarcoid BAL cells irrespective of clinical phenotype. Enhanced expression of STAT3, an essential regulator of Th17 cells, was detected in patients with progressing sarcoidosis. Further studies on the role of STAT3 and Th17 cells in the progression towards the fibrosis in sarcoidosis are needed.

Grant support: IGA MZ CR NS/11/17, IGA MZ CR Ns0267, PU LP_2010_008.

Fibrocytes are circulating precursors for fibroblasts. Their role in the pathogenesis of IPF is debated. Blood Fibrocytes are increased in patients with IPF, but there are no data concerning BAL. The aim of this study was to determine whether fibrocytes are present in the alveolar space and identify their prognostic value.

Methods: We detected and quantified fibrocytes by FACS (CD45+, Collagen1+) in BAL from 26 patients with IPF (3 exacerbations), 8 patients with Systemic Sclerosis and lung involvement, and 11 controls. BAL cells were cultured to isolate alveolar fibroblasts. MCP-1 and CXCL12 were measured in BAL fluid.

Results: Fibrocytes were not detected in controls, but were detected in 14/26 (54%) and 4/8 SSc. Median fibrocyte count was 2.5% ±0.19-7.1% in IPF, 3.0% ±2.7-3.7% in SS (NS). Fibroblasts were cultured from BAL in 12/26 IPF (46%), 5/8 SSc (62%) and 2 controls (P=0.04). The detection of fibrocytes was not associated with diagnosis, fibrosis HRCT score, or survival but was associated with lower DLCO. Fibrocytes did not correlate with MCP-1 and CXCL12 BAL concentration and was not associated with the presence of fibroblasts in culture.

Conclusion: Fibrocytes are detected in BAL fluid in about half patients with IPF and SSc. Their prognostic significance is uncertain.
**P4766**
Expression of transforming growth factor β (TGFβ) receptor, CD105, is declined in Th1/Th17/Th17/Th17 interstitial lung diseases (ILDs)

Andrzej Dyczek1, Jerzy Szczeklik 1, Barbara Balicka-Slusarczyk1, Joanna Chorostowska1, Adam Szpecichinski1, Ewelina Pölgesk4, Marek Jankowski1, Piotr Kopinski1, 1II Dept of Internal Medicine, Centre of Immunological Diseases, Collegium Medicum, Jagiellonian University, Kraków, Poland; 2Dept of Toxicology and Environmental Diseases, Collegium Medicum, Jagiellonian University, Kraków, Poland; 3Laboratory of Molecular Diagnostics and Immunology, Institute of Tuberculosis and Lung Diseases, Warsaw, Poland; 4Dept of Gene Therapy, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland

**Background:** TGFβ, as the most potent activator of lung fibrosis, stimulates fibroblast proliferation and induces secretion of collagen and other extracellular matrix proteins. It reveals its pro-fibrotic effect by receptor complex, including CD105 molecule.

**Methods:** TGFβ levels was examined by ELISA in bronchoalveolar lavage (BAL) supernatants. CD105 expression was tested on BAL macrophages and lymphocytes in primary sarcinocytic cultures (n=16), idiopathic pulmonary fibrosis (n=49), non-specific interstitial pneumonias (n=60) and extrinsic allergic alveolitis (n=77). CD105 appearance was also assessed in model lung cell lines: pneumocytes type 2 (A549) and fibroblasts (HFL-1).

**Results:** IPF was the only disorder with significantly increased TGFβ level. CD105 expression is common on HFL-I (98%), AS49 (63%, median of 5 trials) and alveolar macrophages. In PS significantly decreased CD105 expression on BAL lymphocytes was found (all lymphocytes: 7.2±0.6%, Th cells: 4.6±0.4%). Tc cells: 1.8±0.3%, resp control values: 13.3±4.6%, 6.6±2.6% and 4.7±1.1%, median±SEM, p<0.05). Similar results were observed in EAA. IPF was characterized with remarkably enhanced BAL CD105+ lymphocyte percentage (all lymphocytes: 23.9±8.5%, p<0.05).

**Conclusions:** TGFβ receptor, CD105, is frequently present in lower airways. Lower BAL CD105+ lymphocyte percentage in IPF and, higher one in PS and EAA, may reflect different Th1/Th2 polarization pattern. Summarizing, the key role of diverse lower airway cell reactivity to TGFβ in ILDs should be considered.

**P4776**
Proteological assessment of idiopathic pulmonary fibrosis and hypersensitivity pneumonitis by means of broncho-alveolar lavage

Stijn Willems, Jana Somers, Stijn E. Verleden, Geert M. Verleden, Jonas Yserbyt, Christophe Dooms, Bart Vanaudenaerde, Wim Wuyts. Interstitial Lung Disease Unit, University Hospital Gasthuisberg, Leuven, Belgium

**Introduction and aims:** Idiopathic Pulmonary Fibrosis (IPF) and Hypersensitivity Pneumonitis (HP) are both interstitial lung diseases characterized by a major pathological mechanism and known to have a similar clinical picture.

**Background:** Interstitial lung disease (ILD) is a group of disorders characterized by the presence of pathological processes of the lung parenchyma, not being caused by heart, pleural, vasculature disease, infection or tumors. The most common causes of ILD are autoimmune diseases, exposure to environmental factors, and drug-related ILDs. ILD is not only a medical challenge for patients but also for the healthcare system. In the last years, numerous studies have described and analyzed the expression of specific genes in the patients with ILD. ILD can be divided into idiopathic ILD and specific ILD. Specific ILD can be divided into occupational ILD, drug-induced ILD, and connective tissue disease-related ILD. Idiopathic ILD is further defined into diffuse interstitial lung disease (DILD) and fibrosing alveolitis (FA) (also known as usual interstitial pneumonia (UIP)). In the following, we will focus on the mechanism of FA.

**Methods:** We retrospectively analyzed 49 patients who were suspected as DILD and underwent BAL and LTT between January 2004 and September 2009. The total cell number and the different cellular counts in BAL fluid were determined. The levels of cytokines (tumor necrosis factor-alpha, IL-6, IL-10, IL-12, IP-10, monocyte chemoattractant protein-1, and vascular endothelial growth factor) were determined by multiplex ELISA. It was also evaluated whether these parameters were correlated with the DILD patients.

**Results:** The diagnostic sensitivity and specificity of LTT were 50% and 60%, respectively. These numbers were comparable to those in previous reports. The sensitivity of increased eosinophils (>15%) in BAL fluid was 90%, and the specificity was 22%. The sensitivity of increased lymphocytes (>50%) was 35%, and the specificity was 78%. Furthermore, the positive likelihood ratio of LTT and increased eosinophils and lymphocytes (>10%) in BAL fluid for the prediction of the patient recovery was 6.99, 6.22, and 5.54, respectively. On the other hand, cytokine levels in the supernatant were not correlated with the diagnosis or the prognosis.

**Conclusion:** It was suggested that BAL fluid findings, especially the differential count of leukocytes, may be useful for the diagnosis and the prediction of outcome of the patients with DILD.

**P4769**
Clinical and functional features in idiopathic pulmonary fibrosis (IPF) with and without haemosiderin-laden alveolar macrophages on BALF

Carolina Vitale, Emanuela Carpentieri, Francesco Perna, Manuela Pitassi, Antonio Molino, Anna Stanziona, Matteo Soilia. Dept Respiratory Diseases, University Federico II Naples, Naples, Italy

We have previously reported increased frequency of haemosiderin-laden alveolar macrophages in patients with IPF and without haemosiderin-laden alveolar macrophages on BALF. We performed a retrospective analysis of 49 patients who received diagnosis of IPF. The diagnostic value of IPF was in accordance with the ATS/ERS guidelines. BALF was performed in all subjects. We evaluated the occurrence of haemosiderin-laden alveolar macrophages in patients with IPF. Perls blue staining was used to detect haemosiderin laden alveolar macrophages. >400 MΦ were examined for the number of cells that stained with Perls Blue stain. A score was established by dividing the number of Perls Blue-positive cells by the total cell number of counted cells. Perls positive cells were defined as percentage of BALF MΦ > 50%. Patients were divided in 2 groups based on BALF Perls positivity: IPF-BALF MΦ > 15/49 (30%) and IPF-BALF MΦ < 24/49 (70%). Variables compared between the 2 groups included cellular BALF data, pulmonary function tests, arterial blood gases, and PAPs estimated by echocardiography. DLCO% and oxygen desaturation during 6MWT were significantly reduced in IPF BALF MΦ > 400 in comparison to IPF BALF MΦ < 400, while FVC%th (5.6±1.5 vs 4.7±1.3), FEV1%th (63±9 vs 55±6) and resting PAO2 mmHg (63±9 vs 69±9) were not significantly different.

**Conclusions:** Increased haemosiderin laden alveolar macrophages is associated to more severe impairment of lung diffusion and higher oxygen desaturation during exercise.

**P4770**
Differential cell count in BAL by flow cytometry using CD15

Naoki Hasegawa3, Mitsuru Murata 2, Koichiro Asano1. 1Division of Pulmonary Medicine, Keio University School of Medicine, Tokyo, Japan; 2Department of Laboratory Medicine, Keio University School of Medicine, Tokyo, Japan; 3Division of Infection Control, Keio University School of Medicine, Tokyo, Japan

**Background:** The diagnostic strategy of the drug-induced lung disease (DILD) has not been established. It remains to be determined whether the lymphocyte transformation test (LTT) can be used for the diagnosis of DILD. Although bronchoalveolar lavage (BAL) is often performed, its usefulness in the diagnosis of DILD is still uncertain.

**Aim:** We aimed to evaluate the diagnostic value of BAL and LTT in patients with DILD.

**Method:** We retrospectively analyzed 47 patients who were suspected as DILD and underwent BAL and LTT between January 2004 and September 2009. The total cell number and the differential cellular counts in BAL fluid were determined. The levels of eosinophils (eosinophils > 15%) in BAL fluid was 90%, and the specificity was 22%. The sensitivity of increased lymphocytes (>50%) was 35%, and the specificity was 78%. Furthermore, the positive likelihood ratio of LTT and increased eosinophils and lymphocytes (>10%) in BAL fluid for the prediction of the patient recovery was 6.99, 6.22, and 5.54, respectively. On the other hand, cytokine levels in the supernatant were not correlated with the diagnosis or the prognosis.

**Conclusion:** It was suggested that BAL fluid findings, especially the differential count of leukocytes, may be useful for the diagnosis and the prediction of outcome of the patients with DILD.
Methods: 34 BAL samples were analysed in a 2-laser cytometer (FACSCalibur). The results were compared with those obtained by optical microscopy. The proposed combination of monoclonal antibodies identified key leukocytes as CD8+ cells and lymphocytes as CD15, CD16, and CD68 (NK lymphocytes). HLA-DR- and HLA-DRB1 (B cells and activated lymphocytes) cells; neutrophils as CD15+, CD14-bright+, HLA-DR-bright+ cells; eosinophils as CD11b+bright+, CD66c+bright+, HLA-DR-bright+ cells; and alveolar macrophages as CD11b+, CD16+bright+, HLA-DR-bright+ cells. Macrophage's autofluorescence (AF) was used to compare the monoclonal antibody anti-HLA-DR conjugated with the dye APC as the main identification marker.

Results: Our data showed high correlations (r=0.70 to 0.93; p<0.001) but FCM overestimates lymphocyte population +13 (15.8%), and conversely underestimates alveolar macrophage population -15 (19.6%).

Conclusions: The monoclonal antibodies combination proposed is effective and reliable to identify leukocyte populations in BAL. The process is simpler and faster than manual optical microscopy but some differences in macrophages and lymphocytes counts should be considered.

P4771

LSC 2011 Abstract: Bronchoalveolar lavage in radiation pneumonitis after radiotherapy for breast cancer

Claudia Lucia Toma, Aneta Serbescu, Mihai Alexe, Luminita Cervis, Diana Ionita, Miron Alexandru Bogdan. Pneumology, Carol Davila University of Medicine and Pharmacy, Bucharest, RO Pneumology, Marius Nasta Institute of Pneumology, Bucharest, RO

Radiotherapy pneumonitis is a complication of radiotherapy which limits its application in cancer therapy.

Aim: To compare the bronchoalveolar lavage (BAL) findings in patients with symptomatic radiation pneumonitis (RP) versus asymptomatic RP.

Material and method: We evaluated 65 female patients with RP after radiotherapy for breast cancer.

Results: Forty-nine patients were symptomatic (fever, cough and/or dyspnea) and 16 were asymptomatic. All patients had a newly discovered infiltrate or consolidation on chest radiography, corresponding to the radiation field. BAL in symptomatic patients had an increased number of cells.

Lymphocytosis was present in all patients with RP, but it was higher in symptomatic (34.9±18.81%) vs. asymptomatic (26.4±14.3%). Macrophages were decreased in all patients. Neutrophils were slightly increased (8.88% in symptomatic and 3.34% in asymptomatic) and eosinophils were normal in both groups (2.56% and 1.22, respectively). Almost all lymphocytes were T type (CD3+). CD4+ lymphocytes were increased in both groups with normal CD4/CD8 ratio (2.72 in symptomatic and 1.5 in asymptomatic group).

Conclusions: Lymphocytic alveolitis with T lymphocytes was present in all patients with RP with a higher proportion in symptomatic patients.

P4772

Detection of differences in volatile organic compounds (VOCs) by ion mobility spectrometry (IMS) of exhaled breath in patients with interstitial lung diseases (ILDs) compared to healthy controls (HC)

Olaf Anhenn1, Thomas Rahls1, Ulrike Sommerweck1, Gerhard Weinhre1, Jörg-Ingo Baumbach1, Isabella Kurt1, Kai Durwiche1, Luiz Freitag1, Helmut Teschke1, Ulrich Costabel2, 1Department of Pneumology - Lang Transplantation, Ruhlandlinik, West German Lung Centre at the University Clinic Essen - University Clinic, Essen, Germany; 2Department of Intervential Pneumology, Ruhlandlinik, West German Lung Centre at the University Clinic Essen, Essen, Germany

Introduction: ILDs comprise a heterogenous group of disorders involving the lung parenchyma. Rapid and accurate diagnosis is often complicated by the need of assessing the pathologic changes in the lung parenchyma by bronchoalveolar lavage, tranbronchial biopsies or open lung biopsy. Objective: The aim of our study was to compare the pattern of VOCs in exhaled breath of patients with extrinsic allergic alveolitis (EAA), non-specific interstitial pneumonia (NSIP), idiopathic pulmonary fibrosis (IPF) or sarcoidosis (SA) to healthy controls (HC).

Methods: Detection of VOCs in exhaled breath was performed by ion mobility spectrometry (IMS) coupled to a multi-capillary column (MCC) for pre-separation (MCC-IMS, B&K Analytic). ILD patients with EAA (n = 16), NSIP (n = 28), IPF (n = 26), SA (n = 21) were compared to HC (n = 39).

Results: Overall 215 peaks could be detected in exhaled breath of patients and controls. The EAA and the HC groups differed in 115 peaks. The IPF and the HC groups differed in 26 peaks, the NSIP and HC groups in 63, the SA and HC groups in 3 peaks.

Conclusions: IMS seems to be a promising technique to discriminate different ILDs from healthy controls. However, confirmation of our findings in a larger study population is needed. Also further invesitations have to be undertaken, to address the question, whether different ILDs can be distinguished from one another by distinct peak patterns.

P4773

Phospho-ERM localization in UIP specimens: An immunohistochemistry approach

Simona Inghilleri1, Giulia Maria Stella1, Michele Zorzetto1, Ilaria Campos1, Patrizia Morbini2, Tiberio Oggiorni1, Maurizio Luissuti1, Respiratory Disease, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; 3Department of Pathology-Section of Pathological Anatomy, IRCCS Policlinico San Matteo Foundation, Pavia, Italy

Background: Idiopathic Pulmonary Fibrosis (IPF) is a progressive, fatal lung disease of unknown etiology still lacking effective of therapy. IPF has a poor prognosis with a median survival of 2.5-3.5 years, and it is associated with lung cancer with a prevalence ranging from 4.8% to 46%. Molecular mechanisms of carcinogenesis occurring in IPF remain to be clarified.

Aim and objective: The family of ezrin/radixin/moesin (ERM) proteins is essential for maintaining of cell shape, cell adhesion, migration and division, serving as an important cross-linker between the plasma membrane and cytoskeleton. Recent studies showed that ERM is upregulated in multiple types of metastatic cancers. In the current investigation, we tested the hypothesis that ERM interacts and plays a key role in epithelial-mesenchymal transition (EMT) in alveolar epithelial cells.

Methods: In order to identify the relationship between lung cancer and IPF and we assessed an immunohistochemistry analysis for phospho-ERM in the following pulmonary biopsy specimens: 20 UIP, 4 adenocarcinoma, 6 genetic organizing pneumonia (GOP), and 4 normal controls.

Results: Our preliminary data showed in normal lung samples a totally negative phospho-ERM immunostaining. We found a weak positivity in GOP samples, whereas in UIP samples we found a higher global expression, in particular in activated type II pneumocytes and basal bronchiolar cells.

Conclusion: We hypothesize that activation of ERM proteins could be involved in UIP pathogenesis, leading to possible contribute to the EMT process of lung epithelial cells.

P4774

Serum napsin A is a novel diagnostic and monitoring marker for interstitial lung disease

Takuya Samukawa, Tutomu Hamada, Go Tsukui, Hiromasa Inoue. Department of Pulmonary Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

KL-6, and Surfactant Protein (SP)-A and SP-D have been reported as sensitive markers for interstitial lung disease (ILD). However, a more useful serum marker for diagnosis and activity of ILD may be found in napsin A, a lysosomal protease, mainly expressed in alveolar type-II cells and the kidney. This study sought to evaluate the diagnostic and monitoring value of napsin A in patients with ILD in comparison with KL-6, SP-A, and SP-D, and to determine whether serum napsin A levels reflect renal dysfunction.

Subjects consisted of 34 patients with ILD, 20 patients with lung adenocarcinoma, 12 patients with kidney disease, and 20 healthy subjects. Serum samples were analyzed for each marker by ELISA. The area under the receiver operating characteristic curves (AUC) were used to determine appropriate cut-off levels resulting in optimal diagnostic accuracy using napsin A as a marker; differences in serum levels of these markers were investigated. Further, 10 patients with ILD were treated and evaluated for treatment efficacy and usefulness of napsin A as a monitoring marker.

The AUC values for ILD patients in comparison with control subjects were 0.949 for napsin A, 0.978 for KL-6, 0.896 for SP-A, and 0.672 for SP-D. The accuracy of changes in these serum markers reflecting response to therapy were 80% for napsin A, 50% for KL-6, 70% for SP-A, and 70% for SP-D. Moreover, serum napsin A level reflected no renal dysfunction.

Serum napsin A is a novel diagnostic and monitoring marker for ILD that is superior to SP-A and SP-D, and equivalent to KL-6.

P4775

Extracellular matrix profile of lung in idiopathic pulmonary fibrosis

Susanna Estany1, Vanesa Vicens1,2, Roger Llatrio1, Rosa Penin1, Ignacio Escobar4, Antonio Xaubet5, Jordi Dorca1,2, Maria Molina-Molina1,2.

1Pneumology Research Group, IDIBELL-UB, 2Department of Pulmonology, IDIBELL-UB, 3Department of Internal Medicine, Hospital Universitari de Bellvitge, 4Dental Sciences, Kagoshima, Japan

Idiopathic Pulmonary Fibrosis (IPF) is a progressive, fatal lung disease mainly expressed in alveolar type-II cells and the kidney. This study sought to evaluate the diagnostic and monitoring value of napsin A in patients with ILD in comparison with KL-6, SP-A, and SP-D, and to determine whether serum napsin A levels reflect renal dysfunction.

Subjects consisted of 34 patients with ILD, 20 patients with lung adenocarcinoma, 12 patients with kidney disease, and 20 healthy subjects. Serum samples were analyzed for each marker by ELISA. The area under the receiver operating characteristic curves (AUC) were used to determine appropriate cut-off levels resulting in optimal diagnostic accuracy using napsin A as a marker; differences in serum levels of these markers were investigated. Further, 10 patients with ILD were treated and evaluated for treatment efficacy and usefulness of napsin A as a monitoring marker.

The AUC values for ILD patients in comparison with control subjects were 0.949 for napsin A, 0.978 for KL-6, 0.896 for SP-A, and 0.672 for SP-D. The accuracy of changes in these serum markers reflecting response to therapy were 80% for napsin A, 50% for KL-6, 70% for SP-A, and 70% for SP-D. Moreover, serum napsin A level reflected no renal dysfunction.

Serum napsin A is a novel diagnostic and monitoring marker for ILD that is superior to SP-A and SP-D, and equivalent to KL-6.

Poster Discussion Room G106-107 - 08:30-10:30

Wednesday, September 28th 2011

Abstract printing supported by Chiiesi. Visit Chiiesi at Stand D.30
P4776

Elevation of serum tumor markers in patients with interstitial lung disease
Jianqun Liu1, Haoping Dai1, Lirong Liang1, Lijing Peng1, Jing Yang1,2, Fuqiang Chen1,2, Zijian Chen3,4, Zhiqiang Sun1,2, Jinping Yang1,2

1Respiratory Medicine, Beijing Chaoyang Hospital Affiliated to Capital Medical University, Beijing Institute of Respiratory Medicine, Beijing, China; 2Respiratory Medicine, Beijing Fentai Hospital, Beijing, China

The risk of lung cancer is high in patients with interstitial lung disease (ILD). It was reported that tumor markers were increased in ILD patients. The serum levels of CEA, CA19-9, CA15-3 and NSE were measured in 88 ILD patients and 152 control subjects. The analysis of variance, multiple linear regression, Logistic regression analysis and ROC curve were used for statistical analyses. The mean levels of CEA, CA19-9, CA15-3 and NSE were significantly higher in ILD patients than in control subjects (P<0.05). The multivariate analysis showed that the CEA, CA19-9, CA15-3 and NSE were of diagnostic significance for ILD.

P4777

Interferon-γ or azathioprine plus corticosteroids do not alter the expression of apoptotic markers in alveolar macrophages of patients with IPF
Fotios Drakopanagiotakis1, Aren Xyteri1, Evangelos Tsiamias1, George Vilaras3, Andreas Karakiri1, Constantina Tsakanika1, Vlastis Polychronopoulos1, Demosthenis Bouros1,2,3

13rd Respiratory Medicine Department, Sismanoglio Hospital, Athens, Greece; 2Department of Pneumology, Medical School, Democritus University of Thrace, Alexandroupoli, Greece; 3Pathology and Computerized Image Analysis, NIMTS Hospital, Athens, Greece

Introduction: Pathologic apoptosis is described in IPF. Macrophage activation is implicated in the pathogenesis of fibrotic lung diseases. The apoptotic profile of alveolar macrophages (AM) in IPF is unclear.

Aim: To examine the expression of apoptotic proteins in AM of patients with IPF after therapeutic intervention.

Methods: Twenty newly diagnosed IPF patients were randomised in group A treated by a combination of interferon-γ-1b and prednisolone and group B treated by azathioprine and prednisolone. Groups were compared regarding clinical deterioration, lung function, and bronchoalveolar lavage (BAL) apoptosis markers. We analyzed by immunohistochemistry, the expression of the anti-apoptotic markers bcl-2 and the pro-apoptotic markers bax, fas, fas ligand in AM obtained from BAL before and after treatment. We measured apoptosis by TUNEL.

Results: No difference was observed regarding age, gender, smoking habit between the two groups of IPF patients. The patients of both groups had similar FEV1, FVC and DLCO values at entry and after six months of treatment.

Conclusions: Specifically examined the expression of apoptotic markers in AM of patients with IPF and we report that different treatment options do not affect the expression of these markers in IPF. These results may be related to the ineffectiveness of pharmacological therapies for IPF.