FIBROSING INTERSTITIAL LUNG DISEASES OF IDIOPATHIC AND EXOGENOUS ORIGIN. PHENOTYPE APPROACH.

Conference, Postgradual and Scientific Course

PRAGUE
CZECH REPUBLIC
JUNE 19TH – 21ST 2014
HOTEL ARTEMIS
U SLUNCOVÉ 14, PRAGUE 8

POSTERS ABSTRACTS

hosted by
CZECH PNEUMOLOGICAL AND PHTHISEOLOGICAL SOCIETY

chaired by
PROF. VENERINO POLETTI AND ASSOC PROF. MARTINA VAŠÁKOVÁ

THE CONFERENCE IS HELD UNDER THE AUSPICES OF:
WORLD ASSOCIATION OF SARCOIDOSIS AND OTHER GRANULOMATOUS DISORDERS
ITALIAN ASSOCIATION OF HOSPITAL PNEUMOLOGY (AIPO)

THE CONFERENCE HAS ENDORSEMENT OF EUROPEAN RESPIRATORY SOCIETY

contents

poster nr.: 1

presented by:

Ivan Aleric

Recurrent intrathoracic Hodgkin's lymphoma: an unusual presentation with multiple pumonary ring-like lesions

authors: *I. Aleric, D. Katalinic, I. Neralic-Meniga*

Lung involvement is common in intrathoracic Hodgkin's lymphoma (HL), occurring in 25-40% of patients. The most common radiographic manifestation is mediastinal or hilar lymphadenopathy, which may be accompanied by parenchymal, pleural or chest wall involvement.

We present the case of a 39-year-old woman who was admitted to our hospital with a 2-week history of shortness of breath, dyspnea, haemoptysis and fever. Three years previously, she had been diagnosed with HL with cervical and mediastinal lymphadenopathy. She was treated with chemotherapy and irradiation. A year ago she had been hospitalized because of cavitation in her right upper pulmonary lobe. Relapse of HL was confirmed at thoracotomy. Six months after surgery, a chest x-ray revealed multiple thin-walled, ring-like lesions with right-sided pleural effusion. Fiber-optic bronchoscopy and bronchoalveolar lavage were normal. All microbiology samples were negative. Trans-thoracic fine-needle aspiration of the target lesion confirmed relapse of the HL. The patient underwent chemotherapy and achieved partial remission.

Intrathoracic HL, particularly of the nodular sclerosis subtype, frequently presents with bulky mediastinal disease. In our case, the radiographic presentation was quite unusual. Similar clinical presentation can also be found in primary lung or metastatic carcinoma, abscesses, mycobacterium infection, Wegener’s granulomatosis, rheumatoid arthritis and should be always taken into consideration.

poster nr.: 2

presented by:

Margarida Dias

Association between pulmonary function tests, HRCT and echocardiographic findings at the time of diagnosis of idiopathic pulmonary fibrosis

authors: *M. Dias, A. Gonçalves, F. Costa, M. Guimares, R. Lima, S. Campainha, C. Nogueira, S. Torres, M.C. Brito, S. Neves*

Aims:
To study associations between PFT, fibrosis extent in HRCT and echocardiographic findings in IPF patients at diagnosis.

Method:
We did a retrospective study of IPF patients followed in our ILD outpatient clinic. Demographic data, PFT, echocardiographic features of PHT were evaluated. Fibrosis extent was graded in 4 groups according to parenchyma involved- I: <25%; II: 25-50%; III: 50-75%; IV: >75%. Combined pulmonary fibrosis and emphysema (CPFE) was defined if emphysema extent >10%.

Results:
We included 38 patients, 71% male, mean age: 68±12 years.

FVC was normal in 50% and DLCO in 56%. Regarding the extent of fibrosis: I-22%; II-35%; III-30%; IV-13%. Eleven patients had CPFE. Echocardiography suggested PHT in 24%.

Lower TLC related to greater extent of fibrosis (p=0.015). No association between FVC and fibrosis extent was found but if those with CPFE were excluded, a greater extent of fibrosis was associated with lower FVC (p=0.047).

Fibrosis extent >25% in patients without CPFE and >50% in CPFE patients was needed for median FVC to be abnormal. DLCO wasn't related to extent of fibrosis or CPFE. Extent of fibrosis didn't predict PHT or 6MWT results.

Conclusions:
IPF diagnosis was made mainly at an early stage: most had <50% of fibrosis extent and no changes in FVC. CPFE patients had a different functional status than patients without CPFE. TLC was a better indicator of extent of fibrosis than FVC. This suggests pletismography may have a role in evaluatio

poster nr.: 3

presented by:

Regina Fillerová

Protein levels of CXCL11 and IL-17 in bronchoalveolar lavage fluid and TGF-beta, TNF and CD69 in serum reflect severity and progression in sarcoidosis

authors: R. Fillerova, T. Tomankova, P. Schneiderova, M. Zurkova, V. Lostakova, V. Kolek, E. Kriegova

Aim:
To investigate whether protein profiles in bronchoalveolar lavage (BAL) fluid and serum differ between patients with remitting and progressing sarcoidosis (S) as assessed by 2yrs follow-up.

Methods:
Highly sensitive Proximity Extension Assay (Proseek Multiplex, Olink) was used to detect 92 candidate proteins in BAL fluid and serum obtained from 18 S patients. Immuno-qPCR was used to assess IL-17 protein levels in BAL fluid. Subanalysis was performed in groups according to disease outcome after 2 years (S progressing n=9/remitting n=9).

Results:
Of studied proteins, we observed elevated levels of CXCL11 (fold change 1.78, p=0.05), trend to higher levels of CXCL10 (2.61, p=0.08) and HB-EGF (1.14, p=0.08) in BAL from patients with progressive S comparing to remitting disease. We detected elevated IL-17 protein levels in BAL fluid obtained from patients with progressing S (median, 25th-75th percentile: 107.2, 74.4-177.6 pg/ml) comparing to those with remission (47.1, 30.0-79.4 pg/ml, p<0.0001). In serum, patients with progressive disease had higher levels of LAP TGF-beta-1 (1.80, p=0.01), TNF (1.19, p=0.03) and CD69 (1.68, p=0.04) than remitting patients.

Conclusions:
Protein levels of CXCL11 and IL-17 in BAL fluid and TGF-beta, TNF and CD69 in serum reflect severity and progression in sarcoidosis. Detection of protein profiles in particular sarcoidosis phenotypes may contribute to identification of clinically useful biomarkers.

Grant support: IGA MZ CR NT/11117,LF_UP_14_020

poster nr.: 4

presented by:

Ana Gonçalves

Predicting prognosis in a cohort of idiopathic pulmonary fibrosis patients

authors: *A.F. Gonçalves[1], I. Franco[1], M. Dias[1], S. Campainha[1], C. Nogueira[1], S. Torres[1], M.C. Brito[1], F. Costa[2], A. Sanches[3], S. Neves[1]*
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1- Pulmonology Department
2- Radiology Department
3 –Pathology Department

Introduction:
Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrosing disease of unknown cause with an overall poor prognosis. Scoring and staging systems in IPF may improve prognosis and help guide management decisions.

Objectives:
Characterization of patients with IPF and assess the prognostic value of Composite Physiologic Index (CPI) and GAP index and staging system in these patients.

Methods:
Retrospective study of IPF patients followed in our ILD outpatient clinic was conducted, between January 2002 and December 2013. Data collected: demographics, smoking history, lung function tests, treatment, mortality, CPI and GAP index and staging system.

Results:
48 patients evaluated, 35 included (74, 3% men), with mean age of 67,16 (+/- 11,38) years. 40% non smokers, 25,7% smokers and 34,3% former smokers. Mean % predicted FVC of 81,7% (+/- 21,31), mean % predicted FEV1 of 83,95% (+/-22,05) and mean % predicted DLCO of 61,8(+/-28,2). Mortality rate of 34,3%.Mean GAP index of 3,43 and stage I 48,6% , stage II 42,9% and stage III 8,6%. A higher CPI score and a higher GAP index or stage was associated with a lower overall survival ($p= 0,024$; $p= 0,007$; $p < 0,001$).

Discussion:
In our series a higher GAP index and stage,as well as a higher CPI score, was associated with a worse prognosis. A simple-to-use staging system or score in IPF may become an important tool to accurately inform prognosis and help management decisions(timing for lung transplantation).

poster nr.: 5

presented by:

Ana Gonçalves

Desquamative interstitial pneumonia - an etiologic challenge

authors: *A.F. Gonçalves[1], S. Campainha[1], C. Nogueira[1], S. Torres[1], M.C. Brito[1], F. Costa[2],S. Campelos[3], S. Neves[1]*
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1- Pulmonology Department
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Introduction:

Desquamative interstitial pneumonia (DIP) is associated with tobacco smoke but can occur with occupational exposure to inorganic particles, mycotoxins, connective tissue diseases and pulmonary infections.

54 years old male, former smoker. Worked in a glass fiber mold factory. Had dyspnea, dry cough and weight loss. Presented digital clubbing and bilateral crackles. Chest tomography: ground glass pattern with predominance in the lower regions, and centrilobular nodules. Lung functional tests: mild restriction, mild reduced diffusion capacity of DLCO and PaO2: 53 mmHg.BAL: increased alveolar macrophages. Transbronchial biopsy left B9: inconclusive.Patient without functional conditions to perform lung biopsy. Corticosteroid therapy was started with clinical improvement. Core needle biopsy: intra-alveolar macrophages and identification of particles, birefringent under polarized light . Lung biopsy subjected to scanning electron microscopy and X-ray microscopy: dense particles with composition dominated by O, Si, Al, K, that are associated with other particles – oxide titanium, silica, calcium salts and fragments of stainless steel. Particles found in glass fiber composition. Patient showed clinical and functional improvement under corticosteroid therapy.Conclusion:DIP is not always associated with tobacco smoke. Occupational exposure should always be considered and mineralogical analysis of biopsy samples is an important procedure in etiologic investigation.

poster nr.: 6

presented by:

Helena Hornychová

IgG4 related disease-like changes in tumor induced obstructive pneumonia

authors: *H. Hornychová, M. Nová*

Aim

The authors report a case of patient with lesion fulfilling the histologic criteria of IgG4 related disease in core cut biopsy and small cell lung carcinoma in rebiopsy and the results of a retrospective study describing changes mimicking IgG4 related disease in the obstructive pneumonia in lung parenchyma of patients with lung cancer.

Methods

A series of 19 cases of obstructive pneumonia identified in resection specimens from patients treated by lobectomy for non-small cell lung cancer or carcinoid was evaluated. Immunohistochemistry for IgG and IgG4 was performed. Number of IgG and IgG4 positive cells in high power field was quantified. A IgG4/IgG ratio was calculated.

Results

From 19 cases of obstructive pneumonia 4 cases had more than 50 % IgG4 from IgG positive plasmocytes. Absolute number of IgG4 plasmocytes in these cases was more than 60. Only in one case these changes were found on larger area, in rest of cases it was only small focus in close proximity to the tumor.

Conclusions

IgG4 related disease-like changes can be found in obstructive pneumonia. Diagnosis of IgG4 related disease from core cut biopsy should be therefore established only in cases where the diagnosis of malignancy can be with certainty ruled out. The rare cases of coincidence of true IgG4 related disease and lung carcinoma have been described, however, as the presence of similar changes is relatively frequently associated with malignancy, underdiagnosis of tumor lesion could have fatal consequences.

poster nr.: 7

presented by:

Beáta Hutyrová

Pleural involvement in sarcoidosis

authors: *B. Hutyrová, F. Čtvrtlík, V. Kolek*

Aims:
Pleural involvement was formerly considered to be a rare manifestation of sarcoidosis. This report evaluates incidence of pleural involvement in sarcoidosis detected by high resolution CT (HRCT) scans.

Methods:
In 151 patients with sarcoidosis chest X-ray and HRCT of the lung was performed with detection of pleural changes.

Results:
Pleural involvement was detected in 54 patients (35.8%). No significant differences were found in age and gender between groups of patients with or without pleural involvement. We found pleural nodulation in 12.6%, pleural thickening in 23.2% and pleural effusion in 1.3% cases. Findings in 2 patients with pleural effusion are described. In radiographic stage 0 and I was significantly decreased incidence of all forms of pleural involvement compared to stages with involvement of pulmonary parenchyma II to IV (18.2% vs. 45.8%, p=0.006).

Conclusion:
Pleural involvement in sarcoidosis may be present as pleural nodules, thickening and calcification; clinically more severe forms are pleural effusion, chylothorax, pneumothorax or hemothorax. We found only three types of pleural involvement – pleural thickening, nodules and effusion. Their incidence in our study corresponds with literature data. There was a significant trend towards an increase of incidence of all forms of pleural involvement in dependence on increasing radiographic stage of sarcoidosis.

Grant support: IGA MZ ČR NT11117 a IGA_LF_2014_020

poster nr.: 6

presented by:

Maja Juričić

Interferon beta 1a-induced bronchiolitis obliterans organizing pneumonia: A case report

authors: M. Alilović, T. Peroš-Golubičić, M. Juričić, A. Koprivanac, D. Pelicarić

Recombinant interferons (alpha and beta) are used as immunomodulators in treating viral infections (hepatitis B and C), malignant and lymphoproliferative diseases and multiple sclerosis (interferon beta). Nonspecific side effects of interferon are found in up to 1/3 of patients. Drug induced lung diseases are rare.

We present a 50-year old man who was diagnosed with multiple sclerosis in 2009, and started treatment with interferon beta 1a in 2011. He was receiving it subcutaneously every 14 days. After one year nonspecific symptoms ocured, febrility up to 39°C and dry cough, followed by dyspnea.

Chest X-ray was normal, but HRCT of thorax showed consolidates in both lower lung lobes, tree in bud lesions, bilateral pleural effusions and air trapping during expiration.

PFT's showed restrictive ventilation disorders (FVC 73%, FEV1 62.8%, FEV1/VC 100.8%) and decreased DLco (69%). The diagnosis of bronchiolitis obliterans organizing pneumonia was made by PHD analysis of tranbronchial lung biopsy.

Discontinuation of interferon beta 1a was recommended, which was followed by the regression of lung infiltrates, therefore no corticosteroid therapy was necessary.

Follow-up HRCT of thorax and pulmonary functional tests (FVC 92.5%, FEV1 92.5%, FEV1/VC 108%, DLco 92.5%) after one year were normal.

According to the literature, the case we presented would be the second case of BOOP associated with the use of interferon beta 1a.

poster nr.: 9

presented by:

Maja Juričić

CARDIOVASCULAR DRUG-INDUCED INTERSTITIAL LUNG DISEASE; CASE PRESENTATION

authors: M. Juričić, M. Alilović, A. Koprivanac, D. Pelicarić, S. Smojver-Ježek, L. Brčić, T. Peroš-Golubičić

Cardiovascular drug-induced side effects are seen occasionally, most frequently in patients taking amiodarone, ACE inibitors, anticoagulants, beta blockers and statins. Major pulmonary form is drug-induced interstitial lung disease-DILD.

Pt. M.M. was admitted to hospital due to fever, dyspnoa and pulmonary infiltrates. Since 2011.she has been on amiodarone and in Ocober 2011.implantable cardioverter defibrillator was inserted. The workup among others showed BALF cytoanalysis and transbroncial PHD indicative of DILD. The amiodarone-drug induced lung disease, with peripheral and pulmonary eosinophilia and BOOP was diagnosed. The cesasion of amiodarone and corticosteroids made respiratory failure vane, patient recover and lung infiltrates diminish.

Pt. C.D. experienced fever and cough in January 2013. In outer Institution he received corticosteroids with disappearance of symptoms and multiple interstitial infiltrates. Following the cessation of the steroids all the symptoms (fever, cough) and multiple, migratory pulmonary infiltrates recurred. The workup among others showed BALF cytoanalysis and transbroncial PHD indicative of DILD. The substitution of simvastatin with ezetimib and corticosteroids caused symptoms and pulmonary infiltrates disappear. As ILD has been reported with most statins, suggesting that statin-induced ILD is a class effect and not a specific statin effect we did not substitute simvastatin with another statin but with entirely different compound.

poster nr.: 10

presented by:

Vladimíra Lošťáková

MUSCULOSKELETAL SARCOIDOSIS

authors: *V. Lošťáková[1], V. Kolek[1], J. Lošťák[2], J. Gallo[2], E. Kriegová[3], M. Žurková[1], T. Tichý[4]*
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2- Department of Orthopedics, University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University Olomouc
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4- Department of Clinical and Molecular Pathology, University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University Olomouc

Aims:
Although joint pain is experienced by approximately 25-39% of patients with sarcoidosis, deforming arthritis is rather sporadic.

Methods:
Presented is a case of a 55-year-old female. In 2001, total hip replacement (THR) for degenerative joint disease was done. In November 2009, THR dislocation occurred and revision surgery was indicated. During the revision surgery, a large bursa was found in the quadriceps muscle and excised. Later, however, dislocation reoccurred. In October 2010, therefore, revision surgery was indicated, during which a large cystic mass was revealed on the femur. A granuloma was histologically confirmed. In January 2011, a small reddened area developed in the center of the wound. The patient was referred to a dermatology department for skin excision. Once again, granulomatous reaction resembling sarcoidosis was histologically confirmed.

Results:
The patient was referred to our center. The diagnosis was confirmed. The drug therapy with corticoids and hydroxychloroquine was initiated. Outpatient follow-up showed an improvement in the patient's condition and the local lesion. Given the favorable response to therapy, the left hip prosthesis is to be reimplanted.

Conclusions:
Presented is a case of sarcoidosis with involvement of the lungs, skin, muscles and fasciae. The case report underlined the need for a multidisciplinary approach to the diagnosis and treatment of the condition.

Supported by grants IGA MZ ČR NT11117 and IGA LF 2014 020.

poster nr.: 11

presented by:

Dora Marinova

Heat shock protein 27 and alphaB-crystallin expression in lung tissue from patients with pulmonary sarcoidosis

authors: D. Marinova, Y. Slavova, St. Ivanov

Background:
Sarcoidosis is a granulomatous disorder with unknown etiology which most commonly affects the lungs.The link between infection and autoimmunity is often discussed. Low molecular weight heat shock proteins - Hsp27 and alphaB-crystallin - are molecular chaperones and are associated with proliferation,differentiation, apoptosis and influence the immune response.

Aim:
to investigate the expression of heat shock protein 27 (Hsp27) and alphaB-crystallin (Cryab) in lung tissue from patients with sarcoidosis.

Material and methods:
Lung tissue from 15 patients with sarcoidosis was studied - 7 women and 8 men; mean age 48;1st stage n=2,2nd stage n=11,3th stage n=2; 8 smokers and 7 non-smoker. Immunohistochemical expression of Hsp27, phosphorylated Hsp27, Cryab and phosphorylated Cryab was studied.

Results:
In the studied cases the following expression in granulomas was found:1) Hsp27 is expressed in the cytoplasm of epitheloid cells and giant cells with high intensity;2) phosphorylated Hsp27 is not expressed in these cells;3) Cryab is expressed with high intensity in the cell nucleus and with weak intensity in the cytoplasm;4) phosphorylated alphaBCryab is expressed with high intensity in the cell nucleus and with moderate intensity in the cytoplasm.

Conclusion:
Low molecular weight heat shock proteins play a role in the granulomatous inflammation in patients with sarcoidosis, which requires further clarification of autoimmunity factors in the etiopathogenesis of sarcoidosis.

poster nr.: 12

presented by:

Nesrin Mogulkoc-Bishop

Seven Years' Experience of the Multidisciplinary Diagnosis and Management of Patients with a Definite Diagnosis of Idiopathic Pulmonary Fibrosis

authors: *N. Mogulkoc, Y. Kabasakal, S. Bayraktaroglu, A. Veral, A. Ergonul, F. Bacakoglu, P. Bishop*

67 patients were referred with a presumptive diagnosis of IPF. We classified HRCT appearances as UIP, possible UIP or inconsistent with UIP. A surgical biopsy was obtained in 14 patients and classified as UIP, probable UIP, possible UIP or not UIP. After multidisciplinary team (MDT) review, definite UIP was diagnosed in 24 patients; 18 were men. The average age was 62 years (47 to 75). Five have died; 4 from exacerbations of IPF, one from carcinoma of the lung. The average follow up is 41 months, with two deaths at 3 and 10 months respectively, otherwise the range being 12 to 82 months. Follow up is routinely at 3 monthly intervals in an MDT, with annual HRCT. None have had specific anti-fibrotic drug therapy. At initial presentation, the average FVC was 2.46 L (range 1.24 to 3.90), FVC % predicted was 71% (52% to 93%), DLCO average was 13.6 ml/mmHg/min (4.6 to 23.2), DLCO % predicted average was 56% (16% to 88%). At the last presentation, the average FVC was 2.00 L (1.05 to 3.27), FVC % predicted was 60% (48% to 81%), DLCO average 11.4 ml/mmHg/min (5.6 to 19.3), DLCO % predicted average was 50% (27% to 73%). The change in FVC during follow up averaged -20% (-42% to -2%); 17 patients deteriorated by more than 10%. The change in FVC per annum averaged -8% (-38% to 0%). The change in DLCO over the time of follow up averaged -25% (-51% to -5%); 14 patients deteriorated by more than 15%. The change in DLCO per annum averaged -9% (-23% to -1%).

poster nr.: 13

presented by:

António Morais

Associations between ANXA11 rs1049550 C/T, BTNL2 rs2076530 G/A, HLA class I and II polymorphisms and sarcoidosis evolution.

authors: *M. Vaz[1], B. Lima[2], N. Melo[1], P.C. Mota[1,3], A. Morais[1,3]*
1- Hospital So Joo, Pulmonology Department, Porto, Portugal
2- Oficina de Bioestatistica, Ermesinde, Portugal
3- Faculdade de Medicina do Porto, Porto, Portugal

Aim:
Analysis of associations between ANXA11 rs1049550, BTNL2 rs2076530, HLA class I/II polymorphisms, the potential interaction effect among them and sarcoidosis outcome.

Methods:
138 patients included (37.2±12.1 years, 56.5% women). Evidence of disease after 2 years was considered chronic sarcoidosis. Samples were genotyped for ANXA11 rs1049550 C/T and BTNL2 rs2076530 G/A using rt-PCR and for HLA by PCR-SSP. Differences between groups were evaluated through X2-test (or Fisher exact test) in univariate analysis and logistic regression in multivariate analysis. RR or OR and 95% confidence intervals were calculated.

Results:
66 patients had disease resolution and 72 chronic disease. Comparison of ANXA rs1049550 and BTNL2 rs2076530 allele frequencies didn't show any significant differences. Regarding HLA allele frequencies, only DRB1*03 allele association with disease resolution remain statistically significant after Bonferroni correction (4.9%vs21.2%; RR=0.35; pc<0.01). In the logistic regression models to access the association of HLA alleles and chronic sarcoidosis, adjusted for ANXA11 rs1049550 and BTNL2 rs2076530 only DRB1*03 were significantly protective to chronic evolution after Bonferroni corrections. No significant interaction terms were found in logistic regression analysis.

Conclusions:
In this cohort, only HLA DRB1*03 is associated with disease evolution, when ANXA11 rs1049550, BTNL2 rs2076530 and HLA class I/II polymorphisms were considered either alone or in

poster nr.: 14

presented by:

Sofia Neves

Unclassifiable Idiopathic Interstitial Pneumonias – Reality of an outpatient consultation

authors: *I. Franco, S. Campainha, F. Costa, A. Sanches, A. Goncalves, M. Dias, C. Nogueira, S. Torres, M.C. Brito, S. Neves*

A significant minority of IIP cases cannot be classified even after multidisciplinary discussion (MD). The revision of the ATS/ERS classification of IIP (2013) recognised unclassifiable IIP as a formal entity

Aims:
Determine the prevalence of unclassifiable IIP cases in follow-up in our outpatient consultation, and analyse the characteristics, causes of unable classification and most probable diagnosis.

Methods:
A retrospective analysis of patients data with unclassifiable IIP diagnosed after MD were performed.

Results:
Unclassifiable IIP was diagnosed in 8.1% of the ILD cohort (22 of 272 patients). Exposure to drugs with possible pulmonary toxicity were present in 54.5% and immunological changes in 40.9%. Most usual radiological abnormalities:reticulation (81.8%) and ground glass (81.8%). Most common finding in BAL was lymphocytic and eosinophilic alveolitis (27.3%). Seventeen patients (follow-up 1 year) were classified according to disease behavior: most with stable residual disease (35.3%) and progressive, irreversible disease despite therapy (29.4%). Main causes of unable classification were: no conditions to surgical biopsy (50%) and major discordance beteween clinical, radiologic and pathologic finfings (27.3%). Most probable diagnosis after MD were IPF (31.8%) and HP (31.8%).

Discussion:
Unclassifiable IIP seem to embrace a heterogeneous group of diseases. Assessment of clinical and radiological evolution may allow, in the future, a better management of this entity.

poster nr.: 15

presented by:

Maria Oliveira

Is there a role for core needle biopsy in the diagnosis of interstitial lung disease?

authors: *M. Oliveira, T. Pereira, M. Dias, S. Campelos, A. Sanches, S. Campainha, S. Neves*

Aims:
Evaluation of patients with suspected interstitial lung disease (ILD) who underwent core needle biopsy and the diagnostic utility of this technique.

Methods:
Retrospective analysis of patients followed in our ILD outpatient clinic, that underwent diagnostic core needle biopsy (CNB). Data collected between 08/2010 and 02/2014 included: demographics, smoking habits, comorbidities, CT pattern, prior diagnostic techniques performed, complications and diagnostic results.

Results:
21 patients were included (69.6% men), mean age 65±14 years. 71.4% had smoking history. Heart failure (35.3%), coronary artery disease (17.6%) and COPD (17.6%) were the most frequent comorbidities. Most common CT features were ground glass opacities (52.1%), consolidation (47.8%) and nodules (12.9%). 52.2% of patients were previously performed broncoscopic diagnostic procedures. The main reasons to opt for CNB were patient refusal to surgical lung biopsy (33.3%) and poor surgical conditions (23.8%). Technical complications were observed in 23.8% of cases (14.2% pneumothorax, 14.2% hemoptysis and 4.8% alveolar hemorrhage). No patient required hospitalization. Diagnostic histological features were obtained in 52.3% of the cases (23.8% COP, 9.5% hypersensitivity pneumonia, 9.5% NSIP, 4.8% DIP and 4.8% silicosis).

Conclusion:
CNB was a safe and valid procedure in the diagnostic approach of a selected patient population with suspected ILD, providing histological confirmation in over 50% of patients

poster nr.: 17

presented by:

Martina Plačková

Pulmonary manifestations of Ehlers Danlos syndrome - a case report

authors: *M. Plačková[1], A. Jahodová[1], M. Vašáková[2]*
1- Faculty hospital in Ostrava
2- Thomayer's hospital in Prague

Ehlers - Danlos syndrome (EDS) is a rare hereditary disorder of connective tissue. It is caused by impaired formation or processing of collagen, or possibly other components of connective tissue (proteins that interact with collagen). Collagen is important in structuring skin, joints, muscles, tendons, blood vessels and visceral organs. Its symptoms include striking hypermobility of joints, weakness, vulnerability and hyperelasticity of skin, vascular fragility and the presence of abnormal blood platelets.There is a whole group of disorders that vary in severity from mild to life threatening. EDS is divided into several types. In our report (poster) we would like to remind and show to you pulmonary manifestations of a 41-year- old woman who suffers from one of the most serious forms of EDS - vascular type IV. The diagnosis was made by geneticist in 2011 and confirmed in collaboration with the Clinical Genetics University Gent Belgium - a deletion in exon 47 was found. It is an autosomal dominant defect that can occur in one in 100 to 250 thousand people. Their vessels and organs are fragile and prone to rupture. Typical pulmonary symptoms include emphysema, pneumothorax and pulmonary haemorrhage. The patient was sent to our department for recurrent presence of blood in the mouth, but without dyspnea and hemoptysis. According to HRCT of the lungs it was clear that she suffers from repeated bleeding into the lung tissue with the development of fibrotic lesions and calcifications – this will be presented on HRCT images. Specific treatment of this disease doesn't exist, it is recommended to use vitamin C. The patient is therefore monitored and possible complications will be dealt with.

poster nr.: 18

presented by:

Petr Pohunek

Neuroendocrine cells hyperplasia of the infancy (NEHI) - first documented case in the Czech Republic. A case report.

authors: *P. Pohunek, T. Svobodová*
Pediatric Pulmonology, Dept. of Pediatrics, 2nd Faculty of Medicine and University Hospital Motol, Prague.

We report a case of a boy who had been referred to our department at the age of 5 1/2 month (October 2007) for dyspnea, retractions, tachypnea. He was previously admitted at the age of three months to a regional hospital because of dyspnea and tachypnea noticed during a routine preventative check-up by a GP. For suspected viral pneumonia based on the clinical presentation and the CT scan he was treated with macrolides and bronchodilators with only transient effect. On our ward he deteriorated and received high dose systemic corticosteroids, the effect was only mild and transient. He had an open lung biopsy that did not originally prove any clear interstitial process, only increased number of macrophages and lymphocytes, some collapses and patchy damage to the alveolar walls. He remained oxygendependent for all the time since the original detection. Second reading of the biopsy in Houston, TX, USA (Dr. Megan Dishop) confirmed the hyperplasia of the neuroendocrine cells that we suspected based on the original CT finding. Based on this diagnosis, we have put the child on the long term home oxygen therapy and decided to avoid any further treatment.

He remained closely followed up. In the following time he gradually improved but needed continuous oxygen for about the next two years. The demand gradually decreased, he needed oxygen mainly during the night and during respiratory infections. The oxygen supplementation could be stopped altogether only in November 2011 (age 4 1/2 years). He developed symptomatic bronchial hyperresponsiveness that was treated by a combination of fluticasone/salmeterol with good control.

He is now 7 years old, with no relevant symptoms, normal development, full exercise tolerance. On spirometry he presents with mild decrease of the vital capacity and mild obstructive pattern of the flow-volume loop with some reversibility.

Conclusion: This is to our knowledge the only documented case of the NEHI in the Czech Republic. The development of this case clearly shows the importance of the proper diagnosis in this disease as confirmation of the NEHI implicates no need of any antiinflammatory or immunosuppressive therapy. Oxygen therapy and appropriate therapy of any respiratory infections remain the only treatment needed. Our case confirms the favourable prognosis of this disease if diagnosed early. As this is so far the only diagnosed case, it can not be excluded that there may be some other children with this disease whose diagnosis was not confirmed and who may have been treated by various treatments including oxygen and who eventually improved without having the diagnosis established.

poster nr.: 19

presented by:

Anne Marie Russell

An Exploration of Health Related Quality of Life and symptom Measures in a Cohort of patients diagnosed with Idiopathic Pulmonary Fibrosis (IPF)

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Introduction:
Patients diagnosed with Idiopathic Pulmonary Fibrosis (IPF) experience debilitating symptoms which impact upon health related quality of life (HRQoL). Whilst new therapies are being explored there is a lack of a validated systematic tool for measuring and monitoring HRQoL status in IPF. A Tool to Assess Quality of Life in Idiopathic Pulmonary Fibrosis (ATAQ-IPF) is the first IPF specific measure to be developed. We set out to explore the value of the ATAQ-IPF and contemporary symptom measures in an IPF population.

Methods:
Individuals, diagnosed with IPF were recruited to the PROFILE study, in our unit. Baseline severity was assessed by FVC, DLCo and CPI. Participants completed symptom measures: Hospital Anxiety & Depression scale (HADs); FACIT Fatigue Scale; MRC dyspnoea Scale; Leicester Cough Questionnaire (LCQ) and St Georges Respiratory questionnaire (SGRQ (original)) and ATAQ-IPF(V2). Correlation of baseline questionnaires and correlation between absolute change in HRQoL and symptom measures with FVC% change from baseline to 12 months were determined according to Spearman's rho coefficient. Multivariate regression analysis explored the interrelationship of domains within the HRQoL questionnaires and the individual item components of the symptom measures.

Results:
125 patients completed baseline questionnaires (82% males); mean age 68 (± 8.5) years & 62 patients completed questionnaires at 12 months. ATAQ scores correlate well with severity of disease (CPI: R0.26 p=0.0333) and total SGRQ (R0.72 p=0.00001) at baseline. ATAQ correlates with self-reported symptom questionnaires at baseline but less strongly with MRC score (R0.44 p=0.00001). Strongest correlations were observed with the SGRQ (R-0.40 p=0.0026) and the depression component of the HADS (R-0.47 p=0.0028).

Discussion:
This exploratory data suggests that the ATAQ-IPF is a reliable measure of HRQoL in an IPF cohort but with 89 items it is challenging to administer. The reliability and validity of instrument measures used IPF populations requires further exploration.

poster nr.: 20

presented by:

Anne Marie Russell

Methodology: Development of an Idiopathic Pulmonary Fibrosis (IPF) Patient Reported Outcome Measure (PRoM): An Iterative Approach to Item generation

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Introduction

IPF is associated with significant morbidity and mortality and presents a major challenge to the healthcare clinician. Patients experience debilitating symptoms associated with the disease itself and resulting from side effects of therapies. The USA ATAQ-IPF is currently the only disease specific PRoM available. It requires longitudinal validation but with 89 items it is challenging to administer. We are developing a concise IPF- PRoM (according to FDA criterion) with intended use as a primary endpoint in studies exploring the treatment of symptoms associated with IPF and as a secondary endpoint in clinical trials developing new therapies. Fundamental consideration in the development of the IPF-PRoM is the robust item generation process to support the final conceptual framework of the instrument.

Methodology:

We have conducted 5 Focus groups across 3 UK centres. Participants were stratified for disease severity according to Composite Physiological Index (CPI)(> 45 severe disease). Domains and items from existing symptom and HRQoL measures currently used in IPF have been deconstructed and collated. A group of 10 ILD expert pulmonologists participated in 2 rounds of a Nominal Group. Items generated from these 3 sources are incorporated into a Delphi survey. The survey will run for 3 rounds over 8-10 weekly cycle. Emergent data will undergo Principle component Analysis, followed by application of the RASCH model. The draft instrument will be tested and retested for reliability, repeatability & stability in a population of patients with IPF across a spectrum of disease severity. Participants will engage in cognitive interviewing. The final instrument will undergo validation in a European population.

Patient and Public Involvement

A multidisciplinary Research Support Group has a prominent role in this study with patient and carer representation. Members contribute to the analysis and have the authority to mandate for ‘grey’ items in the Delphi survey.

poster nr.: 21

presented by:

Tereza Tománková

Multiplex protein profiling in serum of patients with IPF-UIP, sarcoidosis and healthy controls

authors: *T. Tomankova*, R. Fillerova*, P. Schneiderova, M. Zurkova, V. Lostakova, V. Kolek, E. Kriegova*
**contributed equally*

Aim:
Idiopathic pulmonary fibrosis (IPF) and sarcoidosis (S) are diffuse lung diseases characterized by a mixture of inflammation and fibrosis. The aim of this study was to compare serum protein profiles between IPF-UIP, sarcoidosis and healthy controls using novel, highly sensitive protein multiplex assay.

Methods:
We analysed protein levels of 92 proteins using highly sensitive Proximity Extension Assay (Proseek Multiplex, Olink) in serum from 13 IPF patients, 18 S patients and 7 healthy controls. Statistical tests and principal component analyses were performed with software package GenEx (Sweden).

Results:
In serum from IPF and S patients, we observed twenty-six deregulated proteins ($p<0.05$). Of these, protein levels of Amphiregulin (fold change 2.46, $p=0.0000001$), HE4 (1.99, $p=0.000008$), Prostasin (1.50, $p=0.00002$), FasL (-1.43, $p=0.0002$), CXCL13 (2.25, $p=0.0002$), GDF-15 (3.45, $p=0.0003$), and HGF (1.82, $p=0.0005$) reached the highest significance between IPF-UIP and sarcoidosis. Sixty proteins were deregulated in IPF-UIP vs controls ($p<0.05$) and sixty-four proteins in S vs controls ($p<0.05$), showing expected similarities but also important differences in both disorders.

Conclusions:
Novel high-sensitive immunoassay identified distinct serum protein pattern in IPF-UIP and sarcoidosis. Identification of disease-specific serum protein patterns may contribute to nomination of new candidate biomarkers for non-invasive blood tests.

Grant support:IGA MZ CR NT/11117,LF_UP_14_020

poster nr.: 22

presented by:

Petal Wijnen

Presence of VKORC1 and CYP2C9 polymorphisms in a family with pulmonary fibrosis

authors: P. Wijnen, A. Bast, J. Verschakelen, O. Bekers, M. Drent

Aim:
Functional gene polymorphisms have been associated with either the incidence or progression of idiopathic pulmonary fibrosis (IPF). We previously found that anticoagulant users with vitamin K epoxide reductase complex 1 (VKORC1) and/or cytochrome P450 2C9 (CYP2C9) variant alleles have a predisposition to develop diffuse alveolar hemorrhage (DAH) events and that these DAH events substantially increase the risk of development or exacerbation of IPF. The aim of this study was to establish if there is a possible link between the presence of IPF and these variant alleles in a family.

Methods:
VKORC1 and CYP2C9 were genotyped in a family with four members suffering from pulmonary fibrosis.

Results:
All nine family members, spanning three generations, possessed at least one of the variant alleles tested. The four female IPF patients possessed VKORC1 allelic variants and all but one possessed a CYP2C9 variant allele.

Conclusions:
Our findings highlight a possible link of these allelic variants with IPF susceptibility in this family with IPF. To evaluate the clinical relevance of this link studies in a cohort of families with IPF are warranted.

poster nr.: 23

presented by:

Monika Žurková

The effect of pirfenidone on impaired lung function as compared with the other treatment modalities in patients with idiopathic pulmonary fibrosis (IPF) in patients listed in the Czech IPF registry

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Background

In June 2012, the Czech national IPF registry was established to monitor epidemiological data, course of the disease, patients survival and the therapeutric effect of novel treatment modalities. Present study used data from the registry to assess how lung function is influenced in IPF patients treated with pirfenidone in comparison with the other treatment modalities.

Patients and methods

The groups treated with pirfenidone, the three-drug therapy and other treatment modalities were compared. The decrease of predicted value (PV) of vital capacity (VC) and transfer factor (DLCO) as well as clinical characteristics and duration of the disease were compared .

Results

The comparison of changes in lung function over a 1-year follow-up showed a significantly larger decrease in the PV of VC in the three-drug therapy group (8.5% vs 1.6%) . The 1-year decrease in the PV of DLCO was also larger in this group (8.2% vs 4.2%), with the result being insignificant. The group with other treatment modalities also showed a significantly larger decrease in the PV of VC than the group treated with pirfenidon (7.5% vs 1.6%).

Conclusion

In present study IPF treatment with pirfenidone was associated with the smallest decrease of lung function in comparison with all other treatment modalities and this study confirmed a positive effect of pirfenidone in the Czech population.

Supported by the Czech Ministry of Health grant NT/11117., IGA LF 2014-020