Background: UIP is the most common form of interstitial lung disease, and has a 3-year median length of survival after diagnosis (1). The histologic appearance of end-stage UIP can be varied. Studies have previously shown evidence of acute lung injury, organizing pneumonia, type II pneumocyte hyperplasia and numerous, large fibroblastic foci (2). The presence of diffuse alveolar damage is inconsistently reported. Occasionally, UIP undergoes acceleration or acute exacerbation with no apparent inciting factor, with mortality as high as 50% (3-4). The natural history of UIP and the cause of this rapid deterioration remain elusive. We use a previously-reported quantitative methodology to evaluate the temporal progression of UIP from diagnosis to transplant or death (5).

Design: With IRB approval, lung tissue from 35 patients (23 biopsies, 8 explants, 4 autopsies) was evaluated: The number of fibroblastic foci (FF), lymphoid aggregates without (LA) and with germinal center (GC) per total tissue area and the ratios of FF area, LA area, and GC area to total area were determined. The presence of superimposed diffuse alveolar damage (DAD) was recorded. Statistical analysis was performed using a Wilcoxon rank sum test.

Result: Compared to biopsy specimens, the explants had a higher FF count, higher FF area, similar LA count, higher LA area, and similar GC counts and areas. The difference in FF area approached statistical significance (p=0.008); none of the differences met statistical significance. The autopsy specimens were excluded from the quantitative analysis because fibroblastic foci were indistinct. None of the biopsy or explant specimens demonstrated DAD. All of the autopsy specimens demonstrated DAD, varying from mild organizing DAD with focal hyaline membranes to diffuse acute DAD with extensive hyaline membranes.

Conclusion: In this longitudinal study of the histology of UIP over time, late-stage UIP (explants) demonstrated increased numbers of larger fibroblastic foci and larger lymphoid aggregates compared to early-stage UIP (biopsies at diagnosis). Acute exacerbation was not a feature of biopsies or explants, but was uniformly present on autopsy specimens, suggesting superimposed acute lung injury as a terminal event. Furthermore, it is worthwhile to note that in the setting of DAD, fibroblastic foci are indistinct, making post-mortem diagnosis of UIP difficult.

References: