EDITORIAL

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The role of neutrophils in the pathogenesis of IPF

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Idiopathic pulmonary fibrosis (IPF) treatment underwent a paradigm shift after all clinical trials of anti-inflammatory and immunosuppressive agents for IPF failed [1]. Current primary IPF treatment is antifibrotic agents. Although immunity and inflammation may not be as important in the pathogenesis of IPF as previously thought, the involvement of innate and adaptive immunity in IPF continues to be reported. Among innate immune cells, macrophages are thought to be the most important cells in fibrotic lung disease [2]. Neutrophils also play roles in fibrotic lung diseases. Neutrophil elastase is involved in extracellular matrix turnover [3], as well as the proliferation of lung fibroblasts and myofibroblast differentiation [4]. And neutrophils participate in the pathogenesis of IPF by controlling the balance of matrix metalloproteinases and tissue inhibitors of metalloproteinases. The neutrophil chemoattractant interleukin 8 and extracellular neutrophil traps are also associated with pulmonary fibrosis [5].

Bronchoalveolar lavage fluid (BALF) lymphocytosis and eosinophilia help differentiate interstitial lung diseases, such as hypersensitivity pneumonitis and eosinophilic pneumonia, from IPF. However, there have been conflicting reports about the significance of BALF neutrophilia. In a retrospective study of fibrotic nonspecific interstitial pneumonia and usual interstitial pneumonia (UIP) patients, the BALF findings did not discriminate between the two entities [6]. In another study, BALF neutrophilia was not significantly related to the survival of IPF patients [7]. However, contradictory results have also been reported. In a cohort of 156 patients with IPF, a high percentage of BALF neutrophils was an independent predictor of early mortality [8]. Recently published data have shown that blood neutrophilia is associated with a decline in forced vital capacity and all-cause mortality in IPF [9], and with progression to IPF in patients with an indeterminate computed tomography pattern for UIP [10].

Although aberrant wound healing is the most important mechanism, the pathogenesis of IPF is highly complex and poorly understood. Multiple factors, including aberrant wound healing and immune mechanisms, are thought to be involved. Lee et al. reported that granulocyte colony-stimulating factor (G-CSF) concentrations were higher in BALF from IPF patients than normal controls. The survival rate of IPF patients was significantly lower in the higher G-CSF concentration group, and the BALF neutrophil count was positively correlated with the G-CSF concentration [11]. This result demonstrates the role of innate immunity in the pathogenesis of IPF.

No single drug is capable of curing or stopping the progression of IPF. Combination therapy targeting multiple sites of

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IPF pathogenesis may be more effective than monotherapy. Innate immunity can be a target for IPF treatment, including via neutrophils. However, although neutrophils could promote lung fibrosis, their recruitment to the fibrotic lung may restore homeostasis [5]. Thus, further studies on the role of neutrophils, as "friend or foe," in pulmonary fibrosis are needed.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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