Topic 35 – Pulmonary hypertension

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PAH in systemic lupus erythematosus

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Introduction: Pulmonary arterial hypertension (PAH) is a rare disease characterized by the progressive increase in pulmonary artery pressures, leading to right heart failure. Systemic lupus erythematosus (SLE) is the second connectivity after Scleroderma can be complicated by PAH. This study aims to estimate the prevalence of PAH in SLE, detected by echocardiography.

Materials and methods: This is a retrospective study of ten years about 80 patients with SLE fulfilling the criteria of the ACR (American College of Rheumatology), followed in our department of internal medicine. Echocardiography with measurement of pulmonary artery pressure was performed in 72 patients. Above 30 mmHg mean arterial pressure was used to define PAH.

Results: Ten patients (7% of cases) had pulmonary arterial pressure greater than 30mmHg. Two of them had lung disease (the first with emphysematous lung and the other a lupus interstitial lung disease). Three patients had mitral insufficiency. A syndrome of anti-phospholipid antibodies (APS) was noted in four patients (40% of cases). Five other lupus patients had isolated PAH (50% of cases). We noted a positive anti-Sm antibody in three patients (40% of cases).

Discussion: PAH is a rare and severe complication of SLE and is a bad prognostic factor. Its detection is based on echocardiography. PAH lupus may be the expression of APS or secondary to pulmonary fibrosis or left valvulopathy. The treatment is based on corticosteroids and immunosuppressive association. Anticoagulants are indicated in cases of APS.

Conclusion: Due to the severity of PAH in SLE, a screening echocardiography should be systematically offered to patients with SLE to treat early this serious complication and to enhance prognosis.

NGF contributes to medial and intimal remodelling of pulmonary arteries in pulmonary hypertension: receptors and signalling pathways involved in smooth muscle and endothelial cell proliferation

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Introduction: We have previously identified critical roles for the nerve growth factor NGF in pathophysiology of pulmonary hypertension (PH). We have here evaluated whether NGF may contribute to medial and intimal remodelling of pulmonary arteries in vivo in PH rat models. We have also investigated the NGF receptors and signalling pathways involved in vitro in NGF-induced proliferation of human pulmonary arterial smooth muscle (hPASMC) and endothelial cells (hPAEC).

Methods: Experimental PH in the rat was induced either by a single injection of monocrotaline (MCT, 60mg/kg), or after 28 days of chronic hypoxia (CH, 0.5atm). Anti-NGF blocking antibodies (10μg/kg ip) were administered as a preventive or a curative treatment. Pulmonary arterial pressure was assessed after 28 days. Medial and intimal remodelling of pulmonary arteries were then evaluated on lung sections after hematoxylin/eosin or Van Gieson stainings. hPASMC or hPAEC proliferation was assessed by the BrdU technique, and involvement of the NGF receptors TrkA and p75NTR was studied by both pharmacological and SiRNA approaches.

Results: In vivo, NGF inhibition with anti-NGF blocking antibodies both prevented and reversed medial and intimal remodelling of pulmonary arteries in MCT and CH rats. In vitro, NGF-induced hPASMC proliferation occurred at low concentrations and only involved TrkA/PI3-kinase dependent signalling pathways. NGF-induced hPAEC proliferation occurred at higher concentrations and involved both TrkA and p75NTR receptors activating PI3-kinase independent/NFκB-dependent signalling pathways.

Conclusion: We show here that NGF contributes to medial and intimal remodelling of pulmonary arteries in vivo in PH rat models. This may occur through stimulation of both hPASMC and hPAEC proliferation, but through distinct receptors and signalling pathways in these two different cell types, thus suggesting that blocking both NGF receptors may be of therapeutical interest in PH.