Abundant IgG4-positive plasma cells in interstitial pneumonia without extrathoracic lesions of IgG4-related disease: Is this finding specific to IgG4-related lung disease?

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Objectives:

There have been few reports on immunoglobulin-G4 (IgG4)-related interstitial pneumonia (IP), and its clinical features remain unclear. The objective of this study was to assess whether IP with marked IgG4-positive plasma cell infiltration without extrathoracic lesions of IgG4-related disease (RD) should be diagnosed as a subtype of IgG4-RD or a separate entity.

Methods:

This retrospective study was conducted at Kanagawa Cardiovascular and Respiratory Center in Yokohama city, Kanagawa, Japan. During January 2001–March 2013, surgical lung biopsies were performed on 640 patients with diffuse lung disease. Patients who had identifiable causes of interstitial lung disease, such as exposure to occupational and environmental agents and complications of connective tissue diseases, were excluded from this study. Patients who had extrathoracic lesions of IgG4-RD were also excluded. Among 314 patients with idiopathic IP proven by surgical lung biopsy, IgG and IgG4 immunostaining was performed in 18 patients because of the presence of numerous infiltrating plasma cells. Five patients with an IgG4/IgG-positive cell ratio of >40% and >50 IgG4+ plasma cells in an HPF were enrolled and investigated in terms of the clinical, radiological, and pathological features.

Results:

All 5 patients were male with a history of smoking. Four patients met the comprehensive diagnostic criteria for IgG4-RD. The remaining one lacked data related to the serum IgG4 level. Histologically, a nonspecific IP pattern was observed in all patients. The key morphologic features of IgG4-RD, such as storiform fibrosis and obliterative phlebitis with lymphoplasmacytic infiltration in a loose background texture, were absent in every patient. In contrast, venule obstruction by densely packed lymphoplasmacytic infiltration was observed in two patients. Marked scarring and remodelling of the lung were also noted, which is not typically seen in IgG4-RD. A favourable response to corticosteroid monotherapy was observed in all patients; however, two patients developed lung cancer during the course of observation.

Conclusions:

There are clear differences in the pathological features between our patients and those with typical IgG4-RD. Therefore, we believe that it is appropriate to regard IP with marked IgG4-positive plasma cell infiltration without extrathoracic lesions of IgG4-RD as a separate entity. Moreover, a favourable response to corticosteroid monotherapy and a high frequency of lung carcinoma were noteworthy, and thus, IgG and IgG4 immunostaining should be performed more aggressively to discriminate such patients from those with idiopathic IP with lymphoplasmacytic infiltration.