

SUPPLEMENTARY MATERIAL

METHODS

Study subjects

All subjects were examined by physicians. Medical histories were taken, including domestic and occupational environmental exposures, chest X-rays, high-resolution chest computed tomography (HRCT) scans, and pulmonary function tests. None of the IPF patients had any clinical symptoms or laboratory test evidence of underlying collagen vascular diseases. The diagnosis of IPF was based on the 2011 [20] and 2018 guidelines proposed by American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS), Latin American Thoracic Association (ALAT) Committee on Idiopathic Pulmonary Fibrosis [21] as follows: detection on HRCT of the pattern of usual interstitial pneumonia (UIP, clinical IPF), and specific combinations of HRCT patterns and histopathology patterns in lung tissue samples (surgical IPF). Pathological recognition of a nonspecific interstitial pneumonia (NSIP) pattern involved exclusion of other patterns of interstitial lung diseases, and categorization of histological features according to the ATS/ERS 2002 classification,

as updated in 2013 [18,19]. Histological classification was based on the amount of inflammation and/or fibrosis in the lung biopsies: Group 1, primarily interstitial inflammation; Group 2, both inflammation and fibrosis present; and Group 3, primarily fibrosis, cellular, cellular and fibrosing, or fibrosing NSIP [22]. The diagnosis of hypersensitivity pneumonitis (HP) was based on compatible clinical manifestations, HRCT, and pathology findings [15]. Video-assisted thoracoscopic surgical lung biopsies showing non-necrotizing granulomatous bronchiolocentric pneumonitis were classified into acute, subacute, and chronic HP, according to HRCT and biopsy findings. Sarcoidosis, diagnosed on the basis of compatible clinical and HRCT findings and histological evidence of non-caseating granuloma, was classified into stages 1 to 4 [16,17]. Of the 10 subjects with NSIP, 4 were group 1, 4 were group 2, and 2 were group 3. Of the 10 subjects with HP, 4 were diagnosed as acute, 5 as subacute, and 1 as chronic. The 10 subjects with sarcoidosis included 3 at stage 1, 5 at stage 2, and 2 at stage 3. Because HP and sarcoidosis were diagnosed after excluding other diseases with similar histological profiles, biopsy tissues were subjected to acid-fast bacilli and Grocott's methenamine silver staining to verify the absence of microorganisms and fungi.