84. Rare diffuse lung diseases

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Interstitial lung diseases in children: The French national cohort study

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Introduction: In France rare orphan diseases as pediatric interstitial lung diseases (ILDs) have been identified as a public health priority. A national pediatric reference center for rare lung diseases, RespiRare, was created several years ago.
Objective: To investigate the prevalence and the expression of pediatric ILDs within a national cohort in France.
Methods: Children presenting with ILD from 1995 to 2010 were identified through the RespiRare network. Clinical, radiological, functional, pathological, biological and genetical longitudinal data were collected by the physicians in charge of ILDs patients using a unique national biomedical database.
Results: Data were available for 197 children presenting with ILD. The mean incidence was 26/year. Median age at diagnosis was 20 months [0-16 years], and the sex ratio was 0.87 male/female. Investigations including thoracic high resolution computed tomography scan (n=197), broncho-alveolar lavages (n=97), lung biopsies (n=30) and analysis of surfactant genes (n=67) led to a diagnosis for 142 out of the 197 children (63.4%): surfactant mutation associated disorders (n=29, 14.7%), haemosiderosis (n=24, 12.2%), sarcoidosis (n=20, 10.2%) and alveolar protéinosis (n=17, 8.6%) were the most common diagnoses. Pulmonary hypertension was observed in 16% cases at diagnosis.
Conclusion: A national database is now used in France for pediatric ILDs and facilitates clinical studies. Based on this experience, recommendations for diagnosis and therapeutic strategies are being established. As a European ILDs consortium is emerging, a European ILDs registry would be the next step to improve the knowledge of pediatric ILDs pathophysiology and their management.

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Diagnostic value of serum VEGF-D in consecutive patients with lymphangioleiomyomatosis

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Background: Serum levels of vascular endothelial growth factor-D (VEGF-D) are increased in patients with lymphangioleiomyomatosis (LAM).
Objective: To explore the value of measurement of serum level of VEGF-D for the diagnosis of LAM.
Methods: Serum levels of VEGF-D were measured prospectively in 45 patients with LAM (mean age, 48±13 years), 13 healthy controls, and 23 patients with multiple cystic lung diseases other than LAM.
Results: Serum VEGF-D levels were significantly higher in patients with LAM (mean, 1856±1742 pg/mL) than in patients with other lung diseases (410±173 pg/mL, $p<0.01$) or healthy individuals (230±69 pg/mL, $p<0.0001$). VEGF-D was elevated (860 pg/mL) in only one patient with Birt-Hogg-Dubé disease with the mutation PQ385X in the *FLCN* gene, with LAM ruled out by lung biopsy. Using 800 pg/mL as a threshold, the specificity of VEGF-D was 98% but sensitivity was only 76%. VEGF-D in LAM was >800 pg/mL in 5/7 transplanted patients, in 6/6 patients receiving sirolimus, and in 4/4 patients treated with doxycycline. VEGF-D levels did not correlate with any pulmonary function parameter.
Conclusion: Serum VEGF-D levels greater than 800 pg/mL contributes to the diagnosis of LAM with false positive only rarely encountered (as in Birt Hogg Dubé disease). Serum VEGF-D level may remain elevated in transplanted patients and those receiving medical therapy.
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Extracellular concentration and enzyme activity of proteasome in BAL of patients with alveolar proteinosis

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Introduction: Pulmonary alveolar proteinosis (PAP) is a rare disorder characterized by alveolar accumulation of surfactant lipoproteins. Proteasomes are responsible for nonlysosomal protein degradation. They are involved in apoptosis, stress response and inflammation. ARDS and sarcoidosis show elevated levels of extracellular proteasome. The aim of this study was to detect proteasome concentration and enzyme activity in BALF in PAP.
Patients and methods: 22 PAP patients (20 with primary, 2 with secondary form) and 18 healthy controls were studied. 20S proteasome subunit (murine monoclonal antibody by Biomol Int. L.P., Exeter, UK) was measured by ELISA in BALF. The cleavage of 3 fluorogenic substrates (Suc-LLVY-AMC, BZ-VGR-AMC and Suc-LLE-AMC) was used to describe the specific enzyme activity (chymotrypsin-, trypsin- and caspase-like) of extracellular proteasome.
Results: Proteasome concentration in BALF of PAP patients was 10-fold higher than in healthy subjects (699±422 vs 60±36 ng/mL, $p<0.0001$). Trypsin- and caspase-like activity of proteasome was significantly increased in PAP compared to healthy subjects (BZ-VGR-AMC 1.5±0.9 vs 0.26±0.27; Suc-LLE-AMC 0.62±0.7 vs 0.07±0.06 pkat/mL; $p<0.01$). Enzyme activity for all 3 substrates correlated directly with the total protein concentration in BALF (r=0.7, p= 0.002; r=-0.56, p=0.02; r=0.85, $p<0.001$) and inversely with TLCO (r=-0.72, p= 0.008; r=-0.7, p=0.014; r=-0.73, p=0.006).
Conclusions: Proteasome alveolar concentration is higher in PAP than in healthy controls. This is associated with an increased trypsin- and caspase-like enzyme activity. Proteasome seems to be significantly involved in the alveolar protein degradation in PAP.

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Chronic eosinophilic pneumonia after radiation therapy for breast cancer

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Background: Several reports have documented the possible appearance of organising pneumonia (OP) as complication of radiation therapy (RT) for breast cancer, but only one has described the occurrence of chronic eosinophilic pneumonia (CEP) in this setting (Cottin V. et al. Eur Respir J 2004; 23:9-13).
Methods and results: We describe 3 new cases of CEP developed after RT for breast cancer. The median time interval between the end of RT and onset of CEP was 4.3 months. All patients were symptomatic for fever or dry cough. None had history of asthma, one was an active smoker. Chest CT showed multiple areas of alveolar consolidation in regions not limited to the irradiated lung. None of the patients had blood eosinophilia >1 G/L. In all cases, the bronchoalveolar lavage (BAL) differential cell count revealed eosinophilia ≥25% (25, 45 and 90% respectively). The respiratory function tests showed normal lung volumes and reduced carbon monoxide transfer factor to 60% predicted in 2 patients. All patients had rapid resolution of symptoms with corticosteroid therapy. 2 patients experienced 2 relapses each after treatment withdrawal. In all patients, therapy could be stopped after a median time of 16 months. All are disease-free after a median time of 85 months.
Conclusions: We confirm the possible onset of CEP as expression of lung injury induced by RT for breast cancer. In contrast to previous observations, CEP after RT may occur in the absence of blood eosinophilia and history of asthma. Since CEP and OP after RT have similar clinical pictures, CEP may be misdiagnosed as OP if BAL is not performed.

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Baseline characteristics of an Italian cohort of pulmonary alveolar proteinosis (PAP) patients

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PAP is a rare disorder, characterized by accumulation of lipoproteinaceous material within alveolar spaces.The clinical course of PAP ranges from spontaneous remission to respiratory failure and whole lung lavage (WLL) currently remains the therapeutic standard.
Methods: Clinical assessment was performed by HRCT scan, BAL, lung biopsy, pulmonary function tests, serum markers (LDH,CYFRA,CEA,NSE) and GM-CSF autoantibodies.
Results: We enrolled 76 PAP patients from 1989 to 2011, divided as follows: Idiopathic PAP (n=70) of which the autoimmune nature was confirmed in 76%, Secondary PAP (n=3, 4%), Congenital PAP (n=1, 1.3%) and PAP-like disorders (n=2, 2.7%). The idiopathic PAP patients showed a prevalence of males (72.8%) over females, with a mean age at diagnosis of 40.7±13. A smoking history (current or former smokers) occurred in 68.5%, with a mean of 27pack/years. The most common presenting symptom was dyspnea, alone (27 patients) or in combination with cough (16 patients). 4 patients were completely asymptomatic. Intercurrent infections were present in 14 cases. Mean GMAbs level was 261±240 μg/mL (n.v. <3 μg/mL). From our whole series, 43 patients were submitted to WLL: 30 (43%) received 1 WLL, whereas 13 (30%) received 2 or more WLLs. Comparison of pulmonary function testing data between not lavaged and lavaged PAP patients showed a significant difference for the TLCO% pred (mean value 60.3±18.4 vs 46±13.7, p=0.011) and for the A-aO2 gradient (35±17vs 45±15.8 mmHg, p=0.043).
Conclusion: The establishment of a reference center for PAP in Italy has allowed to gather and well characterize one of the largest series of PAP patients worldwide.
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Lymphocytes populations in bloods and lungs in patients with auto-immune pulmonary alveolar proteinosis

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Background and aim: Pulmonary alveolar proteinosis (PAP) is a rare lung disease which is characterized by pulmonary surfactant accumulation in the lungs, and a subset of PAP which occurs in association with granulocyte/macrophage colony-stimulating factor (GM-CSF) autoantibodies is recommended to call autoimmune pulmonary alveolar proteinosis (APAP) (Inoue Y et al. Am J Respir Crit Care Med. 2008 177:752). We hypothesize that cellular immunity contributed to pathogenesis of APAP. The aim of this study is to know the lymphocytes populations and to clarify the role of lymphocytes in APAP.
Subjects and methods: Peripheral bloods (PBMC) and bronchoalveolar lavage fluids (BAL) from 30 patients with APAP, 20 healthy volunteers (HV), and 15 patients with other control diseases (CDs: IIPs, sarcoidosis, etc.) were analyzed. CD3, CD4, CD8, CD19, CD20, CD69, CD3/19, CD3/16, CD3/56, CD16/56, CD4/25, CD14/16, and CD19/69 were measured by flow cytometry.
Results: CD3+T cells in PBMC were lower in APAP than HV. CD3+/CD16- in PBMC were significantly lower in APAP than HV. CD4 in PBMC positively correlated with%VC, and negatively correlated with A-aDO2. CD3+T cells in BAL were significantly lower than CDs.
Conclusion: We found abnormal T cell populations in APAP, which suggests possible association of T cell immunity on the pathogenesis of APAP.
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Old and novel surfactant protein C (SP-C) mutations in children

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Genetic variations of SP-C gene are known to cause interstitial lung disease. In previous studies 55 patients have been described focussing on the genetic abnormalities and clinical course.
Here we report the data of children with SP-C mutations collected between 1998 and 2010. Lung biopsy findings and previous radiological imaging studies were re-examined using up to date classifications.
All 11 children identified had heterozygous mutations in the SP-C gene, six of which carried I73T and five other mutations (H59R, G74V, C121F, E191X, A112T). Age at onset of symptoms ranged from birth to 11 years; however most presented with postnatal respiratory distress syndrome or later with tachypnea, cough and failure to thrive. Chest computer tomography showed a variety of different patterns including ground glass attenuation, mosaic pattern, lung fibrosis and cysts. Initial diagnosis was made by genetic testing alone in 6 of 11 cases and by lung biopsy in 5 patients. Histology pattern included non specific interstitial pneumonia and desquamative interstitial pneumonia, chronic pneumonitis of infancy, pulmonary alveolar proteinosis and end stage fibrosis. Average follow-up was 7.1 years (0.8-

18.8), disease progression ameliorated in 6 and remained unchanged in 5 children. During infancy treatments given included corticosteroids and hydroxychloroquine with mixed results. Currently 2 children do not require medical treatment.
The manifestation of interstitial lung disease due to SP-C mutations is variable, however many children present during neonatal period and infancy. Intermediate term course seems favourable. Efficacy of empirical treatments urgently needs to be assessed in randomized trial.

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Serum VEGF-D and VEGFR-3 are biomarkers in lymphangioleiomyomatosis for its diagnosis and impaired pulmonary function
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Background: Lymphangioleiomyomatosis (LAM) is a disease characterized by proliferating LAM cells and LAM-associated lymphangiogenesis. Recently, it has been reported that the serum VEGF-D levels are increased in patients with LAM. Therefore, we hypothesized that VEGF-D and its receptor VEGFR-3 should be biomarkers for LAM.
Objectives: To evaluate clinical significance of serum levels of VEGF-C, VEGF-D and VEGFR-3 in patients with LAM.
Methods: We measured VEGF-C, VEGF-D and VEGFR-3 in serum of 7 patients with LAM, 4 patients with chronic obstructive pulmonary disease (COPD), and 6 normal subjects by enzyme-linked immunosorbent assays, and compared them with pulmonary function.
Results: In patients with LAM, serum VEGF-D levels were significantly increased (2995.1±909.2 pg/ml) compared with patients with COPD and normal subjects (264.7±37.6 pg/ml, 444.9±153.7 pg/ml, respectively). Serum VEGFR-3 levels were also significantly increased in LAM (4511.3±746.7 pg/ml) compared with normal subjects (2633.8±304.1 pg/ml). In patients with LAM, serum VEGF-D levels were negatively correlated with FEV_1/FVC (rs=-0.8630; p=0.0269) and%DLCO (rs=-0.9796; p=0.0035), and serum VEGFR-3 levels were negatively correlated with FEV_1/FVC (rs=-0.8119; p=0.0498).
Conclusion: These results indicate that, in LAM, serum VEGF-D and VEGFR-3 are candidate for biomarkers for the diagnosis and impaired pulmonary function.

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Lymphangioleiomyomatosis – Clinical characteristics and longitudinal follow-up of 36 cases
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Background: Lymphangioleiomyomatosis (LAM) characterized by LAM cells proliferation and cystic lung destruction can occur sporadically (S-LAM) or in association with tuberous sclerosis complex (TSC-LAM).
Aim: To describe the clinical characteristics of subjects with S-LAM and TSC-LAM and to assess changes in pulmonary function test (PFT) during observation.
Methods: Retrospective analysis of 36 women with LAM diagnosed between 1990 – 2010.
Results: There were 25 patients with S-LAM (69%) and 11 cases with TSC-LAM (31%). The mean age of onset of symptoms was 37.4±10.5yr and at diagnosis 40.2±10.1yr. Recurrent pneumothoraces occurred in 22 cases (61%), chylothorax in 4 (11%). Sixteen women (44%) were treated with progesterone. There were 7 deaths, including 4 from respiratory failure (after 6, 7, 11, and 11 yrs). Women with TSC-LAM were younger (32.6±10.2yr vs 43.5±8.3yr; p=0.0018) and more often had renal angiomyolipomas (100% vs 32%; p=0.00003) compared with those with S-LAM. TSC-LAM and S-LAM cases did not differ significantly regarding PFT at presentation. An obstructive pattern was observed in 56% of cases, whereas 35% had normal spirometric results. DLCO was reduced in 83% of patients. The serial biannual measurement of lung function revealed significant reduction in DLCO after 4 yrs (n=13; 49.5±18% pred. vs. 60.8±15.6% pred.; p=0.0038) and it was the earliest significant change in PFTs.
Conclusion: LAM is slowly progressing disease with the first significant deterioration in PFTs after 4 years of follow-up.

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Relationships between respiratory impedance and prognosis in patients with end-stage pulmonary lymphangioleiomyomatosis: A concept based on the Helmholtz resonator
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Background: Patients with lymphangioleiomyomatosis (LAM) are evaluated with multi-directional assessments in the same manner as those with COPD, but the pulmonary physiological features in patients with end-stage pulmonary LAM are complicated because the severe condition of patients caused by disease progression prohibits extensive testing. To complement this, we applied a forced oscillation technique (FOT) for the assessment of patients with LAM, and evaluated the relationship between respiratory impedance and disease severity.
Methods: 9 subjects with LAM were studied cross-sectionally. Lung function tests and respiratory impedance were measured. A concept based on the Helmholts Resonator was used to interpret those respiratory mechanics. A simple 3-element series (RIC) model was used to estimate airway resistance (Raw), airway inertance (Iaw), respiratory capacitance (Crs) and resonant frequency (fres). For the estimation of disease severity, a multifunctional index (BODE index) was used.
Results: The respiratory impedance spectra were fitted to the RIC model, and each value of goodness of fit from the 9 subjects was over 0.9. Raw, Iaw and fres correlated with%FEV1, RV/TLC,%DLCO/VA & the BODE index. Crs correlated with RV/TLC.
Conclusions: The RIC model corresponding with the Helmholtz Resonator provided a reasonable physiological interpretation in which the mechanical parameters reflected airway obstruction and a decrease in capacitive behavior. Thus, non-invasive FOT are useful and represent a potential monitoring tool to evaluate disease severity and prognosis in a cohort of patients with LAM.

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The efficiency of Langerhans' cell hystioctosis treatment (3 years follow-up)
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Aim: To evaluate the efficiency of Langerhans' cell hystiocytosis (LCH) treatment for 3years follow-up.
Methods: 38 patients (pts) with LCH confirmed by immunohistochemistry (IHC) research with monoclonal antibodies CD1a, S-100, LCA, CD68, Ki67, p53, Bax, Bcl-2, cpp32. The basic group (30 pts) was treated with systemic corticosteroids and cytostatics, control group (8 pts) did not receive treatment. All pts were subjected to clinical and radiological examinations and pulmonary function tests (PFTs).
Results: After 3 yrs clinical improvement was noted only in 4 pts (0,17) of basic group, in 16 pts (0,53) clinical picture was stable, in 10 pts clinical deterioration was observed. From them 6 pts complained of increased dyspnea, in 2 cases involvement of other organs was found, 1 pt lost weight, 1 pt complained of increased cough. On CT improvement was found in 11 pts (0,37). In 13 pts CT picture was stable. Deterioration of CT picture was noted in 6 pts (0,2). PFTs improved in comparison with pre-treatment period only in 2 pts. PFTs were stable in 12 pts (0,4), in 15 pts PFTs were deteriorated. After 3 yrs of natural course LCH PFTs worsened in all pts of control group. Clinical deterioration was observed in 50% of pts, and radiological (CT) deterioration – in 1 pt. The radiological symptoms were most stable: in 6 pts (0,74) no changes were noted. This is probably the evidence of inadequate sensitivity of CT for the follow-up of pts with LCH.
Conclusions: 1. After 3 yrs treatment improvement or stabilisation of clinical and radiological data and PFTs was observed in 50% of pts. 2. These data show sensitivity of PFTs for assessment of disease course and treatment efficiency.

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Pulmonary Langerhans-cell histiocytosis – Analysis of 57 cases
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Pulmonary Langerhans'-cell histiocytosis (PLCH) is a rare disease in adults. The clinical spectrum of the disease vary widely and course of it is unpredictable. Regression or stabilisation of the disease after smoking cessation is shown but in other cases progression in spite of treatment is observed. We have reviewed the records of 57 adults (28 women and 29 men in age 15 to 69 year) with histologicaly confirmed PLCH, diagnosed and treated in our Department in a period of 13 years to ascertain their vital status and outcome.
The median follow-up period was 72 months (range 6 to 216 months).All patients were smokers. One woman had disseminated disease, 3 multifocal bone disease, 5 patients had mandible involvement, and in 3 patients skin lesions were revealed. Diabetes insipidus was diagnosed in 8 patients. Clinical and radiological features, pulmonary function tests, will be discussed.
During the time of observation 36 patients were not treated (only stopped smoking) and regression or stabilization of pulmonary lesions were observed. Chemotherapy was administered to 11 patients and steroids to 10 patients, local steroid treatment was applied to 3 patients, radiotherapy in one and in one woman surgical excisions of bone lesions were performed.
One man underwent unilateral lung transplantation at the time of follow-up. Two deaths attributable to respiratory failure were noticed. No case of cancer was observed.

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Long term follow-up in patients with pulmonary alveolar proteinosis

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Pulmonary alveolar proteinosis (PAP) is a rare lung disease characterized by respiratory failure due to surfactant accumulation within the lung. PAP is currently treated by whole lung lavage (WLL).

Since 1977, our cohort is 52 (35 male, 17 female) idiopathic PAP patients. Median age - 37±9 y.o. Most patients are current or former smokers (64%) and have occupational history (55%). Most patients have moderate impairments in functional parameters (mean DLCO - 65±15% pred., mean pulmonary artery systolic pressure - 30±6 mm Hg).

The majority of patients (88.4%) received WLL therapy. 3 patients (5.8%) had segmental lavage, 3 patients (5.8%) - N-acetylcysteine (NAC) as monotherapy. The average number of WLL procedures was 2 (1-7). 34.6% received only one WLL and demonstrated long-term improvement after the procedure.

5-years survival rate is 100%. Spontaneous resolution was observed in 2 patients (3.8%) on NAC treatment. In most cases the course of PAP was slowly progressive. 8 patients (15.4%) had rapid progressive deterioration with respiratory failure despite repeated WLL. Predictors of fast progression were estimated. No associations with gender, age, smoking status were found. Long antibiotics and corticosteroids (CS) intake due to incorrect diagnoses before PAP diagnostic ($p<0.05$) and more than 3 years since first symptoms occurred till PAP diagnostic ($p<0.05$) correlated with progressive deterioration despite repeated WLL treatments. Besides, long CS intake increased the risk of secondary infections: pneumonia in 3 patients (5.8%), tuberculosis in 3 patients (5.8%), aspergillosis – 1 patient (1.9%).

Avoiding of delayed diagnosis/incorrect treatment increases the probability of long symptom-free period after WLL.

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Lymphocytic interstitial pneumonia – Two cases of unusual presentation

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Background: The diagnosis of Lymphocytic Interstitial Pneumonia (LIP) is established by the demonstration of an exuberant lymphoid infiltration. The ATS/ERS statement includes it in the group of idiopathic interstitial pneumonias on the basis that rare cases of histopathological LIP pattern are truly idiopathic.

Case 1: 56-year old male admitted with hemoptysis. Thoracic imaging showed a 1,8 cm solitary nodule in the right upper lobe. Bronchoscopy was negative for malignancy. PET-CT Scan revealed increased uptake. Thoracic surgery and histology revealed dense lymphocytic infiltrate in alveolar septa. Further testing ruled out subjacent causes of LIP.

Case 2: 71-year old female admitted for progressive dyspnoea. Chest CT revealed lung fibrosis and honeycombing mainly in the upper lobes. There was decreased diffusing capacity. Bronchoalveolar lavage revealed lymphocitosis. The histological pattern obtained by surgical biopsy was consistent with LIP with areas of interstitial fibrosis. Secondary causes of LIP were excluded. Treatment with prednisolone was started with clinical and functional improvement.

Comment: LIP represents a benign polyclonal proliferation that can diffusely involve the lung or be a focal process. The combined presence of nodules, cysts and ground glass are suggestive of LIP. Presentation as a solitary pulmonary nodule is rare; it may represent focal involvement of the lymph proliferative disorder. Demonstration of the polyclonality of the usual B cell infiltrates distinguishes LIP from pulmonary lymphoma. Fibrosis is unusual in idiopathic LIP and could be due to long standing disease.The authors emphasize the unusual radiologic presentation of these two cases of idiopathic LIP.

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Abnormalities between down regulation of cyclooxygenase-2 and up-regulation of grow factors in patients with systemic sclerosis

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The main of this study was observed the relationship between COX1, COX2, bFGF, TGFb and apoptosis by TUNEL in 24 surgical lung biopsies from patients with systemic sclerosis.

Methods: Fourteen patients all females (64±8.9yrs) were characterized with SSc. Immunohistochemistry and histomorphometry were used to evaluate the amount of COX1, COX2, bFGF, TGFb, and TUNEL expression. The expression of these markers was tested with their pulmonary function tests.

Results: Higher amount of bFGF and TGFb was observed in these patients contrasting with lower amounts of COX-1, COX-2, and TUNEL, principally in terminal bronchiolar arteries ($p=0.05$).

An important negative correlation was observed between vascular apoptosis and FVC ($r=0.655$, $p=-0.001$), FEV1 ($r=-0.707$, $p<0.001$) and DCO ($r=-0.685$, $p=0.005$) and a positive correlation between total lung COX-2 expression and DCO/VA ($r=0.794$, $p=0.001$).

Conclusions: bFGF and TGFb were increase in lung and in vascular structures of these patients contrasting with lower lung and vascular expression of COX1, COX2 and apoptosis. The vascular apoptosis expression had important impact with pulmonary function tests, suggesting and important participation of this via in the pathway of SSc. The vascular expression of bFGF and TGFb probably are not increasing via COX activation suggesting an insufficient angiogenesis.

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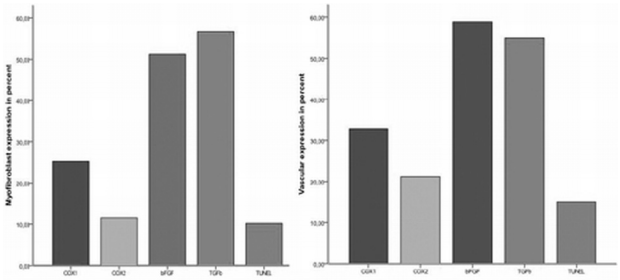

These figures show a higher amount of basic fibroblast growth factor (bFGF) and transforming grow factor beta (TGFb) contrasting with lower amounts of cyclooxygenase-1 (COX-1), COX-2, and TUNEL in myofibroblast of septal interstitium and terminal bronchiolar arteries in patients with systemic sclerosis.

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Features of pulmonary involvement in patients with diffuse connective tissue diseases

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The objective is to study features of pulmonary involvement in patients with diffuse connective tissue diseases

Materials and methods: Retrospective cohort study of 1363 patients. Inclusion criteria: patients at the age of 17-70 with diffuse connective tissue diseases. Exclusion criteria: malignant neoplasms of any localization, concomitant bronchopulmonary pathology. Standard clinical examination, electrocardiography, echocardiogram, spirometry, X-ray study, high resolution computed tomography, ultrasonic scanning of pleura were made.

Results: The involvement of respiratory system was found in 56 (4,11%) of 1363 examined patients. The patients with systemic lupus erythematosus - 25 (44,6%) and rheumatoid arthritis– 19 (33,9%) prevailed. Fewer cases of pulmonary involvement were met in patients with system scleroderma - 9 (16,1%), overlapsyndromes– 2 (3,6%) and idiopathic dermatomyositis- 1 (1,8%). The most common manifestations of pulmonary involvement are bronchoobstructive syndrome - 39,3%, pulmonary fibrosis – 23,2%, pleuritis – 16,1% and pneumonitis – 12,5%. In 3,6% cases vasculitis and in 1,8% - combinations of pleuritis-pneumonitis, pleuritis-bronchoobstructive syndrome and pneumonitis- pleuritis- pulmonary fibrosis were diagnosed.

Conclusion: In 4,11% cases, diffuse connective tissue disorders are accompanied with the involvement of respiratory system that is commonly manifested by bronchoobstructive syndrome, pulmonary fibrosis and pleuritis.

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Arterial stiffness in systemic scleroderma patients with restrictive lung disease

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Systemic sclerosis (SSc) is a chronic disease of unknown etiology, characterized by enhanced fibrosis, and microvascular abnormalities.

To study the stiffness of large arteries in relation to the restrictive lung disease (RLD) aortic stiffness was examined in patients with systemic sclerosis (SSc).

27 non-smoking patients (52,48±7,18 yrs) with diagnosis of SS were included. 17 patient was with RLD (FVC<70%) and 10 patient with normal lung function. Control group consisted of 28 healthy persons, aged 49,82±8,33 years. Arterial stiffness parameters were measured by means of pulse wave analysis using TensioMed Arteriograph (TensioMed, Hungary). Following parameters were detected: aortic augmentation index (AIxAo), aortic pulse wave velocity (PWV), brachial artery augmentation index (AIxB), central blood pressure (SBPao).

Arterial stiffness in patients with scleroderma

	SS with RLD (n=17)	SS without RLD (n=10)	Controls (n=28)
AIxB, %	–3.43±32.56*	–10.13±29.06	–24,76±30.15
AIxAo, %	31.11±13.80*	28.28±12.32	19,41±13.52
PWV, m/s	10.08±2.94*	9.25±2.03	8,44±2.44
Index AIxAo/AIxB	1.97±3.14***	1.40±2.56**	–1.53±2.47
Index PWV/AIxB	0.48±0.83***	0.35±0.77***	–0.55±0.64
Systolic BP	–0.24±8.26*	–2.51±7.98	–7.53±7.25
Index CP	99.30±6.61*	97.96±5.95	93.96±5.33

*p<0.05, **p<0.01, *** p<0.001 with controls. Index CP = (SBPao/brachial systolic BP) × 100.

We noted significantly differences of arterial stiffness parameters between pts with RLD and healthy subjects.
Arterial stiffness infringement in patient without RLD was less experience. We noted decreased differentiation between central and peripheral blood pressure (BP) and increased differentiation between central and peripheral arterial stiffness (index AIxAo/AixB).

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Lung function testing (LFT), diffusing capacity (DC) in patients with rheumatologic disorders: Is spirometry exclusionary?
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Aim: To evaluate ventilatory and lung diffusing capacity (DC) dysfunctions in patients with prior rheumatologic disease diagnosis, correlation with type of rheumatologic disorder, smoking status and establishing if prior normal spirometry is exclusionary.
Method: We performed LFT and DC in 81 patients with rheumatologic disease diagnosis, without prior diagnosis of lung involvement; we assessed lung parameters, status of smoking, Rheumatoid factor (RF) presence and we analysed frequencies and correlations.
Results: 7,4% had lupus eritematosus (LE),67,9% rheumatoid arthritis (RA); scleroderma (SD) 19,7%; spondilitis (Sp) in 4,9%; mean age 56,1±13,7years; smokers were 16%, exsmokers 13,6%, nonsmokers 70,4%; spirometry was abnormal in 61,7%, and DLco in 45,6% (decreased in 91,9%); ventilatory dysfunctions found were: restrictive dysfunction (RD) in RA 20%, in SD 50%, correlation factor (Cf)=0,37, p=0,004; obstructive dysfunction (OD) in RA 9%, in LE 16,6%, no correlation with smoker status; DLco was low in 26% of those with normal spirometry: the lowest values was found in SD and RA with RF+;DLco was decreased in 38,2% in RA; (76,1% in RF+), Cf=0,28; SD 62,5% with Cf=0,319, p=0,003; 25% in Sp; DLco increased in 8,1%.
Conclusions: Prevalence of ventilatory and difussing capacity dysfunctions was high in rheumatologic disorders; DLco was decreased in $\frac{1}{4}$ of patients despite normal spirometry-so,spirometry is not exclusionary for Dlco testing;existed a high correlation between RD and low DLco, RA with RF+ prevalence and low DLco,and SD and low DLco; we cannot found a correlation between smoker status and ventilatory or DLco disorders- (possible because of low prevalence of smoking).

P644
Features of pulmonary involvement in patients with diffuse connective tissue diseases depending on a nosological form
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The objective is to study features of pulmonary involvement in patients with diffuse connective tissue diseases (DCTD) depending on a nosological form.
Materials and methods: Retrospective cohort study of 1363 patients with DCTD. Exclusion criteria: concomitant bronchopulmonary pathology, malignant neoplasms. Standard clinical examination, electrocardiography, echocardiogram, spirometry, X-ray study, high resolution computed tomography, ultrasonic scanning of pleura were made.
Results: The involvement of respiratory system was found in 56 (4,11%) of 1363 examined patients. The patients with systemic lupus erythematosus (SLE) - 25 (44,6%), rheumatoid arthritis (RA) – 19 (33,9%) and systemic scleroderma (SS)-9 (16,1%) prevailed.
In SLE patients pulmonary involvement was commonly manifested by lupus pleuritis (36,0%), pneumonitis (28,0%), bronchoobstructive syndrome (12,0%), pulmonary hypertension (8,0%) and diffuse interstitial pulmonary fibrosis (4,0%). In three patients (12,0%) various combinations of pleuritis, pneumonitis, bronchoobstructive syndrome and signs of interstitial diffuse pulmonary fibrosis were diagnosed. In RA patients, in 100,0% of cases the involvement of respiratory system included bronchoobstructive syndrome manifestations, while in SS patients– fibrosing avleolitis.
Conclusion: In 100,0% cases the involvement of respiratory system with bronchoobstructive syndrome manifestations was more characteristic for RA patients, while for SS patients– fibrosing avleolitis. Pulmonary involvement in SLE patients is more heterogeneous, presented by pleuritis, pneumonitis, bronchoobstructive syndrome and their combinations.

P645
Pulmonary manifestations of systemic sclerosis, a report from Iran
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Background: Systemic sclerosis is a connective tissue disorder, manifesting as skin thickening and multi organ involvement. Scleroderma lung disease is the leading cause of death in this entity. The most common pulmonary presentations are interstitial lung disease and pulmonary hypertension,
Objectives: We investigated different presentations of lung disease in scleroderma patients in Masih Daneshvari hospital between October 2000 and September 2009 in a retrospective study and clinical and paraclinical results were reported.
Results: 42 patients were identified with scleroderma lung disease. The majority of the patients (84%) were female and 23% were male with mean age of 47.26±14.30. The most common complain was dyspnea followed by cough and orthopnea in 93%, 69% and 19% of the patients respectively. Echocardiography demonstrated elevated pulmonary artery pressure (≥30 mmhg) in 17 patients (40.4%). Association of pneumothorax and adenocarcinoma was noted in 3 and 1 of the patients respectively. Finally, 6 patients were deceased and 3 patients are expecting lung transplantation due to advanced lung fibrosis.

HRCT findings

Advanced lung fibrosis	28	66.6%
Reticular pattern	12	54.7%
Ground glass opacity	17	40.4%
Honeycombing	10	23.8%
Alveolar infiltration	12	23.5%
Pleural thickening	7	16.6%
Septal thickening	15	35.7%
Bronchiectasis	10	23.8%
Pleural effusion	6	14.2%
Pericardial effusion	5	11.9%
Mediastinal LAP	9	21.4%
Cardiomegaly	11	26.1%
Pneumothorax	3	7.1%

Conclusion: This study from a tertiary referral hospital in Iran illustrates similar results of pulmonary involvements in systemic sclerosis patients in comparison with previous reports.