

# European Respiratory Society Annual Congress 2013

**Abstract Number:** 4805

**Publication Number:** P425

**Abstract Group:** 1.1. Clinical Problems

**Keyword 1:** Allergy **Keyword 2:** Interstitial lung disease **Keyword 3:** Occupation

**Title:** High levels of vascular endothelial growth factor–C and D are associated with disease severity of hypersensitivity pneumonitis

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**Body:** [Background] The pathogenic roles of angiogenesis and lymphangiogenesis in hypersensitivity pneumonitis (HP) have been remained to be elucidated. [Objective] To characterize the protein expressions of vascular endothelial growth factors (VEGFs) in acute HP, and to explore the clinical significances [Patients and Methods] The concentrations of VEGF–A, –C and –D in the serum and bronchialveolar lavage fluid (BALF) of 29 healthy controls, 10 and 20 patients with idiopathic pulmonary fibrosis and acute HP were determined by ELISA. Formalin-fixed paraffin-embedded lung specimens were used for the immunohistochemical analyses. [Results] The levels of serum VEGF–A and –C, and BALF VEGF–C and –D were significantly elevated in HP, when compared with healthy controls. The results of immunostaining using primary antibodies against the 3 VEGF types revealed that the growth factors were mainly expressed in epithelial cells, macrophages and granulomas. Neither serum nor BALF VEGF-A was associated with inflammatory cells and pulmonary function tests. BALF VEGF–C showed a tendency of inverse correlation with %DLco ( $r = -0.521$ ,  $p = 0.084$ ). BALF VEGF–D was significantly correlated with BAL total cell and lymphocyte counts ( $r = 0.635$  and  $r = 0.720$ ,  $p = 0.0038$  and  $p = 0.00051$ ), and showed a tendency of macrophage counts in BAL. In addition, BALF VEGF–D was inversely correlated with forced expiratory volume % in one second ( $r = -0.495$ ,  $p = 0.031$ ) [Conclusion] Our results indicate that VEGF–C and –D are associated with inflammatory and functional severity of this condition, suggesting that lymphangiogenesis is involved in the pathogenesis of HP.