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Abstracts

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Abstracts

Pulmonary resections for malignancy in patients with severely compromised lung functions

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Background: Significantly impaired lung function has long been considered a contraindication for pulmonary resections. In view if the knowledge gained from lung volume reduction surgery in emphysema patients this paradigm has changed. Lung cancer patients with reduced lung function and hyperinflation who are considered inoperable by classic criteria might experience less loss of lung function than expected or even improve after cancer resection.

Methods: All patients with severely reduced lung function (GOLD stages III and IV, FEV1% < 50%) undergoing lung cancer resection from 1/2006 to 8/2008 at our department were retrospectively analyzed. Postoperative predicted FEV1% was calculated according to the number of resected segments and compared to actual postoperative lung function values.

Results: 31 patients (20 male, 11 female, mean age 61 ± 8 years) with an FEV1% < 50% underwent lung resections for malignancy during the observation period. 27 patients were in GOLD stage III and 4 patients in GOLD stage IV. Average number of resected segments was 3.1 ± 2.5 (16 segmental resections/enucleations, 11 lobectomies, 1 bilobectomy, 3 pneumonectomies). Preoperative mean $PaCO_2$ level was 40.2 ± 4.8 mmHg (range 31.1 to 49.0). Mean preoperative FEV1% was 39.5 ± 8.8%. Mean postoperative predicted FEV1% was 32.5 ± 8.8%. Actual postoperative FEV1% was significantly better with 40.2 ± 10.1% (p = 0.004). Mean preoperative residual volume (RV) was 218 ± 58% and decreased to 206 ± 45% postoperatively, which however was not significant (p = 0.1). 5 patients required prolonged ventilation of more than 24 hours postoperatively. No perioperative in-hospital mortality was observed.

Conclusions: Pulmonary resections for malignancy can safely be performed in carefully selected patients with severely impaired lung function. Postoperative lung function parameters are frequently better than the predicted values and might even improve compared to preoperative lung function due to a volume reduction effect.

Tolerability of inhalative N-chlorotaurine in the pig model

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Objective: N-chlorotaurine, a long-lived oxidant produced by human leukocytes, can be applied in human medicine as an endogenous antiseptic. Its antimicrobial activity can be enhanced by ammonium chloride. This study was designed to evaluate the tolerability of inhalative N-chlorotaurine (NCT) in the pig model.

Methods: Anesthetized pigs inhaled test solutions of 1% (55mM) NCT (n = 7), 5% NCT (n = 6), or 1% NCT plus 1% ammonium chloride (n = 6), and 0.9% saline solution as a control (n = 7), respectively. Applications with 5 ml each were performed hourly within four hours. Lung function, hemodynamics, and pharmacokinetics were monitored. Bronchial lavage samples for captive bubble surfactometry and lung samples for histology and electron microscopy were removed.

Results: Arterial pressure of oxygen (PaO_2) decreased significantly over the observation period of 4 hours in all animals. Compared to saline, only 1% NCT + 1% NH4Cl led to significantly lower PaO_2 values at the endpoint after 4 hours (62 mmHg ± 9.6 vs. 76 mmHg ± 9.2, p = 0.014) with a corresponding increase in alveolo-arterial difference of oxygen partial pressure (AaDO2), (p = 0.004). Interestingly, AaDO2 was lowest with 1% NCT, even lower than with saline (p = 0.016). The increase of pulmonary artery pressure (PAP) over the observation period was smallest with 1% NCT without difference to controls (p = 0.91), and higher with 5% NCT (p = 0.02), and NCT + NH4Cl (p = 0.05).Histological investigations revealed no differences between the test and control groups and no ultrastructural changes of cells in transmission electron microscopy. The surfactant function remained intact. There was no systemic resorption of NCT detectable, and its local inactivation took place within 30 min. The concentration of NCT tolerated by A549 lung epithelial cells in vitro was similar to that known from other body cells (0.25–0.5 mM).

Conclusion: The endogenous antiseptic NCT was well tolerated at a concentration of 1% upon inhalation in the pig model. Addition of ammonium chloride in high concentration provokes statistically significant impact on blood oxygenation.

Alteration of temporal calcium signalling in human pulmonary artery endothelial cells by double-stranded RNA

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Spatial and temporal calcium oscillations regulate multiple signalling pathways in endothelial cells and they are essential for proper endothelial cell function. When the normal pathways for interaction break down, as can occur in disease states, uncontrolled or asynchronous behaviour can occur. Increased levels of circulating RNA may result from excessive cell damage or cancer. We investigated the effect of double-stranded RNA (dsRNA) on calcium homeostasis, gene expres-

sion and proliferation of primary human pulmonary artery endothelial cells (hPAECs).

Fura-2/am loaded hPAECs were used to investigate calcium changes of 24 h incubation with Poly I:C (synthetic dsRNA), dsRNA, natural RNA or control solution by means of live-cell imaging. As a standard stimulus, 100 µM histamine or 15 µM BHQ (a selective inhibitor of sarco/endoplasmic reticulum Ca2+-ATPase (SERCA)) was used in the presence and absence of extracellular calcium. Proliferation tests were performed on Poly I:C, dsRNA or BHQ stimulated cells, by means of 3H-thymidine incorporation. Gene expression of SERCA and toll-like-receptor 3 after dsRNA stimulation was analysed by quantitative RT-PCR. The cellular barrier properties of hPAECs as a read-out for cell function were assessed by measuring changes in the trans-endothelial electric resistance.

The calcium response to histamine showed a significantly prolonged duration after dsRNA incubation, while BHQ-induced Ca2+ response was not changed, pointing to an inhibitory effect of dsRNA on SERCA. Both BHQ and dsRNA inhibited proliferation in the same manner. The quantitative RT-PCR showed that SERCA was 3-fold down-regulated by the dsRNA incubation. The electrical resistance of the monolayer was decreased by 50% after 24 h dsRNA treatment.

In conclusion, it is tempting to hypothesize that the inhibition and down-regulation of sarco/endoplasmic reticulum Ca2+-ATPase by double-stranded RNA in human pulmonary endothelial cells contributes to the endothelial dysfunction.

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Exercise capacity and pulmonary artery pressure-flow relations in patients after successful pulmonary endarterectomy

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Background: Pulmonary endarterectomy (PEA) provides potential cure for patients with chronic thromboembolic pulmonary hypertension (CTEPH). Successfully operated patients have been shown to normalize hemodynamic parameters in long-term studies. The aim of the present study was to assess exercise capacity, and to test the hemodynamic response to exercise at least one year after successful PEA.

Methods: 13 successfully operated CTEPH patients and 14 healthy volunteers underwent cardiopulmonary exercise testing (CPET). In addition, patients and 10 age-matched controls without precapillary pulmonary hypertension underwent right heart catheterization at rest and after 10 minutes of submaximal supine bicycle-exercise. Between-group differences were analyzed utilizing the unpaired t-test, ANOVA or the Fisher's exact test. P-values < 0.05 were considered statistically significant.

Results: Peak work rate (110.5 ± 50.9 Watt) and O2 uptake at maximum exercise (1.8 ± 0.7 l/min) were reduced as compared to healthy volunteers (166.9 ± 49.2 Watt, p = 0.01 and 2.3 ± 0.6 l/min, p = 0.03).

There were no differences between patients and controls with respect to resting hemodynamic parameters. After 10 minutes of exercise, CTEPH patients displayed significantly higher levels of pulmonary vascular resistance than controls with a steeper pressure-flow gradient (p = 0.005).

Conclusions: The decline in PVR that occurs as a physiological reaction to exercise in healthy individuals is reduced in successfully operated CTEPH patients. This abnormal hemodynamic response to physical stress is associated with a limited exercise capacity of CTEPH patients after PEA.

Incidence and outcome of weaning from mechanical ventilation according to the new consensus categories

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Rationale: New guidelines on weaning from mechanical ventilation by the ATS/ERS/SCCM and ESICM categorize weaning as simple, difficult or prolonged. So far it has not been tested whether this new categorization correlates with patient outcome. Specifically, it is not known whether patients with difficult and/or prolonged weaning have increased mortality compared to patients with simple weaning.

Hypotheses: We hypothesized that patient outcome differs between the weaning categories.

Methods: We conducted a prospective cohort study in 5 medical-surgical ICUs in Vienna, Austria. Each ICU prospectively collected patient data during a 6 months period. We included patients who required mechanical ventilation >24 hours and who started weaning without unplanned extubation. Weaning was conducted according to the new guidelines.

Results: From an initial cohort of 510 patients 257 started weaning (53% male, 61 ± 16 yrs, SAPS II score 46 ± 18, 39% surgical admissions). Hospital mortality was increased in patients with prolonged weaning (32%) but not in patients with difficult weaning (9%) as compared to patients with simple weaning (13%), overall $p = 0.0205$. The weaning categories differed with regard to the ventilator-free days within 28 days [simple weaning 26 (18 to 27), difficult weaning 21 (12 to 24), prolonged weaning 1 (0 to 11) days, overall $p < 0.0001$]. In a logistic regression model, prolonged weaning but not difficult weaning was associated with an increased risk of death.

Conclusions: Prolonged weaning but not difficult weaning is a risk factor for increased hospital mortality.

Respiratory symptoms and lung function in adult asthmatic subjects exposed to environmental tobacco smoke (ETS) – Results of a pilot study in Salzburg

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Objective: ETS is a complex mixture of over 4000 chemicals from exhaled mainstream and sidestream smoke. ETS exposure is a risk factor for the development of asthma in childhood and can decrease lung function in children. Our pilot study was performed to examine the acute effect of ETS on lung function and respiratory symptoms in subjects with asthma.

Study population, materials and methods: All 20 participants had well-controlled mild to moderate asthma. They were exposed to artificially produced ETS in increasing concentrations, at weekly intervals for 3 hours. Spirometry was performed with Easy One Spirometer according to ATS-guidelines at given intervals of ETS exposure. Additionally exhaled NO and CO were measured.

The participants' symptoms were evaluated by using the asthma control test (ACT) and a visual analogue scale.

Results: Preliminary results will be presented at the meeting.

A two hour sedimentation of pleural effusion improves the diagnostic yield in patients with suspected malignancy

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Background: The diagnosis of pleuritis carcinomatosa in clinical practice remains difficult. In order to exclude/confirm a malignant pleural effusion, current guidelines recommend two independent samples of pleural fluid aspiration [1].

Aim: The aim of the present study was to evaluate the additional utility in excluding/confirming a suspected pleuritis carcinomatosa using a 2 hour sedimentation of pleural effusion.

Methods: In total 78 patients underwent pleural fluid aspiration (using ultrasound guided thoracocentesis) between March 2007 and March 2009. Cytological analyses has been performed either directly after samples have been taken (method I), or 2 hours after sedimentation (method II). All analyses have been carried out by the same investigator.

Results: 16 patients had to be excluded (no evidence of lung cancer). Of the remaining 62 (male: 62%; age: 66 ± 12, years) 42 were diagnosed with NSCLC (69% adenocarcinoma, 19% squamous cell carcinoma, 12% others), 7 with SCLC, 5 having malignant pleural mesothelioma and 8 having cancer of other lung origin. Using method I, the diagnosis of malignancy was obtained in 25 patients (40.3%). In contrast, when using method II the diagnosis of malignancy was obtained in 30 patients (48.3%). Therefore, the additional diagnostic yield of sedimentation was 8% (95% CI: 4.3–19.8).

Conclusion: Two hour sedimentation of pleural effusion may increase the diagnostic yield in routine pleural fluid aspiration in patients suspected for pleuritis carcinomatosa.

Reference

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Molecular characterization of human malignant pleural mesothelioma cell, lines: impact on response to systemic treatment approaches

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Background: Malignant pleural mesothelioma (MPM) is an asbestos-related highly therapy-resistant malignancy with increasing incidence in industrial countries. In general, the prognosis of MPM is poor with a median survival of 10 to 17 months from symptoms onset. Aim of this study is to improve the understanding of the complex molecular changes underlying the high chemotherapy resistance of MPM.

Material and methods: In this study 6 primary cell lines derived from operation specimens and pleural effusions of patients with the three different histological MPM subtypes (3 epithelial, 1 sarcomatous, 2 biphasic) were used. As a first approach, the cell lines were tested for their sensitivity against 10 chemotherapeutics frequently used in clinical practice. Western blot analysis was performed to evaluate the expression levels of the most important drug resistance proteins.

Results: In general, the tested cell lines strongly differed in their chemotherapy responsiveness. As expected, cis- and oxaliplatin were widely active against the tested MPMs. In case of adriamycin and imatinib, only 2 of 6 cell lines were responsive. Also gefitinib and vinblastine treatment were not very effective against the MPM cell lines. Notably, etoposide, paclitaxel, and BCNU revealed rather promising activity in vitro tests. For all tested compounds, at least 1 resistant cell line was identified. With regard to the expression of resistance-related proteins, ABC-transporter expression was generally rather low in these cell lines. Further no correlation of drug resistance with BCl-2, ERCC1 or CTR1 was found. Notably strong lung resistance protein (LRP) expression was found in 4 cases.

Conclusion: Taken together, our results show that the high therapy-resistance of MPM is very complex and not primarily based on transporter-mediated resistance mechanisms. This indicates that detailed molecular characterization of MPM will be necessary to optimize chemotherapy on a rational basis.

Sind Blutgasparameter im Wachzustand von nächtlicher Schlafapnoe beeinflusst?

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Background-study objective: Sleep disorded breathing is not only associated with nocturnal O2-desaturation but also with chronic (hours), REM-associated (minutes) and/or repeated short phases (seconds) of hypoventilation. If there are longer periods of hypercar-bia bicarbonate should rise as it counteracts hypoventilation. The hypothesis was tested whether morning blood gas parameters correlate with the number or duration of nocturnal apneas/hypopneas and/or

hypoxemia and furthermore whether they could be used as indica-tors for nocturnal breathing disturbances.

Patients-method: In 81 consecutive patients (19 female, 62 male; M ± 2SD age 54 ± 27.4; BMI 32 ± 12.8; AHI 18.4 ± 40.9) of a sleep-outpatient-clinic either arterial or capillary blood-gases (BGA) from hyperemiazed earlobes were drawn at their visit and in the morning after diagnostic polygraphy/polysomnography (PG/PSG). Linear correlations between BMI, pCO2, bicarbonate, aBE, pO2, AaDO2 and medication (diuretics, corticosteroids) with the AH-Index as well the duration of nocturnal hypoxemia were calculated.

Results: Bicarbonate obtained during outpatient clinic visits correlated with bicarbonate in the morning after the sleep study with $r^2 = 0.4827$, aBE $r^2 = 0.3813$, pCO2 = r^2 0.5452, pO2 $r^2 = 0.4822$, and SpO2 $r^2 = 0.396$ – all to some, but limited extent with values obtained in the morning after the sleep-apnea-screening. Comparing nocturnal events with morning BGA:

No correlations between nocturnal AHI and

pCO2morning	=	0.0026*AHI+38.546	$r^2 = 0.0002$
aBEmorning	=	0.0094*AHI+0.573	$r^2 = 0.0143$
HCO3morning	=	0.007*AHI+24.538	$r^2 = 0.0061$

Correlation between aBE in the morning and

diuretics	$r^2 = 0.0493$	
corticosteroids	$r^2 = 0.0179$	
apnea time	$r^2 = 0.0151$	
BMI	$r^2 = 0.0082$	
pCO2morning	$r^2 = 0.2082$	weak but significant

The alveolo-arterial O2-difference in the morning reflected hypoxemia during sleep only poorly.

Conclusion: Blood gas analysis apart from sleep studies compare hardly with parameters obtained immediately after PG/PSGs. Even with BGAs drawn immediately after awaking the different parameters did not correlate with nocturnal events. Neither AaDO2, pCO2, pO2, SpO2 nor bicarbonate or aBE reflected nocturnal hypoventilation. They cannot be used as indicators for sleep related breathing disturbances. Nocturnal hypoventilation might be coun-terregulated sufficiently enough or be too short as to cause lasting blood gas abnormalities.

Early development of pulmonary vasculopathy in scleroderma patients without manifest pulmonary arterial hypertension. A follow-up study

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Systemic sclerosis (SSc) is a known risk factor of pulmonary arterial hypertension (PAH) but the evolution of pulmonary vasculopathy in this condition is not completely understood.

We performed exercise Doppler echocardiography (EDE) and cardiopulmonary exercise test in patients with stable SSc at baseline and after 12 months to investigate changes in the pulmonary hemodynamics. A subset of patients underwent right heart catheterisation (RHC) at both times. Patients with known PAH were excluded.

N = 46 patients underwent baseline and follow-up EDE. Systolic pulmonary arterial pressure (PAP) as determined by EDE was 25 ± 5 vs. 26 ± 5 mmHg at rest, 31 ± 11 vs. 35 ± 11 mmHg at 25W, 37 ± 14 vs. 40 ± 13 mmHg at 50W during baseline vs. 12 month follow-up. Exercise capacity (peak oxygen uptake) was 89 ± 26 vs. 82 ± 22% predicted (baseline vs. follow-up). N = 18 patients had baseline and follow-up RHC. At baseline, all patients had a resting mean PAP <25 mmHg. Pulmonary vascular resistance (PVR) was 104 ± 50 vs. 123 ± 59 dyn at rest, 99 ± 38 vs. 115 ± 53 dyn at maximal exercise; the PVR increase at rest was 18%/yr.

Mean PAP was 16.5 ± 3.5 vs. 18.3 ± 4.1 mmHg at rest, 22.7 ± 4.9 vs. 24.7 ± 4.8 mmHg at 25W and 27.7 ± 5.4 vs. 30.8 ± 8.4 mmHg at 50W (baseline vs. follow-up); N = 2/18 patients developed PAH with a resting mean PAP >25 mmHg.

Non-invasive and invasive measurements showed an increase of PAP and PVR and a decrease of exercise capacity in a 1-year observation period, suggesting that pulmonary vasculopathy progresses in SSc without PAH at baseline and may even lead to the manifestation of PAH. Long-term studies are needed to further explore the development of PAH in SSc and to search for predictors for PAP increase.

Endothelin-1 activates pro-inflammatory signalling pathways via destinct p38MAPK isoforms resulting in downregulation of nuclear p27kip1

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Excessive cell proliferation is a hallmark in pulmonary arterial hypertension. Endothelin-1 (ET-1) acts as an important stimulus of cell cycle progression that relies on the activity of cyclins controlled by cyclin-dependent kinases (CDK). Prevention of abnormal proliferation depends on the function of cyclins and CDKs and are tightly regulated by cell-cycle inhibitors such p27kip1/p27. In malignant cells, p38 mitogen activated protein kinase (MAPK) was identified as important regulator of cell cycle by degradation of p27.

Human pulmonary arterial smooth muscle cells (PASMC) were treated with ET-1 (1 M) or in combination with Bosentan (BOS, 100 M) or SB203580; fetal calf serum (FCS 5%) was used as control. Protein (obtained from nuclear, cytosolic and whole cell extracts) and gene expression for p27 and p38 MAPK were determined by Immunofluorescence, Western blotting and RT-PCR. Cell cycle analysis was performed by flow-cytometry.

Stimulation of PASMC with ET-1 resulted in activation and nuclear translocation of p38 MAPK and decreased nuclear p27 protein. This was inhibited by the addition of the dual endothelin receptor antagonist Bosentan (BOS) or the specific p38MAPK inhibitor SB203580. BOS and SB203580 alone and in combination with ET-1 significantly increased p27 mRNA expression at 6 h ($p < 0.05$) and nuclear protein accumulation ($p < 0.05$), whereas ET-1 alone had no or negative effects. The combination of ET-1 with BOS induced an increase after 6 hours of G1-arrested cells (+6%; $p < 0.036$) while after 24 hours the increase for BOS alone was +9%; $p < 0.015$ and +14.2%; $p < 0.042$ for the combination with ET-1.

In PASMC, the ET-1 induced activation of p38MAPK was effectively blocked by Bosentan and this effect resulted in elevated levels of p27 gene expression and increased nuclear protein levels as well as activation of p27, thereby inhibiting cell cycle progression.

Non-reversible airways obstruction, associated co-morbidities and correlation with the BOD-Index

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Objective: To estimate the burden of co-morbid disease in subjects with non-reversible airways obstruction.

Methods: The Austrian BOLD data were used for this analysis. Participants were aged 40-years and over. Spirometry was done according to ATS-guidelines. Non-reversible airways obstruction (AO) was defined as a post-bronchodilator FEV1/FVC ratio below the lower limit of normal (LLN). The FEV1 was also used to stage AO: mild (FEV1%pred. >70%), moderate (FEV1%pred. 50–70%) and severe-very severe (FEV1%pred. <50%). Reported co-morbidities (heart disease, hypertension, diabetes and stroke) were from BOLD questionnaire. BOD scores (range 0–7) were established from FEV1%, medical research dyspnea scale (MRC) and BMI.

Results: 199 (15.8%) out of 1258 participants presented with non-reversible AO (FEV1/FVC ratio <LLN). Reported co-morbid disease was consistently more frequent among subjects with non-reversible AO, and this difference was significant for heart disease (10.6% vs 16.1%, p = 0.025). The prevalence of reported co-morbidities increased in parallel with severity of AO. The odds-ratio (OR) for severe-very severe AO versus no AO, and adjusted for sex and age, was 2.5 (95% CI 0.7–8.5) for heart disease, 1.18 (95% CI 0.4–3.6) for hypertension, 1.78 (95% CI 0.4–8.4) for diabetes, and 6.1 (95% CI 1.4–26.2) for stroke, respectively. Mean BOD scores increased with severity of AO but did not differ significantly depending on the presence of co-morbidities.

Conclusion: Non-reversible airways obstruction is associated with significant co-morbid disease and prevalence of co-morbidities might increase with severity of airways obstruction.

Gender-related differences in non-reversible airways obstruction – Results from the Austrian Burden of Obstructive Lung Disease (BOLD) study

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Objective: To evaluate gender-related differences in non-reversible airways obstruction (AO).

Methods: We used data from the Austrian BOLD study. Participants were aged 40-years and over. Spirometry was done according to ATS-guidelines. Non-reversible AO was defined as a post-bronchodilator FEV1/FVC below the lower limit of normal (LLN). Men and women with non-reversible AO were compared with regard to age, BMI, risk factors, respiratory symptoms, health-related quality of life, and co-morbidities.

Results: Among 1258 participants 199 (15.8%) fulfilled criteria for non-reversible AO. Even though women were less likely to be ever smokers, the prevalence of non-reversible AO was significantly higher among women than men, 19.4% vs 12.9%, p = 0.002. Among those with non-reversible AO men reported significantly more often ever active smoking (76.1% vs 62.2%, p = 0.035) and occupational exposures to inorganic dusts (14.8% vs 1.8%, p <0.001), gases/fumes and vapours (27.3% vs 4.5%, p <0.001). Respiratory symptoms increased with severity of AO in both men and women, but this increase was more pronounced in women. Both, women and men with non-reversible AO reported relevant co-morbidities. However, there were significant differences between women and men in the presence of reported asthma (19.8% vs 8.0%, p = 0.019) and heart disease (9.9% vs 23.9%, p = 0.008).

Conclusion: The results of this study support the notion that there are relevant gender-related differences in non-reversible AO with regard to risk factors, respiratory symptoms and reported co-morbidities. Gender-specific approaches to prevention, diagnosis and treatment of chronic airway obstruction should be developed.

Reversibility of airways obstruction in COPD – Results from the Austrian Burden of Obstructive Lung Disease (BOLD) study

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Objective: To estimate and characterize the fraction of subjects classified as COPD who present with partial reversibility in FEV1 and/or FVC.

Methods: We used pre- and post-bronchodilator spirometry data from the Austrian BOLD study. Participants were aged 40-years and over. Specially trained and certified technicians conducted spirometry according to American Thoracic Society guidelines. Irreversible airways obstruction was defined as a post-bronchodilator FEV1/FVC below 0.7 (COPD stage I or higher according to GOLD). Partial reversibility was present when the post-bronchodilator FEV1/FVC was below 0.7 but either the FEV1, the FVC or both increased by 12% (and 200 ml) after bronchodilator test (200 µg salbutamol).

Results: 304 (24.2%) out of 1258 participants had a post-bronchodilator FEV1/FVC ratio below 0.7 corresponding with GOLD stage I or higher COPD. Out of these 304 subjects 287 (94.4%) had valid pre- and post-bronchodilator spirometry. Among these 287 subjects (with a post-bronchodilator FEV1/FVC ratio below 0.7) improvements in FEV1 only, FVC only and both FEV1 and FVC were seen in 7%, 13% and 8%, respectively. Overall, 28% (80/287) of subjects with post-bronchodilator airways obstruction (FEV1/FVC <0.7) showed at least partial reversibility after bronchodilator test. Compared to subjects without relevant reversibility (n = 207), participants with partial reversibility (n = 80) were more likely to be female (p <0.001), reported twice often a prior physicians diagnosis of asthma and reported more often the presence of respiratory symptoms (dyspnea, cough and wheezing). No difference was seen in terms of health-related quality of life.

Conclusion: 28% of adults with post-bronchodilator airways obstruction show at least partial reversibilty and present with a distinct clinical profile.

Moderate hypoxia induces hypoxic adaptation in an ex-vivo non-small cell lung cancer model

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Hypoxia is common in solid cancers, such as lung cancer, and promotes aggressive tumor growth and chemotherapy resistance. The molecular mechanisms of adaptation to hypoxia have been largely investigated in tumor cell-lines. They include proteomic changes resulting in loss of apoptotic potential, change of cellular metabolism, and release of angiogenic growth factors. These changes are observed already under moderately hypoxic conditions with O2 concentrations of 1–2% (7–14 mmHg). We developed a novel ex vivo model using fragmented surgery explants in order to investigate mechanisms of hypoxic adaptation in non-small cell lung cancer (NSCLC). The results of our study show that NSCLC fragments can be maintained in culture for four days, both in ambient oxygen and moderate hypoxia (1% O2), without loss of viability, as demonstrated by formazan-based viability assay and histomorphologic evaluation of fragments. Apoptosis rates of tumor cells were investigated in fragments maintained under normoxia or chronic hypoxia for four days using antibodies against cleaved caspase 3 and showed no significant differences between normoxia (5.3% ± 2.6%) or hypoxia (5.7% ± 2.7%, P = 0.92). Cisplatin treated fragments served as a positive control. As a conclusion the novel ex vivo NSCLC fragment model allows the investigation of hypoxic adaptation in short time culture. It combines the advantage of a 3D culture and the use of primary NSCLC tissue instead of cell lines.

Erfolge einer stationären Raucherentwöhnung am Ende des Aufenthaltes und nach einem Jahr in 13 Rehabilitationszentren der PVA 2008

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Introduction: Smoking cessation programmes are offered in the rehabilitation centres (RC) of the Austrian Pension Insurance Company (PVA) for several years. The evaluation of the success, however, revealed diverse standards in implementation. Therefore, the smoking cessation programme in the RC was standardized due to the guidelines of the Austrian Society for Pneumology (ÖGP).

Methods: In a time interval of 6 months all smoking Patients in 13 RC of the PVA who volunteered for the standardized smoking withdrawal were included in a study about the outcome of this programme. The following measures were administered for documentation: measurement of exhaled CO and Fagerström test at T1 (baseline, before rehabilitation), questionnaires about restart of smoking, about smoking habits, and about used supporting means in withdrawal at T2 and T3 (T2 = after 3–4 weeks, at the end of the inpatient rehabilitation; T3 = after one year). Statistical analysis were performed in the Ludwig Boltzmann Institute for rehabilitation in Saalfelden using the programme package SYSTAT, Vs. 11 (Systat Software, USA).

Results: 605 smokers (387 men, 218 women; mean age 51.6 years) took part in the programme and could be included within a half year. The recorded Fagerström-tests for assessment of nicotine dependence resulted in 4.74 points (mean).

After 3–4 weeks (T2) 272 patients (44.96%) had become non-smokers, 237 (39.17%) reduced smoking, 83 (13.77%) went on smoking unchanged, and 13 (2.15%) even enhanced their cigarette consumption. 137 smokers used nicotine compensation therapy (nicotine inhaler n = 174, patch n = 68, nicotine gum n = 36, sublingual tablet n = 19 patients), 118 utilised acupuncture, 70 Champix, and 1 Zyban.

After one year 517 (85.45%) of the 605 patients – a really high percentage – could be reached for telephone or paper-and-pencil interviews. 25.95% were non-smokers at T3, 46.28% reduced smoking, 10.08% continued smoking unchanged in relation to T1, and 3.14% smoked more than at T1. The dropout rate was very low with 14.54%.

Summary: In the rehabilitation centres the PVA provides the majority of inpatient smoking withdrawal in Austria. Our investigations with a representative collective of more than 600 smokers document that the success rate of the launched standardized smoking cessation programme using ÖGP guidelines corresponds to international published experiences, and confirm the efficiency of the smoking cessation programme in the RC of the PVA.

Erhebung des Rauchverhaltens an den berufsbildenden Schulen in Weyer 2007/2008

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Object: Smoking starts at an even younger age. It is questioned how many pupils start smoking in college at age of 14 or later.

Methods: A questionnaire was answered by all pupils of the "Berufsbildende Schulen" in Weyer, supervised by their teachers in March 2007, asking about their smoking patterns. The smokers among them were asked, when and why they had started smoking.

Results: 318 of 364 pupils (87.36%) finished the questionnaire. 166 or 52% are never-smokers. 70 pupils or 22% are smoking only at weekends, 32 or 10% are smoking less than 5 cigarettes per day, 29 of them or 9.5% are smoking 5 to 10 cigarettes, 14 or 4.5% are smoking 10 to 20 cigarettes and only 4 or 1.25% are smoking more than 20 cigarettes per day.

61% of the pupils started smoking before college, only 6 had started in the "Pflichtpraktikum" and 35% started during college. The 2 most often mentioned reasons for starting were curiosity (73 times) and smoking friends.

As a reason for quitting smoking the 115 smokers mentioned health and 101 smokers financial reasons.

Conclusion: Not half of the pupils are smoking. 2 thirds of those started smoking before college. Smoking prophylaxis is rather late for many of the pupils in high school. Smoking cessation should be more encouraged than is the case now.

Varenicline for smoking cessation in a rehablitation center for pneumologic diseases

A. Lichtenschopf

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Object: To evaluate the efficacy and the side effects of varenicline for smoking cessation in a rehabilitation center for pulmonary diseases in 100 patients.

Methods: Observational study on 100 consecutive patients in the year 2007/2008.

Smokerlizertest (exhaled CO) at the end of 3 weeks and Telephon interview after 1 year.

Results: After 3 weeks 57% stopped smoking, 38% had reduced, 3% failed and 2% were lost to follow up. After 1 year 4 patients had died, from the remaining 96, 27 or 28.12% were still abstinent, 27 had reduceand 19 or 19.8% had failed, 22 or 22.9% could not be reached and 2 or 2.08% refused to answer.

68 patients had COPD, 11 asthma bronchiale, 31 had a cardiologic comorbidity.

Side efffects: 79% had side effects, most common nausea 21%, sleep disturbances 16% and mouth dryness 13% 19% had stopped varenicline treatment before time, six of them because of side effects. No serious side effect was observed.

Conclusion: Varenicline is a potential drug for smoking cessation in patients with pulmonary diseases with no serious side effects so far.

Diagnosis and misdiagnosis of COPD in the primary care setting – Results from the Austrian Burden of Obstructive Lung Disease (BOLD) study

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Background: According to current GOLD-guidelines the diagnosis of COPD is based on post-bronchodilator spirometry. Althougth the prevalence of COPD is increasing, the vast majority of COPD cases are still undiagnosed.

Methods: We analysed questionnaire and post-bronchodilator spirometry data from the population-based Austrian Burden of Obstructive Lung Disease (BOLD) study in adults aged 40 years and over. Irreversible airways obstruction was defined as post-bronchodilator FEV1/FVC <0.7 (GOLD I+). COPD GOLD II+ was defined as a FEV1/FVC <0.7 and a FEV1 <80% predicted. The value of a reported prior lung function test on the diagnosis, under- and overdiagnosis of COPD was analyzed.

Results: Out of 1258 participants 304 (24.2%) presented with irreversible airways obstruction corresponding with COPD GOLD stage I+. 269 (88.5%) of those 304 participants were previously undiagnosed. 153 (12.2%) out of all 1258 participants reported a prior lung function test within the last 12 months. Out of these 153 subjects with a reported recent lung function test 60 (39.2%) showed irreversible airways obstruction at the time of the BOLD study visit. However, 83.3% of them (50/60) did not have a prior doctor's diagnosis of COPD and had therefore been false negative. Among 740 participants who did not have any prior lung function test, 22 (3%) reported a doctor's diagnosis of COPD. However, 59.1% (13/22) of those did not show airways obstruction within the BOLD study and had therefore been false positive.

Conclusion: Restrictive utilization and incorrect performance and interpretation of lung function tests contribute largely to the under- and misdiagnosis of COPD.

A simple non-invasive diagnostic algorithm for pulmonary hypertension

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Background: Current guidelines for the diagnosis of precapillary pulmonary hypertension (PH) recommend right heart catheterization (RHC) in symptomatic patients or patients at risk with echocardiographic systolic pulmonary pressures (sPAP) ³36 mmHg. The growing awareness for PH, a high prevalence of postcapillary PH and the inability to discern between pre- and postcapillary PH by transthoracic echocardiography (TTE), have led to unnecessary RHCs. The aim of the present study was to test the ability of standard non-invasive diagnostic procedures to discriminate between pre- and postcapillary PH in a selected patient population with clinical and echocardiographic suspicion of PH.

Methods: In a first step, data from 251 patients with sPAP ³36 mmHg by echocardiography were retrospectively analyzed in a tertiary referral center for PH. The diagnostic value of clinical parameters, blood gas analyses, serum N-terminal brain natriuretic peptide (NT-proBNP) and ECG was assessed. Parameters with independent discriminative abilities derived from logistic regression were used to construct a diagnostic decision tree. In a second step, overoptimistic estimations of the decision tree were corrected by internal and temporal validation. For the latter, data from 121 prospectively recruited consecutive patients were used.

Results: NT-proBNP [OR(95%CI) 2.01(1.21–3.33), p = 0.007] and electrocardiographic right ventricular strain (RVS) [OR (95%CI) 52.931(17.27–162.18), p <0.001] were predictors of precapillary PH. A diagnostic decision tree was derived that stratified patients into a group with and a group without RVS. The latter were further stratified by serum NT-proBNP levels below and above 80 pg/ml. In the diagnostic pathway of precapillary PH, integration of the decision tree subsequent to TTE may increase specificity from 0% to internally validated 17.3% or prospectively temporally validated 26.3%. The validated sensitivity remains high at 97.9% or 100%, respectively.

Conclusion: The incorporation of ECG and NT-proBNP into the work-up of PH provides incremental diagnostic value and may reduce the number of invasive hemodynamic assessments.

P(a-et)CO2 at maximum exercise for early detection of pulmonary involvement in patients with sarcoidosis

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Study objectives: Sarcoidosis is a systemic granulomatous disease of unknown origin. The pulmonary involvement and degree of functional impairment is important for the diagnosis and prognosis of the disease. However, lung function impairment often occurs late in progressive pulmonary sarcoidosis. Aim of this study was to assess whether cardiopulmonary exercise testing (CPET) with gas exchange measurements at exercise allows for earlier detection of pulmonary impairment.

Methods: Sixty-five patients with biopsy-proven sarcoidosis stage I–IV (10.8%, 72.2%, 6.2%, and 10.8% in stage I, II, III,

and IV, respectively) underwent pulmonary function testing with diffusion capacity of carbon monoxide (DLCO) and incremental cycle CPET with blood gas analysis at rest and maximum exercise.

Results: Maximum exercise capacity was limited in patients with stage I (Wattmax 86.2 ± 9.8%) with normal lung function and decreased with clinical stages (Wattmax 74.6 ± 22.5%, 61.2 ± 11.0%, 66.8 ± 22.5% in stage II, III, and IV, respectively). P(a-et)CO2 at maximum exercise was significantly different between all stages ($p < 0.001$). PaO2 and AaDO2 at maximum exercise both reached significant differences for stage III versus I ($p = 0.036$ and 0.011 for PaO2 and AaDO2, respectively), stage IV versus I ($p = 0.005$ and 0.012) and stage IV versus II ($p = 0.004$ and 0.019). DLCO was only significantly different between stage IV and I ($p = 0.045$) and stage IV and II ($p = 0.003$).

Conclusion: P(a-et)CO2 at maximum exercise showed the highest significant differences between stages in patients with sarcoidosis and could help for early diagnosis in pulmonary involvement.

A role for PECAM-1 in venous thrombus resolution

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is characterized by intraluminal thrombus organization and fibrous obliteration of pulmonary arteries, with concomitant endothelial dysfunction. Thrombi resolve by a process of organization and recanalization. Leukocyte recruitment and angiogenesis are key components of this process. Platelet endothelial cell adhesion molecule-1 (PECAM-1 or CD31) is a molecule expressed on all cells within the vascular compartment, and plays an important role in leukocyte-endothelial cell adhesion and transmigration. Thus, PECAM-1 represents a link between these two key components of thrombus resolution. We investigated the role of PECAM-1 in a murine model of stagnant flow venous thrombosis.

Methods: Thrombosis was induced in the infrarenal vena cava of PECAM-1 –/– mice on an FVB/n background by creating a venous stenosis with a silk suture. Thrombi were harvested on days 3, 7, and 14 after surgery for analysis ($n = 8$ per time point). Wild-type mice served as controls.

Results: Thrombus cross-sectional area analysis demonstrated a significant increase in thrombus area over time in PECAM-1 –/– animals compared with controls (ANOVA < 0.05). Immunohistochemical staining using antibodies against F4/80 for detecting thrombus macrophages revealed a decreased number of macrophages in PECAM-1 –/– animals compared with controls (ANOVA < 0.05). The number of Isolectin B4-positive micro vessels was significantly decreased on days 3 and 7 in PECAM-1 –/– mice (ANOVA < 0.05).

Conclusion: Deletion of PECAM-1 results in misguided thrombus resolution with a decrease of monocytes and micro vessels. PECAM-1 is critically involved in venous thrombus resolution.

Abnormal phospholipid profiles in misguided thrombus resolution after splenectomy

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Purpose: Splenectomy is associated with an increased risk of chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is a life-threatening condition characterized by single or recurrent pulmonary thromboemboli that obstruct the pulmonary vascular bed. In 20% of cases CTEPH is associated with phospholipid-antibodies. The aim of our study was to analyze circulating phospholipids after splenectomy.

Methods: We utilized a mouse model of stagnant flow venous thrombosis to characterize thrombus resolution. Vena cava ligation was performed one month after splenectomy. At days 3, 7, 14 and 28 after vena cava ligation thrombi were harvested for histology and electrospray ionization – mass spectrometry analysis.

Results: Thrombus areas of splenectomized mice were significantly larger than those of controls at all time points (ANOVA, $n = 8$, $p < 0.03$). Whole blood FACS revealed higher counts of CD41-platelet microparticles (day 14: 3216 versus 927 cells/µl, $p < 0.05$) and leukocyte/platelet aggregates (day 14: CD11b/CD41, 56.4 versus 38.7%, $p < 0.05$). The composition of phospholipids enclosed in the thrombus was significantly different between thrombi of splenectomized mice and controls.

Conclusion: An altered thrombus phospholipid profile may derive from platelets and leukocytes after splenectomy. The loss of mechanical filtering function of the spleen permitting the accumulation of phospholipids in the peripheral circulation appears to be a key modifier of thrombus resolution.

MDR-TB an der 1. Internen Lungenabteilung Otto Wagner Spital Wien 2006–2008

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Background: Multidrug-resistant tuberculosis (MDR-TB), and extensively drug resistant tuberculosis (XDR-TB) are a growing source of concern globally. Compared to TB infections with fewer resistances to first and second line TB drugs, these infections are associated with poorer treatment outcome, longer hospitalization and treatment, higher mortality and a higher rate of adverse effects under therapy.

Method: In this retrospective analysis of 35 cases of MDR-TB, including 3 cases of XDR-TB, treated on a specialized TB ward from 2002 to 2008, we investigated patient characteristics, therapy administered, serious adverse effects, duration of treatment and hospitalization, and therapy outcome. A standardized data collection form and data from patient documentation at the ward as well as resistance testing performed by the national reference laboratory was used. All patients were treated with individualized regimen according to the results of resistance testing.

Results: 35 Patients, 25 male, age 31.9 yrs. (SD: 10.3). Patients came from 12 countries, mainly from the Russian Federation ($n = 15$), the majority of which ($n = 12$) came from the Chechen Republic, 8 Patients from Georgia, and 3 patients from Romania.

Treatment outcome: Healed 16 (46%); Ongoing Treatment – improvement under therapy 12 (34%); Unknown 5 (14%);

Died 2 (6%). Concomitant diseases were common. 22 patients had a psychiatric diagnosis, 6 patients had viral hepatitis, and 3 patients were diagnosed with neoplasia.

Conclusions: MDR-TB should be treated with individualized regimen according to accepted treatment principles. Side effects and patients' adherence should be monitored closely. Treatment of MDR-TB is long, should be reserved for specialized centers. Under these conditions, cure is an achievable goal.

Sleep disordered breathing and cardiac performance indices in patients with stable chronic heart failure

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Introduction: The aim of this study was to investigate neurohumoral activation and cardiac performance indices in patients with stable severe chronic heart failure and Cheyne-Stokes-Respiration (CHF-CSR) and heart failure patients with obstructive sleep apnea (CHF-OSA).

Methods: We studied 8 patients with polysomnographically diagnosed CHF-CSR and 8 age, gender, body-mass-index, and apnea-hypopnea index (AHI) matched patients with CHF-OSA. Hemodynamic measurements of stroke index (SI) and cardiac index (CI) were recorded using impedance cardiography. N-terminal pro brain natriuretic peptide levels (pro-BNP) were assessed by ELISA technique. Preliminary data from an ongoing study are presented (NCT00863421).

Results: The two groups did not differ with respect to left ventricular ejection fraction using echocardiographic measurements, pharmacologic treatment, or etiology of heart failure. Mean AHI was 24 ± 13/hr in patients with CHF-CSR as compared to 25 ± 19/hr in patients with CHF-OSA. Patients with CHF-CSR had significantly lower SI (30 ± 3 vs. 37 ± 7 ml/min per square meter body surface area, $p < 0.05$) and CI (2.1 ± 0.1 vs. 2.5 ± 0.5 L/min per square meter body surface area, $p = 0.06$) than patients with CHF-OSA. Consistent with these findings, NT-proBNP levels were significantly higher in chronic heart failure patients with CSR than in those with OSA (3200 ± 3293 pg/ml vs. 940 ± 596 pg/ml, $p = 0.04$).

Conclusions: Differences in neurohumoral activation between CHF-CSR and CHF-OSA patients may be related to cardiac performance indices rather than apnea severity.

Difficulty in initiating and maintaining sleep in patients with stable mild to moderate chronic obstructive pulmonary disease

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Introduction: Sleep problems associated with chronic obstructive pulmonary disease may have an important impact on quality of life and health outcome measures in patients. The aim of this study was to prospectively assess differences in symptom profile and polysomnographic parameters in patients with stable mild to moderate COPD and age, gender, and body-mass-index matched controls without airflow obstruction.

Methods: The Sleep Disorders Questionnaire was administered to both patients and controls prior to clinical and polysomnographic evaluation. Responses obtained from the questionnaire were used to construct four independent symptom scales: sleep apnea, periodic limb movement syndrome, psychiatric sleep disorder, and narcolepsy. Associations between each diagnostic scale and sleep parameters were considered by means of multiple analyses of covariance.

Results: Patients with COPD had overall lower sleep efficiency (75 ± 13 vs. 82 ± 11, $p < 0.01$), a lower total sleep time (4.7 ± 1.0 vs. 5.5 ± 0.8, $p < 0.05$) and lower mean overnight oxygen saturation (89 ± 3% vs. 93 ± 2% SaO2, $p < 0.05$) compared to controls. Patients with COPD were significantly more likely to report symptoms of the periodic limb movement and psychiatric sleep disorder scales such as insomnia and difficulty in initiating and maintaining sleep, resulting in overall higher scale scores in patients compared with controls. Minimum oxygen saturation was an independent predictor for all symptom scales. After correcting for potentially confounding factors, including pack years of smoking, total sleep time, sleep efficiency, arousal index, mean and minimum oxygen saturation, and apnea-hypopnea-index, the between group-differences for both the periodic limb movement and psychatric sleep disorder scale scores remained statistically significant.

Conclusions: We observed significant differences in both quantity and quality of sleep between patients with stable mild to moderate chronic obstructive pulmonary disease and respective controls.

Bronchiolitis obliterans in haematopoetic stem cell transplantation following non-myeloablative conditioning

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Introduction: Advances in allogeneic HSCT-management have significantly decreased the risks of early post-transplant infectious complications in the last decade. As a result, late noninfectious pulmonary complications, including bronchiolitis obliterans (BO), are increasingly of interest due to their growing influence on morbidity and mortality, the overall incidence of BO ranging up to 14% with mortality rates up to 50%. Over the past few years reduced intensity conditioning (RIC) has been offered as alternative to conventional conditioning regimens for patients with advanced age or comorbidities undergoing allogeneic HSCT.

Aim: It is argued that a RIC-regimen is likely to produce considerably less organ toxicity and, therefore, less pulmonary complications. This abstract reviews our experiences with BO in allogeneic-RIC-HSCT over the past eight years.

Methods: Between 2000 and 2008 61 patients underwent allogeneic-RIC-HSCT at our Division of Haematology. These patients were screened for airflow limitation by pulmonary function test prior to transplantation as well as three to six, and nine to twelve months after transplantation. In case of newly onset irreversible airflow obstruction, and exclusion of infection, diagnosis of BO was made.

Results: None of the 61 patients had airflow limitations prior to transplantation. Twenty patients died within the observation period, mostly due to acute GvHD. No one died of BO. Seven patients are lost to follow up. Two of the remaining 34 patients developed an obstructive airflow limitation which was reversible in one patient. In the other diagnosis of BO was made.

Conclusion: Regarding the incidence of BO in relation to the intensity of the conditioning regimen, our observation shows an incidence of BO following allogeneic-RIC-HSCT of

2.9%. Keeping in mind the small amount of patients as limiting factor, using a RIC-protocol showed a lower incidence of BO as compared to the published overall rates of BO after allogeneic HSCT.

Raucherstatus Erwachsener in Österreich, Trends bei repräsentativen Stichproben 2005–2008

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The following questions/items have been asked in April 2005 and 2008 and trends analysed about: Risk of smoking, guess of how much life is shortened by smoking and how many smokers will suffer health problems, segments of smokers and non-smokers, use of tobacco products, regular consumption of at least one cigarette a day, number of cigarettes a day, first cigarette in the morning, age of first cigarette in life, start of regular smoking, serious attempts and methods of quitting smoking, readiness of quitting, whether warnings on cigarette packs detain from smoking; should bars and restaurants be smokefree, readiness of visiting restaurants despite smoking, leaving bars and restaurants because of smoking, smoking at home and the workplace. Others like: Personal experience with spirometry, suffering from diseases like hypertension, diabetes, respiratory and cardiovascular disease, thromboembolism, cancer; present body mass index, attitudes towards smoking (clean air vs clean water, smoking when driving, respecting non-smoking individuals).

Method: Representative random check by SPECTRA with face-to-face interviews in 1031 persons 2005 and 1027 subjects 2008 (Figs. 1 and 2).

First cigarette in the morning – nicotine dependence was likely in 47–48% of smokers, but note that less subjects were found smoking 2008.

Selected details of this large inquiry will be shown on the poster. This most recent update on smoking habits in Austria funded by Österreichische Krebshilfe is rather relevant information for medicine and health politics as well.

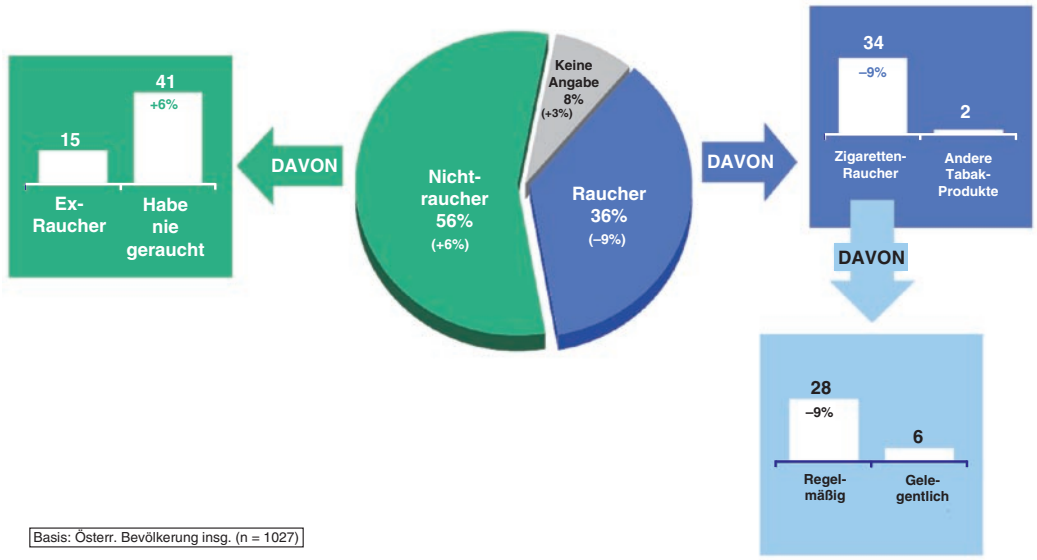

Fig. 1. Übersicht der Raucher-/Nichtraucher-Segmente im Trend

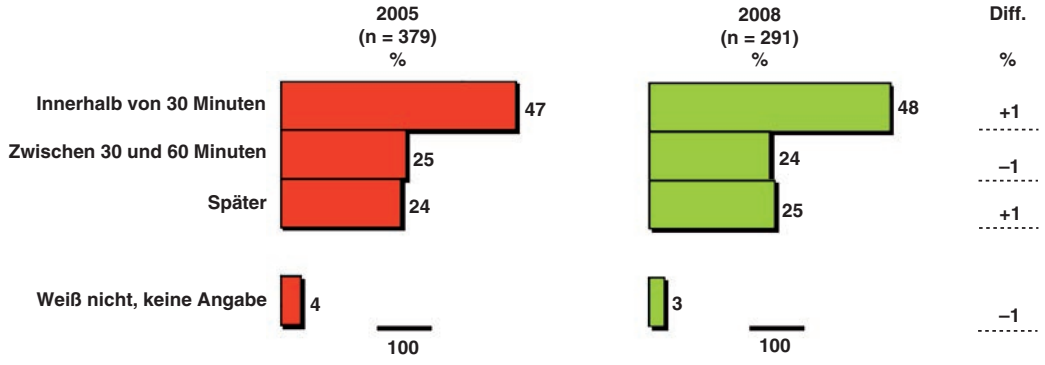

Fig. 2. *Trend towards nonsmoking* has significantly increased between 2005 and 2008. A turn around?

Raucherstatus von Teens in Oberösterreich, Trends bei repräsentativen Stichproben 2005–2008

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Method: Representative random check by SPECTRA with face-to-face interviews in 529 students 2005 and 569 teens 2008 of Upper Austria aged 13–18 years.

Items asked were considered hazard of smoking, distribution of never/irregular/regular smoking, first cigarette tried ever, start of regular smoking 3+ and number of cigarettes a day, attitude towards smoking, smoking among peers, persons smoking at and within home, spending pocket money, and body mass index (BMI).

The answers were stratified by sex, age, type of school attended, number of persons and smokers in the common household, way of spending expenses and leisure behaviour, caring about health, and smoking status.

Summary: The number of teens having ever tried cigarettes remained about the same (183/569 – 32%). The percentage of regular smokers between age 13–18 was 12.5% (109/569). The number of never-smokers increased, the one of smokers of 3+ cigarettes fell slightly. Regular smokers consumed 2008 one cigarette more than 2005. Smoking was considered less risky in 2008. Smoking in the common household promoted smoking, non-smoking favoured non/never-smoking. Unfortunately did environmental tobacco smoke exposure at home increase by 14% from 41 to 59%. Only one third of persons left the living quarter for smoking. Regular consumption of cigarettes dropped in students aged 13–14, of secondary modern and grammar schools. On opposite an upward trend was found with students of the polytechnical year and vocational schools. Smoking friends stimulated tobacco use. Paradoxically did subjects concerned about health and nutrition smoke more. The first cigarette was tried on average at age 12.3. Regular smoking (mean 12–13 cigarettes/day) was taken up 1.5 years later, but the starting age dropped from age 14.2 to 13.7.

Risk profile: Smoking behaviour of teens is coined by 4 features: (non)smoking at home, level of education, pressure of the peer group and expenses on the triad alcohol-cigarettes-disco.

The impact of immediate postoperative pulmonary vascular resistance on survival in patients with chronic thromboembolic pulmonary hypertension

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Background: Pulmonary endarterectomy (PEA) is the treatment of choice for patients with chronic thromboembolic pulmonary hypertension (CTEPH).

In a series of 1500 PEA cases an immediate postoperative pulmonary vascular resistance (PVR) of above 500 dynes.s.cm-5 was predictive of poor outcome within 30 days after a discharge.

We sought to investigate whether PVR measured invasively in the intensive care unit right before removal of the Swan Ganz catheter ("immediate PVR") is predictive of PVR at one year after surgery, and has an impact on long-term survival.

Methods: We collected immediate PVR data from 56 patients who underwent PEA between 1994 and 2006, and were followed for 70.9 (14; 97) months. From 56 patients, who underwent a baseline right heart catheterization (RHC), 45 underwent a RHC one year after PEA.

Results: Mean immediate postoperative PVR was 382.6 ± 176 dynes.s.cm-5. There was a significant correlation between immediate PVR and PVR 1 year postoperatively ($r = 0.6$, $p < 0.0001$). Immediate postoperative PVR had a significant influence on survival/freedom of lung transplantation ($p < 0.0001$). Immediate PVR could predict death/lung transplantation with a sensitivity of 79% (0.67; 0.89) and a specificity of 95% (0.86; 0.99), at a cut-off of 446 dynes.s.cm-5 (estimated area 0.87).

Conclusions: Immediate PVR is a predictor of one-year PVR, and of long-term survival in CTEPH patients undergoing PEA.

Formula for predicting mean pulmonary arterial pressure using systolic pulmonary arterial pressure in chronic thromboembolic pulmonary hypertension

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Rationale: Pulmonary hypertension (PH) is defined by an invasively measured mean pulmonary arterial pressure (mPAP) above 25 mmHg. The formula for predicting mPAP from systolic pulmonary arterial pressure (sPAP) was calculated in patients with pulmonary arterial hypertension using high-fidelity catheters (mPAP = 0.618*sPAPinvasive+2 mmHg).

Objectives: We searched for a formula to predict mPAP from sPAP by echo (sPAPecho) in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: We collected data from 190 patients diagnosed with CTEPH who underwent right heart catheterization (RHC) and echocardiography at the time of diagnosis.

Measurements and main results: Over a wide range (19 to 92 mmHg) mPAP and invasively measured sPAP (sPAPinvasive) were correlated ($r = 0.9$, $p < 0.001$).

Regression analysis allowed us to propose the formula 0.55* sPAPinvasive + 4.2 mmHg ($r2 = 0.823$; validation sample bias, 0 ± 5 mmHg, $p < 0.008$) for estimation of mPAP. SPAPinvasive was correlated with Doppler-derived sPAP values ((sPAPecho), $r = 0.674$, $p < 0.001$). Regression analysis allowed us to propose the formula (0.73* sPAPecho + 23.6 mmHg) for estimation of mPAP ($r2 = 0.45$; validation sample bias, 0 ± 16 mmHg, $p < 0.001$) from sPAPecho.

Conclusions: Mean PAP can be accurately predicted from invasively and Doppler-derives sPAP values according to the formulas: 0.55 * sPAPinvasive + 4.2 mmHg, and 0.73* sPAPecho + 23.6 mmHg, respectively, in patients with CTEPH undergoing RHC using fluid-filled catheters.

The Veres-method and transcutaneous CO2-monitoring during supraglottic high-frequency jet ventilation with laryngeal mask airway for interventional bronchoscopy

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Background: The aim of this report was to detect the transcutaneous CO2 using the Veres-method (supraglottic high frequency jet ventilation [HFJV] with laryngeal mask airway using specific Veres-connector) in adults during fiberoptic invasive diagnostic and interventional therapeutic bronchoscopy.

Methods: 30 adults between 32 and 76 years were recruited. We used a tcpCO2, and tcpO2 monitor (Radiometer TCM 40 TINA) that also determines transcutaneous oxygen saturation (SpO2) by means of a sensor placed on front of the chest wall at a temperature of 42 C. After inducing general anaesthesia using remifentanil and propofol, facemask ventilation was followed by the insertion of a size 4 or 5 LMA (laryngeal mask). A specific Veres-adapter connected the proximal end of the LMA with the anaesthetic circuit of the high frequency anaesthesia system (TwinStream Firma Reiner). The procedures involved were intra- and transbronchial biopsy, endobronchial ultrasound with TBNA, cryobiopsy, bronchial lavage, haemostyptic therapy, tumor resection or excision and diagnostic bronchoscopy. Transcutaneous carbon dioxide and oxygen, oxygen saturation, and arterial blood gas were recorded and analyzed.

Results: There were no significant differences comparing transcutaneous carbon dioxide or arterial blood gas value during the intervention. The tcpCO2 and paCO2 values ranged between 33–70 mmHg (mean 45.3 mmHg). The surgical intervention time was 8–84 min (mean 31.63 min). No major respiratory complications primary to the ventilation technique were observed.

Conclusions: In our report on patients undergoing interventional bronchoscopy using the Veres-method with transcutaneous carbon dioxid monitoring, we were able to achieve optimal surgical access, and provide adequate ventilation without notable carbon dioxide retention. Measuring transcutaneous CO2 offered accurate respiratory monitoring of the Veres-method. The described technique may provide an improvement for controlling the respiratory parameters in patients undergoing interventional and diagnostic bronchoscopy requiring HFJV.

Key words: Veres-method, transcutaneous carbon dioxid, bronchoscopy, ventilatory monitoring.

Effect of bilevel ventilation on respiratory capacity in various diseases

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Introduction: Bilevel ventilation improves ventilatory and sleep related parameters in various disorders. However, little is known about the effect on respiratory capacity measured by P 0.1 max.

Methods: Retrospective chart review of all patients on bilevel ventilation from October 2006 to January 2009 in the sleep laboratory of the Medical University Graz and analysis with regard to sleep related parameters, oxygenation and P 0.1 max.

Results: 19 patients were treated with bilevel ventilation, 12 patients received additional oxygen. The underlying diseases were kyphoskoliosis/post-polio-syndrome (n = 2), sleep apnea-hypopnea syndrome (SAHS, n = 6), lung fibrosis (n = 1), obesity-hypoventilation syndrome (OHS, n = 5), COPD (n = 4) and Pompe's disease with respiratory insufficiency (n = 1). 12 patients were able to perform the P 0.1 max manoeuvre and had more than one control polysomnography and P 0.1 max manoeuvre.

10 patients improved in terms of P 0.1 max (%pred) with a baseline mean of 28.1% (± 10.8) to a mean of 36.1% (± 13.7) at maximum, one patient (OHS) is planned for further pressure optimization, one patient (SAHS) has reached her baseline level (68%pred) with bilevel ventilation after initial deterioration with CPAP. The results correlate with improvement in clinical symptoms, lung function and oxygenation.

Discussion: Efficacy of bilevel ventilation in sleep disordered breathing and oxygenation in various diseases is widely accepted. However, changes in respiratory capacity as basic mechanism has not been proven so far. Although the P 0.1 max manoeuvre is limited by the patients' ability to cooperate, nearly all patients improved in P0.1 max regardless of the underlying disease.

Conclusion: Measurement of P 0.1 max as substitute for respiratory capacity may guide and reflect optimal treatment with bilevel ventilation.

Endothelial dysfunction and systemic inflammation in stable and exacerbated patients with COPD

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Background: Chronic obstructive pulmonary disease (COPD) is associated with a 2–3 fold increased risk of cardiovascular morbidity and mortality. Besides this, low-grade systemic inflammation has also been shown to be a feature characteristic in patients with clinically stable COPD compared to healthy peers, which transiently increases during acute COPD exacerbations. Endothelial dysfunction is suspected to be a possible link between the low-grade systemic inflammation and the increased cardiovascular risk in patients with clinically stable COPD. So far, no data exist about endothelial function in COPD patients during an acute exacerbation.

Aim: Therefore, the aim of the present study was to investigate endothelial function and systemic inflammatory biomarkers during acute exacerbation and to evaluate a possible improvement after acute exacerbation in patients with COPD.

Methods: In a prospective study COPD patients admitted to hospital due to an acute COPD exacerbation were investigated. Besides lung function (using standardized spirometry), subjects flow mediated dilatation (FMD) of the brachial artery (using ultrasound) was measured according to recommended guidelines. Furthermore, systemic inflammatory biomarkers, such as C-reactive protein (CRP) and leukocytes were assessed. All measurements were done at baseline, and after 6 weeks and confirmed clinical stability.

Results: Four patients were available for analysis (male: n = 3; age: 67.25 ± 10.31, years, FEV1: 36.50 ± 6.14, %pred.; FEV1/FVC: 34.25 ± 11.64, %pred.). During acute exacerbation COPD patients showed an FMD of 8.75 ± 5.16%, a CRP of 19.8 ± 20.5, mg/l and leukocytes of 8.06 ± 3.27 G/l. After 6 weeks and confirmed clinical stability an improvement in FMD (10.6 ± 3.82%) as well as a decrease of systemic inflammatory biomarkers (CRP: 6.50 ± 1.91 mg/l; leukocytes: 6.59 ± 1.12 G/l) was observed.

Conclusion: Our preliminary findings strengthen the hypothesis of a risk for future cardiovascular events triggered by the frequent occurrence of acute exacerbations and the entailed systemic inflammation in patients with chronic obstructive pulmonary disease.

Pulmonary, pleural and thoracic wall woud infection with rhizopus oryzae

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Introduction: Zygomycosis is a rare infection caused by ubiquitous fungi. It usually occurs in immunocompromised hosts. The course of the disease is very often acute and rapidly fatal with very high reported mortality rates.

Case report: A 52 year old caucasian female patient with B-cell chronic lymphatic leukemia and several previous infectious complications including cerebral toxoplasmosis and herpes simplex pneumonia was admitted because of cough and fever. The thoracic CT scan was consistent with pleural empyema and a thoracic drain was inserted. The CRP kept rising up to 511 mg/L (normal <8 mg/L) and the clinical course deteriorated and thus a thoracotomy was performed.

Histology of the resected pleura revealed invasive fungal disease. Cultures from the wound revealed the zygomycete *Rhizopus oryzae*. Subsequently the fungus infiltrated the wound and surrounding skin. Treatment with liposomal amphotericin B was initiated. This was followed by a significant clinical improvement and a sharp decline in the CRP value. Three weeks later the antifungal therapy was changed to posaconazole leading to shrinkage and drying off of the mycetoma. Finally it was sequestered from the thoracic wall revealing the lung and resected rib. Debridement and a thoracostomy were performed and the patient discharged again in good clinical condition. After fifteen weeks two of the three wounds were closed and the third one was healing without any sign of infection while the patient remained in excellent clinical condition.

Six months after initial presentation the patient died due to hemorrhagic pneumonia. From autopsy specimens no zygomycete could be cultured, but pseudomonas was found in the lung tissue.

Discussion: This case illustrates the severity of invasive fungal disease due to emerging zygomycetes in immunocompromised patients and underlined the necessity for invasive diagnostic procedures in order to establish timely diagnosis.

Size reduced lung transplantation – 9 years of experience by a single centre

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Background: Expanding the donor pool for patients on the waiting list is still a great challenge in lung transplant surgery. Size reduced lung transplantation is an opportunity to offer lung transplantation to young patients or adults with small chests. Nevertheless, size reduced lung transplantation is still not a standard procedure.

Patients and methods: We retrospectively reviewed all 162 patients (m = 71, f = 91, mean age: 40 + 17a) who underwent size reduced lung transplantation from January 2000 to January 2009 at our institute. All patients (pts) were analysed with regard to postoperative outcome and were compared to all other pts who underwent standard lung transplantation (n = 434) during the observation period.

Results: During the observation period 27.2% (n = 162) of all 596 lung recipients underwent size reduced lung transplantation. Downsizing was achieved by lingula resection n = 13 (8%), lobar transplantation n = 136 (84%) and split lung transplantation n = 13 (8%). Underlying diseases in the size reduced group: CF n = 54, COPD n = 44, Fibrosis n = 37, PPH n = 10, others n = 17. Within the observation period 49 pts died (infections: n = 26, graft failure: n = 5, bronchiolitits: n = 4, others: n = 14) in the size reduced group and 133 pts in the standard group. There was no statistically significant survival difference (Log Rank p = 0.259) between the size reduced group (mean 1962 + 117, range 0–2951 days) and the standard transplantation group (mean 2175 + 72, range 1–3691 days).

Conclusions: Size reduced lung transplantation, including split lung transplantation, lobar transplantation and peripheral segmental resection, is a reliable procedure providing equal survival results compared to standard lung transplantation.

Double-stranded RNA affects the TRPC channel expression in human pulmonary artery endothelial cells

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Background: The role of endothelial cells is to maintain the integrity of the vessel wall, preventing inappropriate thrombogenesis and maintain the vascular tone. Transient receptor potential canonical (TRPC) channels take part in the endothelial barrier regulation. They are voltage-independent, non-selective cation channels, which are activated by increased cytosolic calcium. During viral infection increased levels of circulating double-stranded (ds)RNA may occur and lead to changes in the endothelial permeability. This process is dependent on calcium entry e.g. TRPCs. We investigated the effect of dsRNA on the expression and function of TRPC channels of primary human pulmonary artery endothelial cells (hPAECs).

Methods: Changes in the expression of TRPC1-7 and toll-like-receptor 3 genes after dsRNA stimulation were analysed by quantitative RT-PCR. Fura-2/am loaded hPAECs were used to investigate calcium changes after 24 h incubation with dsRNA, synthetic dsRNA (Poly I:C) or control solution by means of live-cell imaging. To deplete the intracellular calcium stores 15 µM BHQ (a selective inhibitor of sarco/endoplasmic reticulum Ca2+-ATPase (SERCA) was used for 10 minutes with calcium free extracellular solution. After activation of TRPC channels, 1.8 mM extracellular calcium was added and the increase in the intracellular calcium level was monitored.

Results: The quantitative RT-PCR showed that from the 7 known isoforms only TRPC1, 3 and 4 were expressed by hu-

man PAECs. Incubation with dsRNA induced a 2-fold increase in the expression of TRPC3 and a 5-fold increase in the TRPC4 expression, whereas the level of TRPC1 was not significantly changed. The calcium measurements showed an increased calcium influx after dsRNA incubation.

Conclusion: Our data suggests that TRPC channels are regulated by dsRNA. This causes increased calcium influx in human pulmonary artery endothelial cells and may lead to changes in vascular tone.

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Limitations of immune-based diagnostics in patients suspected for pulmonary tuberculosis

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Background: Presence of early secretory antigenic target (ESAT)-6 specific, interferon (IFN)-γ expressing T cells in blood is thought to accurately identify infection with Mycobacterium tuberculosis (MTB). However its role together with pro- and anti-inflammatory cytokines like TNF-α, IL-2, TGF-β or IL-10 is controversial and has not been studied so far.

Aims: Aim of our study was to elucidate the relevance of new immune-based diagnostics in patients suspected for pulmonary tuberculosis (TB).

Methods: 135 patients suspected for TB were prospectively studied. Flow cytometry for intracellular detection of IFN- γ, TNF-α, IL-2, TGF-β or IL-10 in CD4+ T cells was performed after stimulation of peripheral blood mononuclear cells (PBMC) with ESAT-6. Additionally, levels of IFN-γ, TNF-α and IL-10 were studied in plasma and supernatants by ELISA.

Results: In 69 patients active TB was confirmed by positive culture. ESAT-6 stimulation of PBMC was associated with increased secretion of IFN-γ in the TB group, while IL-10 levels were lower. 70% of TB patients responded to ESAT-6 stimulation. An increased frequency of CD4+ T cells expressing INF-γ was found in TB patients ($p < 0.001$). The additional determination of TNF-α, IL-2, TGF-β and IL-10 expressing CD4+ T cells was not superior to INF-γ for the diagnosis of active TB. The same was true with with regard to plasma levels.

Conclusions: Enhanced MTB-specific type 1 reactivity is evident in patients with active pulmonary TB. INF-γ-responder rates of 70% question the usefulness of ESAT-6 based immunological methods for the diagnosis of active disease, determination of other pro- and anti-inflammatory cytokines does not increase specificity and sensitivity.

Fall des Jahres

Management einer Ösophago-bronchialen Fistel bei hochmalignem Non-Hodgkin-Lymphom

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Bei dem 65-jährigen Patienten wird Ende 2007 ein niedrigmalignes NHL diagnostiziert. Schon damals fallen in der Gastroskopie Schleimhautinfiltrationen im mittleren Ösophagusdrittel auf, welche bioptisch als lymphozytäre Infiltrate identifiziert werden.

Es folgen mehrere Zyklen kombinierter Chemo-Immuntherapie bis März 2008.

Im September 2008 erfolgt die Aufnahme auf der Lungenabteilung aufgrund pulmonaler Infiltrate. CT-morphologisch zeigt sich ein neu aufgetretenes mediastinales Lymphknotenpaket. Zusätzlich wird der Verdacht auf eine Ösophago-bronchiale Fistel geäußert, welche im Anschluss sowohl gastroskopisch als auch bronchoskopisch verifiziert wird und der ursächlich eine Lymphominfiltration mit Exulceration des Ösopagus bzw. der Atemwege zugrunde liegen dürfte.

Hämatologisch ist es zu einer Transformation in ein hochmalignes Lymphom gekommen.

Bereits nach dem ersten Zyklus einer neuerlichen Chemotherapie zeigt sich ein ausgezeichnetes Ansprechen der Lymphome, andererseits entsteht ein grosser ösophago-bronchialer Parenchymdefekt.

In mehreren interdisziplinären Besprechungen entscheidet man sich zu einem endoskopisch interventionellen Vorgehen. In einer Sitzung wird Fibrin injiziert sowie ein Ösophagusstent bzw. ein Bronchialstent implantiert, welche jedoch allesamt im Laufe einer Woche dislozieren und entfernt werden müssen bzw. vom Patienten sogar abgehustet werden.

Überraschenderweise kommt es in der Folge zu keinen weiteren Aspirationen mehr, die Fistel ist nicht mehr darzustellen. Offensichtlich hat die kurze Zeit der Stentschienung ausgereicht um den Defekt zu verschliessen.

Das „acute chest syndrome“ im Rahmen einer Sichelzellanämie

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Anamnese: plötzlich auftretende Rippenschmerzen links Mitte September 2008. 1–2 Tage später Fieber bis 39 °C, daraufhin Vorstellung beim Lungenfacharzt, der eine Ventilations-Perfusionsszintigraphie bei klinischem Verdacht auf Pulmonalembolie veranlasste. Nach negativem Befund Therapie mit Avelox. Trotzdem kommt es zu einer Verschlechterung des Allgemeinbefindens mit zunehmender Dyspnoe und Tachykardie, weshalb die Überweisung an unsere Abteilung erfolgte.

Vorerkrankungen: Sichelzellanämie, Allergie auf Beifuß und Schimmel

Aufnahmestatus: Die 19-jährige Patientin befindet sich in reduziertem AZ, ist hypoxämisch, tachykard und präsentiert sich klinisch mit Dyspnoe, Husten und Rippenbogenschmerzen links ventral.

Körpergröße: 170 cm
Körpergewicht: 53 kg
Auskultation: Vesikuläratmung bds., keine RG's,
Lungenfunktion: mittelschwere Restriktion (TLC 2,77 L 49%; VC max 1,55 L 36%)
Labor: normochrome, normozytäre Anämie Hb 9,2 g/dl, Thrombozytose 629 G/l D- Dimer 7100 µg/l, Leukozytose 18,5 G/l CRP 5,0 mg/dl Differentialblutbild: Targetzellen, Sichelzellen, Riesenthrombozyten
Blutgasanalyse: pH 7,47 pCO2 31 mmHg pO2 64 mmHg AaDO2 47mmHg
EKG: S1/QIII-Typ, Sinustachykardie von 104/min.
Multi-Slice CT: regelrechte Perfusion, Infiltrate in beiden Unterlappen mit Winkelergüssen
Bronchoskopie: makroskopisch das Bronchialsystem diffus entzündlich
Histologie der TBB aus dem linken Unterlappen: Alveolitischer Prozess mit intraalveolären Blutungen und Fibrinmembranen.

Es wurde eine breite, antibiotische und antientzündliche Therapie durchgeführt, wobei sich die Patientin rasch erholte und nach Hause entlassen werden konnte.

Nach nur einer Woche erfolgt eine erneute Vorstellung der Patientin mit nun rechtsthorakalen Schmerzen, Fieber und ähnlicher Befundkonstellation wie beim Voraufenthalt. Wieder wurde eine bilaterale Pneumonie festgestellt. Aufgrund dieses ungewöhnlichen Verlaufes haben wir uns eingehend mit der Vorerkrankung der Patientin, der Sichelzellanämie auseinandergesetzt und darin die Ursache für das Auftreten einer zweimaligen bilateralen Pneumonie und der rezidivierenden Knochenschmerzen gefunden. Das „Acute Chest Syndrom“: Hb S ersetzt bei Patienten mit Sichelzellanämie postnatal das Hb F. Im oxygenierten Zustand verhält sich das Hb S normal. Bei Sauerstoffmangel, Fieber, Unterkühlung und bei hypertonem Serum können die Hb S-Moleküle vom Sol- in den Gelzustand überwechseln wobei die Erythrocyten sichelförmig und damit unelastisch werden, was zu Kapillarokkulsionen in verschiedenen Organsystemen führen kann, die sich als schmerzhafte Krisen äussern. Im Bereich der Lungen wird diese Situation auch „akutes Thoraxsyndrom“ genannt. Die Verschlüsse der Pulmonalarterien entstehen durch Erythrocytenaggregationen oder Fettembolien aus ischämischem Knochenmark und können ihrerseits zu Lungeninfarkten führen. Die Patientin wurde im St. Anna Kinderspital bei Dozent Minkov, einem Spezialisten für Sichelzellanämie, vorgestellt und befindet sich nun bei ihm in weiterer Betreuung. Unter Litalir-Therapie sind bisher keine weiteren Schmerzkrisen mehr aufgetreten.

Rezidivierende Pneumonien – Röntgenivisible Raumforderung

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Vorgeschichte: Pneumonie rechter Lungenunterlappen 4/08 – Antibiose, vollständige Abheilung. Rezidivpneumonien im selben Lungenlappen 9/08 und 11/08 – jeweils vollständige Abheilung unter Antibiose.

Aktuelle Erkrankung: Vorstellung an unserer Abteilung 2/09 nach neuerlicher Pneumonie im rechten Lungenunterlappen. Nach Antibiose zum Begutachtungszeitpunkt bereits deutliche Rückbildung des Infiltrates.

Auskultation: Verlängertes Exspirium, keine feuchten RG's.

Labor: Leukozyten 8,7 G/L, CRP 14 mg/l, BSG 44/62 mm

Durchleuchtung: kein Mediastinalpendeln, keine Raumforderung.

Auswärtiges CT Thorax: primär keine Raumforderung beschrieben, lediglich geringes Restinfiltrat.

Aufgrund des bisherigen Verlaufes Indikationsstellung zur endobronchialen Evaluierung mittels Bronchoskopie: gestielter endobronchialer Polyp im distalen Zwischenbronchus (Abb. 1).

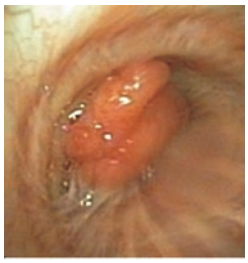

Abb. 1

Retrospektiv bereits im auswärtigen *CT Thorax*-Bild polypoide Veränderung im Zwischenbronchus rechts erkennbar (Abb. 2).

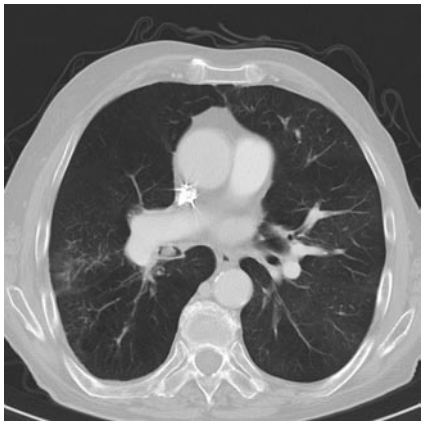

Abb. 2

Therapie: Bronchoskopische Abtragung des Polypen, Antibiose mit Sulbactam/Ampicillin

Histologie: Partiell chondromatöses Hamartom

Nach Abtragung des Polypen vollständige Rückbildung des Lungeninfiltrates

Respiratorisches Versagen einer 18-jährigen Patientin mit Niereninsuffizienz: pulmorenal oder renopulmonal?

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Wir berichten über eine 18-jährige Patientin, die vom niedergelassenen Lungenfacharzt wegen Hämoptoe eingewiesen wurde. Sie klagte über Husten mit blutig tingiertem Sputum, sowie Belastungsdyspnoe. Sie war noch nie zuvor im Krankenhaus gewesen, hatte keinerlei Vorerkrankungen und keine Dauermedikation.

Bei Aufnahme wurden eine Sinustachykardie (Herzfrequenz 121/min) sowie ein Blutdruck von 209/144 und eine Körpertemperatur von 38° C erhoben.

Im EKG zeigten sich linksventrikuläre Hypertrophiezeichen. Laborchemisch auffällig waren erhöhte Nierenretentionsparameter (Kreatinin 8,8 mg/dl, Harnstoff 181 mg/dl) bei Proteinurie, erhöhte Entzündungswerte (CRP 10,6 mg/dl), eine mikrozytäre Anämie (Hb 10,3 g/dl) sowie ein massiv erhöhtes pBNP von 107.000 pg/ml. Das echokardiographische Korrelat war eine konzentrische Linksherzhypertrophie mit zirkulärem Perikarderguss ohne hämodynamische Relevanz.

Übersichtsradiographisch zeigten sich alveolär konfluierende Strukturverdichtungen beidseits mit rechtsseitigem Pleuraerguss. Im CT wurden die Veränderungen als symmetrische Konsolidierungen epihilär mit ground-glass-Phänomen in den basalen Lungenabschnitten beschrieben. Aufgrund der progredienten respiratorischen Insuffizienz wurde die Patientin auf die Intensivstation verlegt und invasiv beatmet.

Die Autoantikörperdiagnostik (ANA, ANCA, Anti-GBM, ds-DNA, C3/C4-Komplement, Kryoglobuline) war negativ. Im Rahmen der bronchoskopischen Abklärung erfolgte die Entnahme von transbronchialen Biopsien. In der histologischen Aufarbeitung wurde ein intraalveoläres fibrinöses Exsudat beschrieben. Die bronchioloalveoläre Lavage zeigte ein reaktiv entzündliches Zellbild.

Der Schnelltest auf Influenza war primär positiv, wurde jedoch bei neg. Influenza A/B RNA (PCR) nicht bestätigt.

Unter antihypertensiver Therapie, Hämodiafiltration und negativer Bilanzierung sowie antibiotischer Abschirmung erholte sich die Patientin rasch und konnte nach 3 Tagen extubiert werden. Die Nierenbiopsie ergab das Bild einer malignen hypertensiven Nephrosklerose mit höchstgradiger Arterio- und Arteriolosklerose.

Ein pulmorenales Syndrom wurde ausgeschlossen.

Es besteht eine dialysepflichtige Niereninsuffizienz bei maligner Nephrosklerose und arterieller Hypertonie. Ursächlich für die pulmonale Symptomatik war eine pulmonale Stauung mit Permeabilitätsödem.

Pneumothorax bei einer 43-jährigen Frau

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Das konventionelle Thoraxröntgen gehört zu den Basisuntersuchungen der Pneumologie. Folgender Fall zeigt, wie leicht dabei ein augenfälliger Befund andere wichtige Pathologien verdrängen kann.

Anamnese: Eine 43-jährige Frau sucht nach der Rückkehr von einer Parisreise aufgrund linksthorakaler Schmerzen ihren Hausarzt auf. Sie wird von ihm deswegen im BWS-Bereich paravertebral infiltriert, worauf es zu einer von Belastungsatemnot begleiteter Zunahme der Beschwerden kommt. Am Folgetag wird die Patientin deswegen an unsere Abteilung zugewiesen. Sie ist Raucherin (ca. 25 packyears) und leidet weder an bekannten Allergien noch Vorerkrankungen.

Aufnahmebefund: Vesikuläratmen – links apikal abgeschwächt, paravertebraler Muskelhartspann, sonst unauffälliger Status.

Pathologische Laborbefunde: CRP 13,7 mg/l (<9), D-Dimere 0,53 mg/l (<0,5).

Blutgasanalyse: gute Oxygenierung (pO2 75 mmHg) grenzwertige Hyperventilation (pO2 34 mmHg), Säure-Basen-Status ausgeglichen.

Thoraxröntgen: acht Zentimeter breiter apikaler Pneumothorax ohne Mediastinalshift, minimaler Randwinkelerguss links, Lingula-Teilatelektase, sonst unauffällig.

Verlauf: Die Patientin wird zur Observanz stationär aufgenommen und analgetisch therapiert. Wegen der, durch den Pneumothorax nicht erklärbaren, Minderbelüftung im Lingulabereich in Verbindung mit den erhöhten D-Dimeren wird eine Computertomographie mit PAE-Protokoll durchgeführt. Hier zeigen sich die Pulmonalarterien frei perfundiert sowie bekannter Pneumothorax links und bekannte Lingulaatelektase.

Aufgrund besagter Minderbelüftung, der Laborbefunde sowie Anamnese und Klinik wird zur genaueren Beurteilung der pulmonalarteriellen Endstrombahn noch zusätzlich eine Lungenszintigraphie angeordnet, die Pulmonalarterienembolien im Bereich der Segmente L3 bis L5 zeigt.

Die Patientin wird nach Ausschluss einer Beinvenenthrombose mittels Phlebographie als Ursache der Embolie oral antikoaguliert und beschwerdefrei nach Hause entlassen. Der Pneumothorax bildet sich spontan zurück.

Fazit: Ein ins Auge springender Röntgenbefund bietet oft eine rasche Erklärung für die vom Patienten geschilderten Beschwerden. Dennoch ist eine systematische Befundung des Röntgenbildes auch in diesem Fall unabdingbar. Zur Vermeidung von Fehlern, welche durch die sogenannte „Satisfaction of Search" ausgelöst werden, ist es notwendig, sämtliche radiologische Veränderungen mit Anamnese, Klinik und Laborparametern in Einklang zu bringen.

Chronischer Husten und Trachealstenose

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Eine 61-jährige Patientin präsentierte sich mit Husten seit mehreren Jahren mit Expektoration eines gelblichen Sputums, sie betrieb bis vor 10 Jahren einen Nikotinabusus. Atemfunktionell bestand eine geringgradige obstruktive Ventilationsstörung, ein mittelgradig erhöhter zentraler Atemwegswiderstand, es fand sich kein Hinweis für eine funktionell wirksame Stenose. Im Thoraxröntgen zeigten sich ab dem mittleren Anteil der Trachea bis in die Hauptstammbronchien enge Lumina, im Thorax-CT eine unregelmäßige und leicht verdickte Trachealwand. Bronchoskopisch fand sich eine mäßiggradigradige Einengung der Trachea bis in beide Hauptbronchien, die Schleimhaut der Trachea und der Bronchien war makroskopisch hochgradig pathologisch verändert mit blumenkohlartigen Veränderungen; es wurden ausgiebige Schleimhautbiopsien entnommen, histologisch zeigte sich eine Tracheobronchopathia osteochondroplastica, durch eine Mischflora superinfiziert.

Therapeutisch begannen wir eine Antibiose mit Amoxicillin/Clavulansäure und Metronidazol zur Keimsanierung, weiters erhielt die Patientin Salmeterol/Fluticasonproprionat sowie Azithromycin 3-mal wöchentlich zur Immunmodulation. Im Verlauf kam es zum Sistieren des Hustens, atemfunktionell ist die Patientin unauffällig. In den Re-Bronchoskopien nach 6 und 12 Wochen zeigte sich ein unveränderter makroskopischer Befund.

Die Leiden des jungen W.

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Die ABPA stellt eine komplexe Hypersensitivitätsreaktion (Typ I und III) der Lunge dar verursacht durch eine Kolonisation mit Aspergillus und betrifft 1–2% der Asthmatiker und bis 15% der CF-Patienten.

Frühzeitige Erkennung und Therapie mit system. Steroiden können den Lungenfunktionsverlust und strukturellen Lungenumbau hintanhalten. Es besteht jedoch eine hohe diagnostische Latenz, bei später Diagnosestellung handelt es sich oft um Patienten mit schwer beherrschbarem Asthma und nicht reversibler Atemwegsobstruktion.

Die häufigsten radiologischen Befunde stellen neben zentralen Bronchiektasien ein- oder beidseitige Infiltrate dar, die zumeist als Pneumonie fehlgedeutet werden.

Dies war auch bei W., 18 Jahre, im Verlauf der vergangenen 18 Monate mehrfach der Fall, die Behandlung erfolgte jeweils mittels peroraler Antibiose, bildgebende Verlaufskontrollen wurden nicht veranlasst.

Obiger Patient wurde uns schließlich aufgrund beidseitiger OL-Infiltrate sowie zystisch-kavernös imponierender Strukturveränderungen mit Verdacht auf Tb. pulm. zugewiesen.

Der Auskultationsbefund war obstruktiv, es bestand eine ausgeprägte Hustensymptomatik mit zähem putridem Sekret. Die Entzündungsparameter waren nur gering ausgelenkt, auffällig waren eine periphere Eosinophilie von 14% sowie ein gesIgE von über 2500 IU/ml. Anamnest. hat seit Kindheit ein allergisches Asthma bronchiale bestanden. Lungenfunktionell zeigte sich eine mittelgradige obstruktive Ventilationsstörung unter regelmäßiger inhalativer Therapie mit einem Kombinationspräparat. Weiters waren die spezif. IgE-AK für Aspergillus fumigatus erhöht. Tuberkulintest und bronchoskop. Aktivitätsbeurteilung blieben negativ, der histolog. Befund beschrieb Granulationsgewebsbildung mit Eosinophilie. Im Bronchialsekret gelang der Nachweis einzelner Pilzhyphen.

In Zusammenschau der Befunde wurde eine allerg. bronchopulmonale Aspergillose diagnostiziert; es wurde eine system. Steroidtherapie beginnend mit 1 mg/kg KG etabliert. Nach 7-monatiger Therapie ist der Patient klinisch beschwerdefrei, nativradiologisch derzeit kein Infiltratnachweis. Lungenfunktionell besteht weiter eine fixierte obstrukt. Ventilationsstörung.

Morbus Castleman: selten – oder nur selten erkannt?

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Fallvorstellung: Ein junger Mann (31 Jahre) nimmt als gesunder Proband an einer COPD Raucherstudie teil. In der obligatorisch vorgeschriebenen Computertomograpie des Thorax zeigt sich als Zufallsbefund eine 3 x 1,5 cm große weichteildichte Formation paraaortal links. Da vom radiologischen Aspekt ein Malignom nicht ausgeschlossen werden kann, wird eine Onko-PET-Untersuchung durchgeführt, in der die Läsion eine deutliche pathologische Glucosespeicherung zeigt.

Zur weiteren invasiven Abklärung wird der Patient an unser Thoraxzentrum zugewiesen. Durch das aortopulmonale Fenster hindurch wird die Formation mittels EBUS-gezielter transbronchialer Nadelaspiration punktiert. Zytologisch ist aus dem repräsentativen Material lymphatisches Gewebe nachweisbar, wobei eine klare Diagnose nicht möglich ist,

aber ein Malignom nicht ausgeschlossen werden kann. Aufgrund dieser Befundlage wird die Indikation zur videoassistierten Thorakoskopie gestellt. Die Weichteilformation kann vollständig reseziert werden. Histologisch stellt sich die Diagnose eines unizentrischen Morbus Castleman vom hyalinvaskulären Typ.

Beim Morbus Castleman (angiofollikuläre Lymphknotenhyperplasie) handelt es sich um eine selten auftretende lymphoproliferative Erkrankung mit zwei prognostisch Krankheitsbildern. Für die Lungenheilkunde interessant ist vor allem der unizentrische Morbus Castleman. Mit 80 bis 90% der Fälle ist er viel häufiger als die multizentrische Form, der aufgrund des klinischen Bildes und Verlaufes eine Domäne der Hämatoonkologie ist.

Die Hauptlokalisation des unizentrischen Morbus Castleman sind die mediastinalen, hilären sowie intrapulmonalen Lymphknoten. Weitaus seltener kommt er im Abdomenbereich sowie in peripheren Lymphknoten vor.

Die meisten Patienten mit einem unizentrischen Morbus Castleman sind klinisch völlig asympotmatisch und jung (Durchschnittsalter: 35 Jahre). Histologisch handelt es sich meist um den hyalin-vaskulären-Typ. Als Therapieoption wird die operative Sanierung empfohlen. Eine maligne Entartung (NHL, Hodgkin Lymphom) trotz Operation wurde beschrieben, ist aber selten.

Beim multizentrischen Morbus Castleman sind die Patienten deutlich älter (Durchschnitt 60 Jahre) und zeigen Symptome wie Fieber, Nachtschweiß, Gewichtsverlust und Abgeschlagenheit. Oft ist diese Erkrankung mit einer HIV- und Herpesvirus 8 Infektion assoziiert. Histologisch herrscht der Plasmazell-Typ vor. Eine maligne Entartung (NHL, Hodgkin Lymphom, Kaposi-Sarkom, POEMS-Syndrom) ist häufig, die Prognose ist trotz Therapie (Steroide, Chemotherapie, antivirale Therapie, Rituximab) schlecht.

Diskussion: Aufgrund der modernen bildgebenden Diagnostik werden zunehmend solitäre intrathorakale Lymphadenopathien zufällig entdeckt. Da es sich häufig um asymtomatische jüngere Patienten handelt, stellt sich die Frage, ob die diagnostischen sowie operativen Risiken überhaupt gerechtfertigt sind, vor allem dann wenn in Verlaufsbeobachtungen keine Größenprogredienz erkennbar war und zur definitiven Diagnosesicherung größere Lungenanteile geopfert werden müssen.

Neben den vorgestellten Patienten konnten wir in einem ähnlich gelagerten Fall die gleiche Diagnose histologisch sichern. In zwei weiteren Fällen besteht zumindest ein Verdacht auf das Vorliegen eines Morbus Castleman, wobei sich sich in der bildgebenden Diagnostik eine solitäre hiläre bzw. intrapulonale Lymphadenopathie zeigt. Trotz umfassender Diagnostik (EBUS-TBNA, transthorakale Nadelaspiration, PET-CT) ist keine Diagnosesicherung möglich, da zur Diagnosesicherung eines Morbus Castleman zytologisches Material nicht ausreicht und nur eine histologische Aufarbeitung des gesamten Lymphknoten die Diagnosestellung erlaubt. Eine operative Entfernung der pathologisch vergrößerten Lymphknoten wäre in beiden Fällen mit einer Pneumonektomie verbunden, weshalb auf eine Operation verzichtet wurde und die Patienten in die Verlaufsbeobachtung genommen wurden. Bisher war keine Größendynamik erkennbar.

Da in der Literatur keine großen Fallzahlen beschrieben wurden und in unserem Krankenhaus die Diagnose Morbus Castleman in den letzten 10 Jahren abgesehen von den beiden oben beschriebenen Fällen nur ein weiteres Mal gesichert wurde, stellt sich für uns die Frage ob es sich um eine zufällige Häufung handelt oder ob der Morbus Castleman aufgrund der oftmaligen Schwierigkeit der Diagnosesicherung und des eher gutartigen Verlaufes bisher eher zu selten diagnostiziert wurde.

Wir meinen, dass in Fällen einer solitären intrathorakalen Lymphadenopathie bei jungen Patienten differentialdiagnostisch unbedingt ein Morbus Castleman zu erwägen ist.

Seltener blutender Trachealtumor – mediastinales Angiosarkom (Case Report)

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Bei einem 75-jährigen Patienten mit Hb-wirksamen Hämoptysen konnte als Ursache ein mediastinales Angiosarkom diagnostiziert werden. Mittels interventioneller bronchoskopischer Maßnahmen wie Argonplasmabeamer-Therapie, Freitagstentapplikation und Brachytherapie konnte die endobronchiale Blutung gestillt und die zentralen Atemwege offen gehalten werden.

Anamnese: Seit 3 Wochen zunehmend blutig tingierter Auswurf, geringe Atemnot, keine Thoraxschmerzen, kein Fieber, keine bekannten pulmonalen Vorerkrankungen.

Status: 75 a, guter AZ, adipöser EZ, Vitalparameter im Normbereich, kardiopulmonal unauffällig, auch sonst keine wesentlichen Befunde.

Befunde: Labor: Hb 9,7 g/dl (Z.n. 2 EryKonz. auswärtig), INR(TT) 2,3 (AOK wegen chron. VHF).

Thoraxröntgen: Mikronoduläre Infiltrate bds.

Bronchoskopie: Blutende tumoröse RF mittlere/distale Trachea, Probenentnahme, Beamertherapie zur TU-Abtragung und Blutstillung.

Histopathologischer Befund: Epitheloides Angiosarkom.

Staging mit CT und PET: Mediastinaler Tumor mit Befall Trachea, Ösophagus und Schilddrüse, cT4N3M1 mit ossärer Metastasierung.

Zusammenfassung und Verlauf: Nach Erstdiagnose, mechanischer Tumorabtragung und lokaler Blutstillung mittels Argonplasmabeamer-Therapie wurde eine systemische Polychemotherapie vom Patienten abgelehnt. Bei fortschreitendem lokalem Tumorwachstum (nach 4 Monaten) musste zur Sicherung der zentralen Atemwege ein Bifurkationsstent gelegt werden. Da am distalen Stentende im Bereich beider Hauptbronchien eine tumorbedingte Obliteration drohte, wurde dreimal eine endoluminale Bestrahlung mit Erfolg durchgeführt. Schließlich verstarb der Patient 7 Monate nach Erstdiagnose an den Folgen der zerebralen Metastasierung.

Pulmonale Amyloidose bei SLE und MGUS

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Wir berichten über den außergewöhnlichen Fall einer pulmonalen Amyloidose einer 45-jährigen Patientin mit systemischen Lupus erythematodes (SLE) und monoklonaler Gammopathie unklarer Signifikanz (MGUS), die wegen Fieberschüben bis 39 C, Polyarthralgien und Myalgien zutransferiert wurde. Auswärts war bei fehlendem Hinweis für eine Infekti-

* Beide Autoren haben in gleichem Ausmaß beigetragen.

on ein SLE-Schub suspiziert und eine Kortikosteroid-Therapie begonnen worden, unter der es zu keiner Besserung kam.

Auffällige laborchemische Befunde waren ANA 1:2560, ds-DNA-AK 653,9 IU/ml, AK vs. Histone 113 U/ml, Paraproteinämie Typ IgG-Kappa und IgG-Lambda mit freien Kappa- und Lambda-Leichtketten, CRP 22,6 mg/dl, erhöhte Leberfunktionsparameter, sowie eine Anämie. Sämtliche mikrobiologische Befunde (Blutkulturen, Harn, Liquor) waren negativ.

Bei anhaltendem Fieber erfolgte eine empirische Antibiotikatherapie mit Piperacillin/Tazobactam, worunter es wiederum zu keiner klinischen Besserung kam. Im weiteren Verlauf traten bei vorbestehenden geringgradigen Pleuraergüssen und sauerstoffpflichtiger respiratorischer Verschlechterung pulmonale Infiltrate beidseits auf, die zunächst als pneumonisch, in der Verlaufskontrolle als Ödem interpretiert wurden. Eine Pleurapunktion ergab ein Transsudat ohne Keimnachweis. Es erfolgte eine Bronchoskopie, wobei es zu einer intubationspflichtigen respiratorischen Insuffizienz kam. Die BAL ergab Klebsiella pneumoniae 103, empfindlich auf Piperacillin/Tazobactam. Weiters entwickelte die Patientin Zeichen einer disseminierten intravasalen Gerinnung. Bei weiterhin unklaren therapierefraktären pulmonalen Infiltraten erfolgte eine offene Lungenbiopsie. Bei Verdacht auf SLE-Schub als Ursache der respiratorischen Insuffizienz erfolgte eine Hochdosistherapie mit Prednisolon. Darunter kam zu einer raschen Besserung der respiratorischen Situation und Extubation. Die Infiltrate und Pleuraergüsse waren rückläufig, das Fieber sistierte. Alle Laborparameter normalisierten sich nahezu, einschließlich einer Abnahme der ds-DNA-AK auf 37 IU/ml.

Die Histologie der offenen Lungenbiopsie ergab das überraschende Ergebnis einer diffusen Amyloidose. Die Immunhistochemie zeigte eine Non-AA-Amyloidose, am ehesten eine primäre AL-Amyloidose. Biopsien von periumbilikalem Fettgewebe, Rektum und Leber zeigten keinen Hinweis für eine Amyloidose.

Zusammenfassend sind kombinierte Fälle von SLE und MGUS bekannt, jedoch beschreibt dieser Fallbericht unseres Wissens erstmalig überhaupt eine Amyloidose bei SLE und MGUS, im Besonderen eine pulmonale Amyloidose.

Vermeidung der nicht-invasiven Beatmung bei einem Patienten mit idiopathischer bilateraler Phrenicusparese – Effekte des inspiratorischen Atemmuskeltrainings

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Ein 44-jähriger männlicher Patient wurde an unserer Abteilung aufgrund von Dyspnoe, welche im Liegen an Intensität zunahm, aufgenommen. Bis auf eine beidseitige Pulmonalembolie im Jahr 2001 bei bekannter Faktor V Leiden Mutation waren keine wesentlichen Vorerkrankungen erhebbar.

Im Thoraxröntgen zeigte sich ein beidseitiger Zwerchfellhochstand sowie eine paradoxe Zwerchfellbewegung beim Hitzenberger-Schnupfversuch während der Durchleuchtung. Die Lungenfunktion ergab einen deutlichen Abfall der inspiratorischen Vitalkapazität (VCin) im Liegen gegenüber der VCin im Sitzen (siehe Tabelle 1). Die elektrophysiologische Untersuchung zeigte eine pathologisch verlängerte distale Latenz des N. phrenicus beidseits (rechts 13,2 ms, links 15,1 ms), womit die Diagnose einer bilateralen Phrenicusparese gestellt wurde. Die ätiologische Abklärung blieb ohne Befund.

Da die nächtliche Pulsoxymetrie eine durchschnittliche Sauerstoffsättigung von 85% zeigte und die transcutane CO2 Messung 59 mmHg ergab, war eine nächtliche nichtinvasive Beatmung (NIV) mittels BIPAP indiziert.

Zusätzlich zur nichtinvasiven Beatmung absolvierte unser Patient täglich ein Atemmuskeltrainingsprogramm, bestehend aus Kraft- und Ausdauerübungen, mit dem Gerät Respifit S.

Der während einer maximalen Inspiration erhobene Munddruck (MIP) und der 12 s-MVV-Test dienten als Parameter für Kraft- und Ausdauer der Atemmuskulatur.

Nach 5 Monaten täglichen Atemmuskeltrainings und der BIPAP-Beatmung wurde eine signifikante Besserung sowohl der VCin als auch der 12s-MVV und MIP festgestellt.

Da die nächtliche Pulsoxymetrie ohne Beatmung nun eine durchschnittliche Sauerstoffsättigung von 96% und die transcutane CO2 Messung 42 mmHg ergab, wurde die NIV abgesetzt.

Nach 2 sowie 18 Monate nach Beendigung der NIV, unter Fortsetzung des täglichen Atemmuskeltrainings, erfolgte eine neuerliche Evaluierung der Parameter. Dabei konnte trotz Fortbestehen der beidseitigen Phrenicusparese, nachgewiesen durch die elektrophysiologische Untersuchung, eine suffiziente nächtliche Sauerstoffsättigung ohne CO2-Retention sowie eine weitere Besserung der Parameter für Kraft und Ausdauer der Atemmuskulatur nachgewiesen werden.

Sichtlich kann spezifisches inspiratorisches Atemmuskeltraining trotz sistierender bilateraler Phrenicusparese durch verstärkte Rekrutierung der Restmuskulatur der inspiratorischen Atempumpe das Auftreten relevanter nächtlicher Desaturationen verhindern.

Unseres wissens nach, ist dies der erste Fall, wo durch individuelles Atemmuskeltraining die nichtinvasive Beatmung bei einem Patienten mit bilateraler Phrenicusparese vermieden werden konnte.

Grillen – eine neue Berufskrankheit?

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Anamnese: 60-jähriger Mann, seit 10 Jahren Exraucher. Über Jahre zunehmende Atemnot insbesondere bei körperlicher Belastung. Keine lungenfachärztlichen Besuche in der letzten Dekade. Stationäre Aufnahme wegen Husten, zunehmender thorakaler Beklemmung, immer wieder glasig bis putrider Auswurf.

Berufsanamnese – gelernter Koch, seit ca. 15 Jahren tätig in einem mexikanischen Restaurant meist am offenen Griller.

Körperlicher Untersuchungsbefund: 60-jähriger Mann, 176 cm, 98 kg, BMI 31,6. Atemfrequenz in Ruhe 18/min., auskultatorisch beidseits über den Mittel- und Untergeschossen ausgeprägte Sklerosiphonie, kein Giemen, kein Stridor.

Spirometrie-Bodyplethysmografie: Befund einer mäßiggradigen primär restriktiven Ventilationsstörung (TLC 4,55 L – 70,1%) mit Hinweis auf erhöhte Lungensteife. Zusätzlich leichtgradige obstruktive Komponente bei erhöhtem Atemwiderstand (Rtot 0,44–0,23 vor/nach 3 Hub Sultanol) mit Besserung um 47. FEV1 2,06–2,40 L (56,5–66% Norm), FEV1%VCmax 74,4–77,4%

Kapilläre Blutgasanalyse: In Ruhe pCO2 39,8, pO2 77,6 mmHg. Nach leichter Belastung mit Laktatanstieg von 0,9 auf 2,2 mmol/L: Abfall des pO2 auf 61,8 mmHg bei gleich bleibendem pCO2.

TLCO SB: 49,1% des Solls, TLCO/VA: 77,3%, VA 63,5% des Solls.

Routine-Laborbefunde: unauffällig, keine erhöhten Entzündungsparameter, keine LDH-Erhöhung, kein Hinweis für eine Autoimmunkrankheit.

Thoraxröntgen pa/lat mit ausgedehnten beidseitigen Zeichen einer Lungenfibrose über allen Abschnitten.

Thorax-CT: ausgeprägte fibrosierende Strukturveränderungen über beiden Lungen mit subpleuralem Honeycombing.

Bronchoskopie: zentral unauffälliges Bronchialsystem, BAL ohne Aktivitätshinweise.

Nach 6 Monaten systemischer Kortikosteroidgabe weder eine radiologische, klinische noch funktionelle Besserung. Indikation zur thorakoskopischen Lungenbiopsie.

Histologie: Endstage-Veränderungen einer Wabenlunge neben dem Bild einer chronischen Bronchiolitis obliterans wie auch konstriktiven Bronchiolitis.

Diskussion: Bei Berufsanamnese einer 15-jährigen Grilltätigkeit mit Verwendung von Margarinen mit Diacetyl als Geschmacksverstärker z.B. beim Grillen von Maiskolben und vorliegendem histologischen Befund einer Bronchiolitis obliterans besteht der hochgradige Verdacht auf eine Diacetyl-bedingte fibrosierende Lungenerkrankung.

Zwischen 1992–2000 wurde von der NIOSH Diacetyl als Hauptkomponente des butterartigen Aromas von Geschmacksstoffen der Nahrmittelindustrie identifiziert und in Folge eine Assoziation mit chronisch obliterierender Bronchiolitis bewiesen.

Seltene Differenzialdiagnose pulmonaler Infiltrate: Intravasculäres Lymphom

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Eine 49-jährige Patientin wurde wegen Nachtschweiß, Leistungsabfall, Reizhusten und Inappetenz seit drei Monaten zur Abklärung pulmonaler Infiltrate beidseits aufgenommen. Sie präsentierte sich in mittlerem AEZ, cardiorespiratorisch unauffällig, palpatorisch Hepatomegalie. Nikotin- und Allergie-Anamnese waren leer.

Die Blutgase zeigten eine Partialinsuffizienz, das Thoraxröntgen Infiltrate in beiden Oberfeldern. Bodyplethysmographie, EKG und Bronchoskopie waren unauffällig, die Tuberkulose-Diagnostik negativ. In der Ganzkörper-^{18}FDG-PET ergab sich keine Befunderweiterung.

Laborchemisch auffällig waren Anämie und Erhöhung von Leberparametern, CRP und LDH, letztere im Verlauf steigend.

Bei klinisch-radiologischem Verdacht auf eine interstitielle Lungenerkrankung wurde mit oralem Kortison therapiert, die radiologische Kontrolle (Abb. 1) zeigte eine Persistenz der Infiltrate.

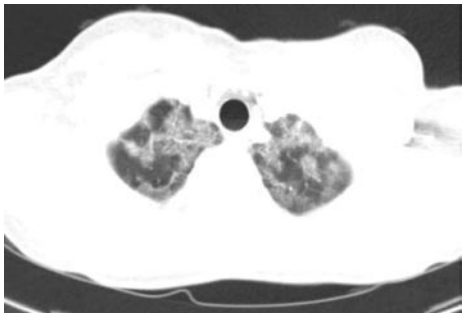

Abb. 1. Flaue Infiltrate in beiden Oberlappen

Die Patientin verließ das Krankenhaus gegen Revers. Sie wurde in reduziertem AZ an der Thoraxchirurgischen Abteilung wiederaufgenommen, wo eine Keilresektion im Segment R1 komplikationslos durchgeführt wurde. Postoperativ kam es jedoch zum Multiorganversagen. Die Histologie ergab ein intravaskuläres großzelliges B-Zell-Lymphom (Abb. 2). Die Patientin verstarb vor Verabreichung einer Rescue-Chemotherapie am neunten postoperativen Tag.

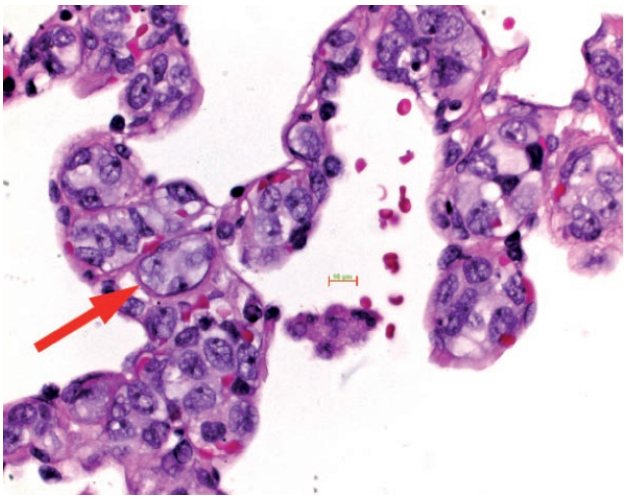

Abb. 2. Kapillaren von Tumorzellenb ausgefüllt; Referenzlinie 10 µm

Diskussion: Das Intravaskuläre B-Zell-Lymphom ist eine seltene Ursache pulmonaler Infiltrate. Diagnostische Probleme ergeben sich durch die uncharakteristischen klinischen und radiologischen Befunde. Bei rechtzeitiger histologischer Diagnosestellung kann mittels Chemotherapie (R-CHOP) eine Remission erreicht werden. Komplikationen ergeben sich aus dem endoluminalen Wachstum mit Obstruktion des Kapillarbettes.

Bei diffusen Lungeninfiltraten, subfebrilen Temperaturen, Hypoxämie und extrapulmonalen Symptomen muss differentialdiagnostisch an das IVL gedacht werden.

Mikroskopische Polyangitis beim Kleinkind

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Ein 5 7/12 Jahre altes bis dahin gesundes Mädchen wird am 01.05.2008 aufgrund von Husten und Fieber seit einer Woche an unserer Abteilung vorstellig. Sie war bereits mit Amoxicillin über 5 Tage erfolglos behandelt worden. Aufgrund von Anamnese, Befund, Labor und Röntgenbild wurde bei vorübergehend spontaner Besserungstendenz von einer viralen Bronchopneumonie ausgegangen. Wiedervorstellung nach einer Woche bei deutlich schlechterem Allgemeinzustand mit auffallender Blässe, stärkerem Husten und persistierendem Fieber. Im Labor bestätigt sich jetzt eine Anämie, das Röntgenbild zeigt zunehmende fleckförmige alveoläre Verschattungen. Der Harn ist im Sinne einer Glomerulonephritis auffällig. Es entwickelt sich ein nephritisches Syndrom mit Zeichen des beginnenden akuten Nierenversagens. Die Nierenbiopsie zeigt eine pauci immune crescentic Glomerulonephritis als Hinweis für eine Nierenbeteiligung im Rahmen einer systemischen Vaskulitis. Es besteht der klinische Verdacht eines pulmorena-

len Syndroms, was sich durch Nachweis von Siderophagen in der bronchoalveolären Lavage bestätigt. Bei Nachweis von p-ANCA#s und fehlendem Nachweis von granulomatösen Entzündungszeichen ist in Zusammenschau von Klinik, Labor, Histologie und Zytologie das Krankheitsbild einer mikroskopischen Polyangitis zu diagnostizieren. Es wird eine Therapie mit Steroid- und Cyclophosphamidboli eingleitet. Hierunter gelingt eine Remission, die Erhaltungstherapie erfolgt mit Prednison und Azathioprin.

A case of easily cured pulmonary hypertension

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Patient: A 57 year old female presented with progressive dypnoea, impairment of daily living activities and of memory. Physical examination revealed obesity, global cyanosis, slight leg oedema and slowed mental state. Previous medical history comprised cerebral aneurysmatic bleeding with a prolonged ICU stay, arterial hypertension and smoking of 15 packyears.

Findings. Arterial blood pressure at admission was 148/90, ECG showed an incomplete right bundle-branch block, pulmonary function test revealed slight obstruction, arterial blood gas analysis hypoxaemia (pO2 38.7 mmHg) and hypercapnia (pCO2 67.4 mmHg). Laboratory findings were within normal limits except NT-proBNP of 1728 pg/ml and haematocrit of 48.3%. 6 minute-walking test was 288 m with BORG 5. Echocardiography yielded impaired left ventricular relaxation, dilated right atrium and ventricle and tricuspid regurgitation equivalent to 50 mmHg. These findings led to right heart catheterization with following results: mean pulmonary arterial pressure 34 mmHg, wedge pressure 12 mmHg, pulmonary vascular resistance 259 dyn*s*cm-5, suggesting pulmonary hypertension as main cause for the patient´s symptoms.

Diagnostic test: Further exploration revealed excessive daytime sleepiness, so polysomnography was performed and yielded severe obstructive sleep apnoea syndrome (apnoea-hypopnoea index 110/h, maximal apnoeic event 50.8 seconds, mean oxygen saturation 77%, minimal 55%).

Diagnosis: Obesity-hypoventilation syndrome with severe obstructive sleep apnoea, secondary leading to pulmonary hypertension.

Treatment and follow-up: Bilevel ventilation and oxygen lead to normalized breathing pattern, laboratory findings and right heart catheter parameters and weight loss as well as elimination of complaints and symptoms.

Ein 18-jähriges Mädchen mit Fieber, Husten und zystischen Läsionen in der Lunge

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Klinische Fallbeschreibung: Eine 18-jährige Patientin wurde an unsere Abteilung mit einer typischen Infektanamnese, seit einigen Tagen zunehmendem Fieber mit Temperaturen bis 38,5 Grad C stationär aufgenommen.

Initial war sie von einem Matura-Urlaub in der Türkei vor einer Woche zurückgekehrt, wo sie im Rahmen des „Summer Splash" einerseits viel Spass gehabt hatte, sich jedoch „entweder durch die Klimaanlage oder beim Rückflug vor einer Woche verkühlt hatte". Sie war unmittelbar nach Ankunft zu Hause im KH Eisenstadt stationär, hier erfolgte eine CT, die eine Infiltration mit Spiegelbildung von zystischen Läsionen im re. OL aber auch im Bereich der UL-Spitze zeigte. Diesbezüglich war eine antibiotische Therapie mit Augmentin i.v. begonnen worden.

Bei uns präsentiert sich eine Pat., die klinisch überraschenderweise kaum Beschwerden angibt, bei max. In- u. Exspiration verspürt sie einen geringen stechenden Schmerz re. thorakal, ansonsten ist sie im Wesentlichen asymptomatisch. Altersentsprechender AZ u. EZ, 170 cm, 60 kg, RR 100/70, Pulsfrequenz 80, Rachen: gerötet, SD: schluckverschieblich, Cor: HT: rein, rhythmisch, normofrequent. Pulmo: Atemfrequenz 10, Perkussion: sonorer Klopfschall, Basen frei verschieblich Auskultation, VA, minimale bronchitische RG's re. Sonstiger Status: altersentsprechend unauffällig.

BGA mit Raumluft: p02 77 mmHg, 96%, pCO2 32 mmHg, pH 7,49, BE 1,4 mmol/L.

EKG: Sinusrhythmus, Normallagetyp, 81 Frequenz, P u. PQ unauffällig, QRS 0,08, regelrechte R-Progression, Transition V 3/V 4, keine Repolarisationsstörung.

Die Entzündungsparameter sind bei Aufnahme erhöht (CRP 87 mg/l, Leuko 16.5 G/l), auch die vorliegenden Bilder sprechen für eine floride Infiltration, sodass die antibiotische Therapie mit Augmentin fortgeführt wurde. Zusätzlich lagen uns folgendes Röntgen und CT vor (Bilder).

Diagnostisches Vorgehen: Zur Abklärung der sekreteingefüllten Zysten erfolgte eine Bronchoskopie. Diese zeigt eine Stenose der Bronchien im Bereich des re. OL, aber auch im Bereich der re. UL-Spitze. Die nachgeschalteten Segmentbronchien sind stenosiert, ein Vorschieben einer Kanüle in diese Bereiche ist zwar möglich, es können nur sehr geringe Mengen von leicht eingetrübtem Sekret aspiriert werden.

Die uns vorliegenden zytologischen Untersuchungen zeigen einen benignen Zellbefund mit stellenweise vermehrten Leukozyten (PN II). Unter lfd. antibiotischer Therapie kommt es zu einem Rückgang der Entzündungsparameter, in einem Kontrollrö. zeigt sich jedoch im Wesentlichen unverändert eine 10 cm große flüssigkeitsgefüllte zystische Läsion im re. OL mit zwei weiteren kleineren flüssigkeitsgefüllten Läsionen im re. OL sowie im Bereich der UL-Spitze.

Es konnten Vorbilder der Patientin aus dem Jahre 2004 gefunden werden, in denen ebenfalls Lungenzysten ohne Sekretspiegel zu sehen waren, ebenfalls im Jahre 2004 war daraufhin eine CT des Thorax zur Diagnose von Zysten im re.OL durchgeführt worden.

Sonographie Abdomen: Kein HW auf zystische Veränderungen im Abdomen. Gyn. Konsil unauffällig.

Am ehesten ist das Vorliegen einer kongenitalen zystisch adenomatoiden Malformation (CCAM), hierbei handelt es sich um angeborene zystische Veränderungen der Lunge. Aufgrund der Komplikation mit Sekretretention in mehreren Zysten wurde eine operative Sanierung im interdiziplinären Konsil besprochen.

Diskussion: Nach weiterführender antibiotischer Therapie, ausführlicher, präoperativer Aufklärung der Patientin erfolgt am 18.09.2007 die Operation, wobei der rechte OL reseziert wurde, des weiteren wurde eine atypische Segmentresektion aus der UL-Spitze rechts durchgeführt. Der intraoperative Verlauf gestaltete sich komplikationslos. Die Histologie bestätigte den V.a eine CCAM.

Die Genese dieser Erkrankung ist nicht geklärt, eine definitive Diagnose ist erst durch Gewebsentnahme möglich. Der Typ I der CCAM ist die häufigste Form, die Unterscheidung erfolgt morphologisch, wobei typischerweise bis zu 10 cm große dünnwandige Zysten, die einzeln oder mulitlokolär vorliegen, können auftreten (Bild). Dies ist bei unserer Pat. der Fall. Es kann durch die auch bei uns vorliegenden Stenosierungen zur Entwicklung eines Hydrops und Sekundärinfektionen kommen.

Typ 1:
– am häufigsten
– wenige, große, dünnwandige Cysten (d = 2–10 cm)
– Luft- oder Flüssigkeitsgefüllt

Typ 2:
– multiple kleinere Cysten (d = 0,5–2 cm)
– Assoziation mit anderen kongenitalen Fehlbildungen in bis zu 60% (Ösophagusatresie, Tracheoösophageale Fisteln, bilaterale Nierenagenesie, andere Lungenfehlbildungen …)

Typ 3:
– oft sehr große Läsionen, ev. über mehrere Lappen
– bestehend aus zahlreichen winzigen Cysten (d < 0,5 cm) sehr seltene Formen: Typ 4: große Cysten (d bis zu 7 cm Typ 0: winzige Cysten (d < 0,5 cm)

In der Literatur sind dzt. nur wenige Fälle beschrieben, im Wesentlichen wird vor allem bei symptomatischen Patienten eine chirurgische Intervention empfohlen. Hier ist vor allem bei der CCAM Typ I die Prognose exzellent. Begründet wird dies mit einerseits rezidivierenden Komplikationen wie Infektionen, es wird jedoch auch eine Assoziation mit epithelialen u. mesenchymalen Neoplasien vermutet, weshalb im Speziellen bei symptomatischen Pat. eine Intervention empfohlen wird. CCAM Typ 2 und 3 sind von einer schlechteren Prognose begleitet auf Grund der anderen, assoziierten Fehlbildungen (Typ 2) bzw. der stärkeren Größenausdehnung der Läsionen (Typ 3).

Beidseitige Pleuraergüsse bei Rosai-Dorfmann Syndrom und serologischem Verdacht auf Lupus erythematodes

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Eine 62-jährige Patientin wird mit progredienter Dyspnoe und Gewichtsverlust von 5 kg ambulant vorstellig. Im Lungenröntgen zeigen sich beidseitige, handbreite Pleuraergüsse, die Lungenfunktion ist restriktiv (FVC 43%, FEV1 46%, Tiffenau Index 87%). Die Zytologie des Pleurapunktates (1200 ml) ist negativ (Transsudat, PN II, ZN negativ). Laborparameter: CEA, SCC, NSE & Cyfra 21.1 negativ; Blutsenkung 124 mm/h, mikrozytäre Anämie Hb 9,1 g/dl, MCV 72 fl, Hypocalciämie 2,03 mmol/l, passagere Erhöhung des beta-2-Mikroglobulins auf 3,1 mg/l und CRP bis 140 mg/l. Cervikal und axillär imponieren beidseits gut verschiebliche bis 2 cm im Durchmesser haltende Lymphknoten. Die Punktion eines cervikalen Lymphknotens ergibt einen unklaren Befund: PN II, dentritische Mesothelzellen und Mesothelzellverbände. Erst die chirurgische Lymphknotenextirpation bringt die histologische Diagnose eines Rosai-Dorfman Syndroms (Emperipolesis, S100 pos, CD1a neg.), eine benigne lymphoproliferative Erkrankung.

Da das Autoantikörperscreening einen positiven Befund auf ANA 1:320, anti-dsDNA 32,9 IU/ml, Antikörper gegen Histone und Nukleosomen je >200 IU/ml zeigte, besteht der Verdacht auf Lupus erythematodes. Die dermatologische Begutachtung war negativ, auch waren sämtliche Lupuskriterien (ACR) bis auf Serositis und positiver ANA und anti-dsDNA negativ (nicht hämolytische Anämie, Harnbefunde unauffällig, Herzecho unauffällig, systolischer PAP 31 mmHg).

Eine spezifische Therapie für das Rosai Dorfman Syndrom existiert nicht, aufgrund des Lupusverdachtes wurde die Patientin mit Aprednislon 1 mg/kg/KG anbehandelt. Die Plaeuraergüsse zeigten nach 4 Wochen Therapie völlige Regressio, die Lungenfunktion verbesserte sich auf eine FVC 66%, FEV1 68% und Tiffenau Index 84%. Die Steroiddosis beträgt derzeit 0,5 mg/kg/KG, zusätzlich geben wir 100 mg Azathioprin.

