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Response to Letter to Editor regarding "Sarcoidosis and IPF in the same patient-a coincidence, an association or a phenotype?"

To the Editor:

We thank Drs. Valentin, Hyde, Gomez and Patel for commenting on our recently published article “Sarcoidosis and IPF in the same patient-a coincidence, an association or a phenotype?” [1]. Indeed, one of our objectives in reporting our observations was to provoke further interest in the scientific community regarding such patients and conduct of clinical studies in such cohorts.

We appreciate the suggested term “Sarcoidosis with UIP pattern”. In fact, we have discussed this as a possibility in the manuscript: that sarcoidosis and UIP in the same patient may suggest that sarcoidosis should be added to the list of conditions such as connective tissue diseases, chronic hypersensitivity pneumonitis and asbestosis where patients can manifest UIP. Our intent in labeling such patients as “Combined Sarcoidosis and IPF” or CSIPF was to generate interest and explore the possibility of therapeutic interventions with currently available antifibrotics for these patients as we do not know whether this is a coincidence, phenotype or common final pathway of disease. Since the patient cohort of patients with CSIPF in our series clinically behaved similarly to those with Lone-IPF, we believe it is reasonable to consider and treat such patients similarly to those patients with Lone-IPF.

The question of the use of antifibrotic agents in such patients in the real world setting needs to be addressed. It is hoped that the results of an ongoing trial comparing pirfenidone to placebo among patients with advanced fibrotic sarcoidosis (NCT03260556) and a trial (INBUILD) designed to determine safety and efficacy of nintedanib among patients with progressive pulmonary fibrosis in interstitial lung diseases including sarcoidosis (NCT02999178) will demonstrate a decrease in the rate of disease progression (measured by FVC) as seen in patients with IPF [2,3]. However, these trials do not isolate patients with sarcoidosis and UIP and entry criteria consist of a diagnosis of sarcoidosis and > 20% fibrosis on CT scan of the chest for the pirfenidone trial and > 10% fibrosis on CT scan of the chest for the nintedanib trial, which may not necessarily be the UIP pattern we describe in our case series [1–3]. Patients with radiographic stage 3 and 4 pulmonary sarcoidosis in our series (more than half of whom had predominantly fibrotic changes on HRCT chest) had a significantly longer mean survival from diagnosis compared to those with UIP (CSIPF) as demonstrated in Fig. 1 below. Therefore, if pirfenidone and/or nintedanib are not found to have effect in the ongoing trials, that does not necessarily mean that these medications would not be efficacious for the small subset of patients who have CSIPF or sarcoidosis with UIP pattern.

While our case series leaves unanswered questions and calls for further study, we suggest that a trial of antifibrotics in patients with CSIPF or sarcoidosis with UIP to treat the UIP component be considered

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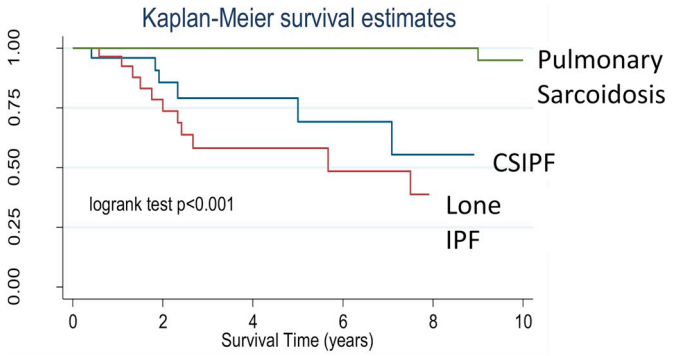

Fig. 1. Years from diagnosis of IPF to death, transplant, or date of censor for patients with CSIPF (blue line)) and Lone-IPF (red line). Years from diagnosis of pulmonary parenchymal sarcoidosis (stage III or IV; green line) to death, transplant or date of censor for patients with pulmonary sarcoidosis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

given clinical behavior/survival was clearly similar to patients with Lone- IPF (mean time from IPF diagnosis to death was 3.2 years for patients with CSIPF and 3.6 years for patients with lone IPF, log rank p value of 0.49) and clearly differed from those with pulmonary sarcoidosis-the majority of whom had fibrosis on CT chest (mean time from diagnosis to death of 21.4 years) in our case series.

In essence, further studies are warranted to better understand the clinical course and management of this cohort of patients with sarcoidosis who also manifest a UIP pattern on CT chest or histopathology. Genotyping in such patients would be of particular interest.

References

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