IMAGES IN SARCOIDOSIS

Histopathologic overlap between fibrotic sarcoidosis and UIP pattern

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Case presentation

The histological hallmark of sarcoidosis is the presence of non-necrotizing granulomas distributed along bronchovascular bundles and lymphatics. In this setting, the granuloma formation represents the attempt by the immune system to contain a persistent or unidentified antigen. In most cases, inflammation resolves without major sequelae; however, approximately 20% of patients develop a chronic or progressive fibrotic course, leading to irreversible parenchymal remodelling ranging from linear scarring to end-stage fibrotic destruction (1-5). Here, we present a case of 59-year-old man who received a diagnosis of sarcoidosis ten years before. The patient was a former smoker (20 pack-years). He recently presented with dyspnoea and cough, after a recent Sars-Cov2-infection. High-resolution CT (HRCT) (Figure 1A–F) revealed diffuse ground-glass opacities (red star) with upper lobe bronchial distortion, including traction bronchiectasis (yellow arrows), airway angulation, and peribronchovascular thickening (black arrows). Honeycomb-like cystic structures were present in both lower lobes (red arrows); unlike the classical subpleural honeycombing of usual interstitial pneumonia (UIP), these cysts were larger and centrally located. Mediastinal-window images showed enlarged right paratracheal and subcarinal lymph nodes. PET-CT excluded extrapulmonary disease. The patient underwent EBUS-TBNA of stations 4R and 7 and transbronchial cryobiopsy in the right upper lobe. EBUS-TBNA confirmed sarcoid-related microgranulomas, whereas transbronchial cryobiopsy showed parenchymal fibrosis containing non-necrotizing granulomas in a perilymphatic distribution (Figure 2A). At higher magnification (Figure 2B), fibrosis entrapped residual alveolar spaces. At the edge with not fibrotic tissue, cystic structures lined by bronchiolar epithelium and with a few discrete ellipsoidal structures in the wall consisting of extracellular myxoid matrix in which myofibroblasts were embedded resembling UIP-like

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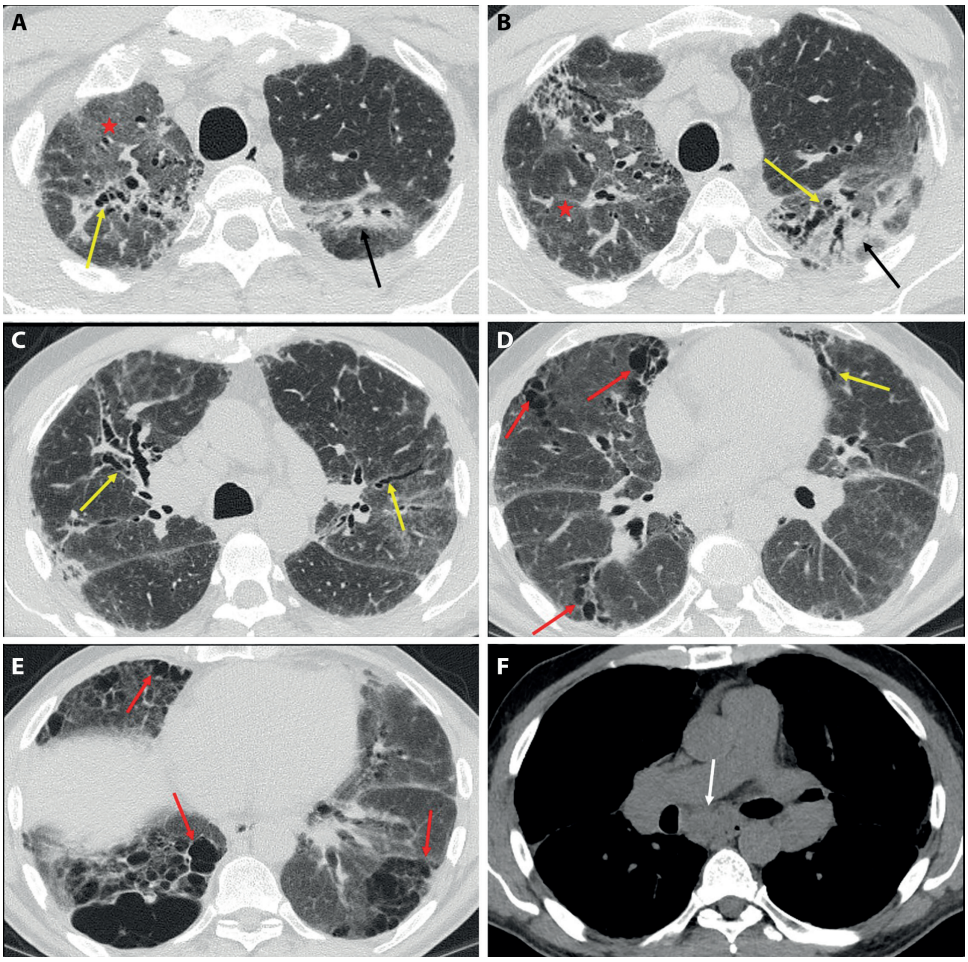

Figure 1. HRCT of the thorax in axial view in lung (A-E) and mediastinal window (F) demonstrated diffuse ground glass opacities (red star) with bilateral upper lobe bronchial distortion such as traction bronchiectasis (yellow arrows), airway angulation and peribronchovascular thickening (black arrows). Presence of honeycomb-like structures in both lower lobes (red arrows) were also present. Multiple enlarged right paratracheal and subcarinal nodes (Figure 1F).

fibroblastic areas were detectable. The final diagnosis was fibrotic sarcoidosis. The 2024 Delphi consensus defines fibrotic sarcoidosis by bronchocentric reticulation, with or without dense parenchymal opacification, cavitation, fibrobullous destruction, or large bronchocentric masses resembling progressive massive fibrosis. Honeycomb-like changes may occur but tend to be centrally distributed, in contrast with the subpleural basal honeycombing characteristic of UIP (6). In the case hereby described the UIP-like appearance in CT scan corresponds to fibrotic areas with entrapped alveolar structures, containing scattered granulomas and cysts whose walls include fibroblastic foci. The presence of fibroblastic foci in the wall of cystic structure covered by a bronchiolar epithelium might explain the progressive phenotype seen in a subset of patients with sarcoidosis, suggesting that a UIP-like pattern and the underlying biological mechanisms links sarcoidosis to other fibrosing interstitial pneumonias manifesting a progressive phenotype (7-10).

Conflict of interest: The authors of this manuscript have no conflict of interest.

Declaration on the use of AI: AI has been used exclusively for English editing.

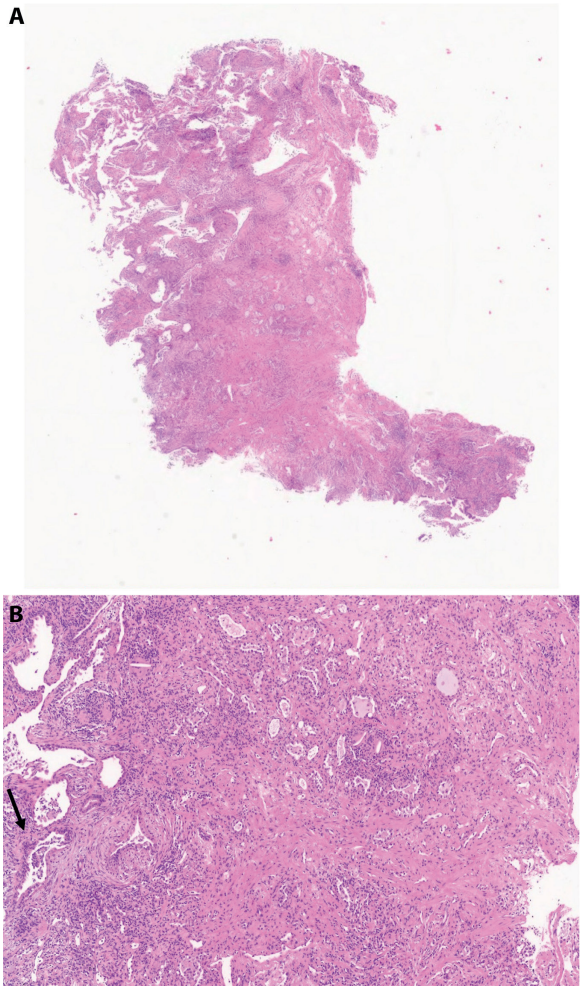

Figure 2. Figure 2A. Areas of parenchymal fibrosis abutting with lung parenchyma with preserved architecture containing non-necrotizing granulomas with a peri-lymphatic distribution (H&E). Figure 2B. At high power, remnants of alveolar spaces are intrapped inside fibrosis and at the periphery of this fibrotic area cystic spaces surrounded by loose fibrotic tissue and covered by bronchiolar epithelium are evident (H&E).

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