



Molecular mechanisms underlying fibrosis and elastin destruction in childhood interstitial lung diseases

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Abstract:

Objective This study aimed to evaluate fibrosis and elastin destruction in childhood interstitial lung disease (chILD) patients. **Methods** Sixty patients and twenty healthy children were recruited. On admission, evaluation of chILD severity was made using Fan chILD score. Participants provided urine and blood samples. Plasma levels of transforming growth factor (TGF)- β 1, connective tissue growth factor (CCN2), soluble factor related apoptosis (sFas) and long non-coding RNAs and urinary levels of desmosine/urinary creatinine (UDes/UCr) were measured. **Results** In patients, clinical findings were crackles (100.00%), tachypnea (65.00%), cardiomegaly (45.00%), digital clubbing (43.30%), cough (33.00%), cyanosis (26.70%), hepatomegaly (28.30%) and wheezes (23.30%). Categorizing of the patients with Fan chILD clinical score revealed that most patients 33.30% scored (3, symptomatic with abnormal saturation/cyanosis during exercise) then 28.30% scored (5, symptomatic with clinical and echocardiographic features of pulmonary hypertension), 18.30% scored (2, symptomatic with normal room air saturations), 15.00% scored (1, asymptomatic) and 5.00% scored (4, symptomatic with abnormal room air saturation/cyanosis at rest). TGF- β 1, CCN2, sFas, lncRNA-2700086A05Rik relative gene expression and UDes/UCr levels were higher in patients than controls ($P = 0.002$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, respectively). In patients, significant positive correlations were found between TGF- β 1 and CCN2, sFas, UDes/UCr; between CCN2 and both sFas and UDes/UCr; between UDes/UCr and sFas. Morbidity and mortality rates were 46.70% and 10.00%, respectively. **Conclusion** Markers of fibrosis (TGF- β 1, sFas, CCN2) and elastin destruction (UDes/UCr) were increased in chILD especially in patients with long disease duration. So blockage of their pathways signals may offer novel therapeutic targets. **Abbreviations** ARDS, acute respiratory distress syndrome; AECs, alveolar epithelial cells; BMI, body mass index; CXR, chest X-ray; chILD, childhood interstitial lung disease; CPI, chronic pneumonitis of infancy; CCN2, connective tissue growth factor; CT, critical threshold; ECM, extracellular matrix; DIP, desquamative interstitial pneumonitis; DAD, diffuse alveolar damage; EMT, epithelial-mesenchymal transition; ERS, European Respiratory Society; HRCT, high-resolution computed tomography; lncRNAs, long non-coding RNAs; LIP, lymphocytic interstitial pneumonia; NSIP, idiopathic interstitial pneumonias; IPF, interstitial pulmonary fibrosis; OP, organizing pneumonia; PAP, pulmonary alveolar proteinosis; sFas, soluble factor related apoptosis; TGF- β 1, transforming growth factor- β 1; UDes/UCr, urinary levels of desmosine/urinary creatinine; UIP, usual interstitial pneumonia

Keywords:

Connective tissue growth factor (CCN2); Interstitial lung disease of children; Long non-coding RNAs; Transforming growth factor (TGF)- β 1; Urinary desmosine (UDes)

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