Bleomycin-induced pulmonary fibrosis in cynomolgus monkeys

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【Purpose】

Idiopathic pulmonary fibrosis (IPF) is a progressive and intractable lung disease characterized by the proliferation of fibroblasts and loss of pulmonary function. Although many bleomycin-induced pulmonary fibrosis has been studied as IPF model in rodent, IPF model in nonhuman primates has not been reported. In this study, we investigate a cynomolgus monkey model of bleomycin-induced pulmonary fibrosis by IPF related biomarker and pathology.

【Methods】

Two cynomolgus monkeys were injected transtrachealy with bleomycin (2mg/kg) once a week for the first 2 weeks. The blood and bronchoalveolar lavage fluid (BALF) were collected at 0, 1, 4, 7, 9, 14, 21, 28 days after the first bleomycin injection, and cytokine levels were measured. On day 29, lung hydroxyproline content was measured. The formalin fixed lungs were stained with HE or Masson's trichrome for microscopic observation.

【Result and Discussion】

After bleomycin injection, BALF IL-1β levels were significantly increased on day 1 and returned almost normal level on day 4. The BALF MCP-1 levels were gradually increased and reached peak from day 4 to day 9. The BALF TGF-beta1 levels reached the maximum on days 7 or 9. The serum TGF-beta1 levels showed almost the same tendency as the BALF levels. The lung hydroxyproline contents of bleomycin injected monkeys were increased about 1.4 times more than normal. Histological examination showed a significant interstitial fibrosis with destruction of the alveolar architecture and was similar to IPF of human. This study provided new model using nonhuman primate for drug development in IPF.