

THE ANGIOGENETIC AXIS ANGIOPOIETIN-1 AND -2/TIE-2 IN NONSMALL CELL LUNG CANCER: A BRONCHOALVEOLAR LAVAGE AND SERUM STUDY

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Angiopietin-1 (Ang-1) and Angiopietin-2 (Ang-2) have both been identified as ligands for Tie-2, a receptor expressed on endothelial cells, and it has been shown previously that Ang-1 and Ang-2 play critical roles in angiogenesis, in concert with VEGF. Angiogenesis plays important role in tumor growth and development. Increasing evidence implicates angiogenesis in the pathogenesis of interstitial lung diseases. The aim of this study was to evaluate the concentration of Ang-1, Ang-2, Tie-2, Interleukin-18 (IL-18), Transforming Growth Factor beta 1 (TGF β 1) and VEGF domain in serum and in BALF of lung cancer patients before chemotherapy. We studied 45 Nonsmall Cell Lung Cancer patients (38 males; mean age 61.9). Control groups consisted of 15 Sarcoidosis patients (13 males; mean age 58.3), 15 Hypersensitivity Pneumonitis (13 males, mean age 59.5) and 15 Healthy Persons (13 males; mean age 60.1). The highest levels of Ang-1 were in serum of HP patients, lower in NSCLC, Healthy and lowest in Sarcoidosis (51.01 vs 43.01 vs 32.87 vs 24.24 ng/ml, $p < 0.05$). Serum levels of Ang-2 were highest in NSCLC, lower in HP, next in Sarcoidosis, lowest in Healthy (2.6 vs 2.35 vs 1.94 vs 1.72 ng/ml, $p < 0.05$). The levels of Ang-2 in BALF were highest in HP, lower in NSCLC, next in Sarcoidosis and lowest in Healthy (62.95 vs 62.28 vs 61.6 vs 59.57 pg/ml, $p < 0.05$). The levels of IL-18 in BALF were highest in HP, lower in Sarcoidosis, next in Healthy, lowest in NSCLC (64.01 vs 28.99 vs 12.07 vs 10.65 pg/ml, $p < 0.05$). Receiver-operating characteristics (ROC) curves were applied to find the cut-off serum levels of Ang-1 (NSCLC vs Sarcoidosis: 24.52 ng/ml, Sarcoidosis vs HP: 95.5 ng/ml), Ang-2 (NSCLC vs Sarcoidosis: 0.801 ng/ml, NSCLC vs Healthy: 1.19 ng/ml), IL-18 (NSCLC vs Healthy: 118.11 pg/ml), TGF β 1 (NSCLC vs Sarcoidosis: 18.84 pg/ml). ROC curves were also applied to find the cut-off BALF levels of Ang-2 (NSCLC vs Healthy: 54.16 pg/ml), Tie-2 (NSCLC vs HP: 2.86 pg/ml), IL-18 (HP vs Healthy: 33.37 pg/ml). We didn't found any correlation between the levels of the Ang-1, Ang-2, Tie-2 and stage of the tumor, response treatment (prospectively). We conclude that angiogenetic axis Angiopietin-1 and -2/Tie-2 may play important role in lung cancer development and their concentrations may be useful at the time of initial diagnosis of lung cancer.