Spectrum of HIV-Associated Kidney Disease in the Era of Combination Antiretroviral Therapy

John Booth¹, Lisa Hamzah², Sophie Jose¹, Stephen Mcadoo³, Emil Kumar³, Catherine Horsfield¹, Patrick O'Donnell¹, Rachael Jones⁵, Caroline Sabin¹, Frank A. Post²
¹University College London, London, United Kingdom, ²King’s College London, London, United Kingdom, ³Imperial College London, London, United Kingdom, ⁴Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom, ⁵Chelsea and Westminster NHS Foundation Trust, London, United Kingdom

Background: Immune complex kidney disease (ICKD) has become the dominant pathology in renal biopsy series of HIV+ patients. The natural history of ICKD and risk factors for ICKD remain poorly studied.

Methodology: We reviewed consecutive renal biopsies (1998-2012) of HIV+ patients attending eight clinics in the UK. ICKD was defined by the unequivocal presence of glomerular immunoglobulin deposits and corroborated, where available, by the presence of electron dense deposits on electron microscopy. We compared patients with ICKD to those with HIV-associated nephropathy (HIVAN) and patients in the UK CHIC cohort. Kaplan-Meier analysis was used to estimate progression to end-stage kidney disease (ESKD), and Poisson regression analysis to examine factors associated with ICKD and HIVAN in the UK CHIC cohort.

Results: Of the 250 diagnostic biopsies, 88 showed ICKD and 67 HIVAN. ICKD comprised a spectrum of patterns including membranous (n=17), membrano-proliferative (n=5) and ICKD-not otherwise specified [NOS] (n=34); these groups displayed considerable overlap in both glomerular morphology and location of deposits and were hence considered together as ‘core’ ICKD. The remaining ICKD biopsies showed IgA nephropathy (n= 26) and lupus (n=6) nephropathy; these patients were analyzed separately and excluded from the present analyses. Patients with ICKD and HIVAN differed by ethnicity (black: 54% vs. 98%), median known duration of HIV (6.2 vs. 0.1 years), degree of immunodeficiency (median CD4 nadir 155 vs. 54, median CD4 at biopsy 382 vs. 116 cells/mm³) and severity of kidney disease at biopsy (median eGFR 53 vs. 22 mL/min/1.73m²) (p<0.001 for all). At biopsy, 59% vs. 41% of patients had initiated combination antiretroviral therapy (ART) (p=0.01) and 66% vs. 34% had HIV RNA <200 c/mL (p=0.0008); at 1 and 5 years post-biopsy, 4% vs. 29% and 13% vs. 45% of patients had progressed to ESKD (p<0.0001 for both). Of the 31,483 patients in the UK CHIC cohort, 32 developed HIVAN and 44 ICKD during follow up. In multivariable analyses, black ethnicity (IRR 2.23 [1.13, 4.40]) and HIV viraemia (1.48 [1.17, 1.86] per log₁₀ increase in HIV RNA) were associated with ‘core’ ICKD, and black ethnicity (IRR 9.94 [3.69, 26.75]), HIV viraemia (1.35 [1.02, 1.79]), and current CD4 cell count (0.78 [0.68, 0.88] per 50 cell increase) with HIVAN.

Conclusions: This is the first study to demonstrate a relationship between HIV replication and ICKD. Compared to HIVAN, ICKD was associated with less advanced immunodeficiency and a lower rate of progression to ESKD. The observed association with HIV viraemia for both ‘core’ ICKD and HIVAN may imply a pathogenetic role of HIV replication and its associated immune activation; it also suggests that suppressive ART may reduce the risk of developing these types of kidney disease.