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RENAL PATHOLOGY OF HUMAN IMMUNODEFICIENCY AND HEPATITIS C VIRUS INFECTED PATIENTS

10year Eperience of a Portuguese Hospital

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Objective

Renal injury secondary to Hepatitis C virus (HCV) and Human immunodeficiency virus (HIV) infections is nowadays well recognized and has an important impact on patients outcome and their survival. However, the long-term outcome of HCV- and HIV-associated nephropathies remains ill-defined. The present work aims to characterise the pathological pattern and clinical data and to evaluate prognosis of HCV and HIV infected and co-infected patients submitted to renal biopsy.

Methods

The present work is a retrospective review of all renal biopsies of HIV and/or HCV infected patients received in our laboratory, between January 2003 and December 2012. Tissues for optical microscopy were stained with haematoxylin-eosin, periodic acid Schiff, Masson's trichrome, methenamine silver and Congo red. Immunofluorescence was performed in frozen sections, using IgA, IgG, IgM, C1q, C3, C4, kappa and lambda light chains and fibrinogen. Indirect immunofluorescence using formalin-fixed paraffin embedded section was performed when no frozen fragment was available. Every case was submitted to ultrastructural evaluation.

Clinical and laboratory data were obtained.

Chi-square test, t-test and Mann-Whitney were used when required. Statistics were performed with SPSS 20.0.

Results

In 390 biopsies registered in our laboratory between January 2003 and December 2012, 27 corresponded to HIV, 19 to HCV infected patients, 5 of them being HIV-HCV co-infected. Four patients were excluded because of insufficient clinical and/ or inadequate pathological sample. 41 biopsies were analised, corresponding to 39 patients.

Mean age 47.9years (SD12.9), 75,6% men and 51,2% Caucasian. 82.5% of the HIV infected patients had AIDS.

The clinical data and histological patterns of each groups are detailed in table 1 and table 2, respectively.

55,6% of HIV infected patients and 42.9% of HCV infected patients became dependent on hemodialysis ($p>0.05$). Renal survival median time was 532.8 days (+/- 850.2) for HIV infected patients and 693.1 days (+/- 965.0) for HCV infected patients. The HIV-HCV co-infected patients had the lowest renal survival median time- 137.8 days (+/- 200.7). In a logistic regression model, the grade of interstitial fibrosis and tubular atrophy in the renal biopsy and creatinine at time of admission were associated ($p<0.005$) with progression to dialysis.

The mortality reached 31.8% for HIV infected patients and 28.6% for HCV patients. The survival time was 1092.2 days (+/- 1099.8) for HIV infected patients and was 1014.9 (+/- 964.3) for HCV infected patients. ($p>0.05$)

Conclusion

As in others studies, HIV-associated nephropathy (HIVAN) was the predominant lesion in HIV infected patients. (figures 5 to 8) As documented in the literature, the strongest association with HCV is that of membranoproliferative glomerulonephritis (MPGN) and the majority of cases had concomitant clinical features of mixed cryoglobulinemia; in the present work, the 4 HCV infected patients with MPGN had cryoglobulinemia. (figures 1 to 4) Other renal lesions that are associated with HCV and HIV infections have been documented in several papers: membranous glomerulonephritis, IgA nephropathy, focal segmental glomerulosclerosis (FSGS), fibrillary glomerulonephritis and immunotactoid glomerulopathy, postinfectious glomerulonephritis and lymphoma in HCV infected patients; thrombotic microangiopathy, immune-complex glomerulonephritis, tubulointersticial nephropathy, FSGS and lymphoma in HIV infected patients. On the other hand, the introduction of combined anti-retroviral therapy changed the spectrum of renal disease in HIV infected patients, reducing the incidence of HIVAN and increasing diabetic nephropathy, hypertension and nephrotoxicity.

HIV infected patients have a worse renal survival and higher mortality when compared with HCV infected patients.

Patients infected with HIV and HCV can develop diverse renal pathologies. No correlations between clinical data and pattern of renal disease have been seen and it seems that is not possible to predict the renal disease based on clinical criteria alone. Renal biopsy remains the gold standard for establishing the diagnosis and can help predict renal prognosis.

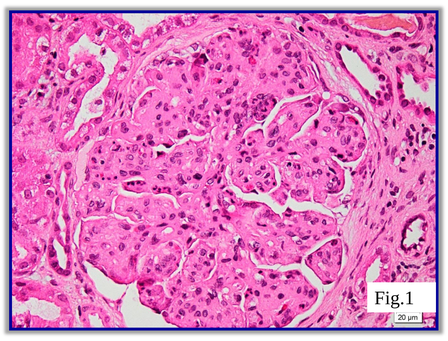
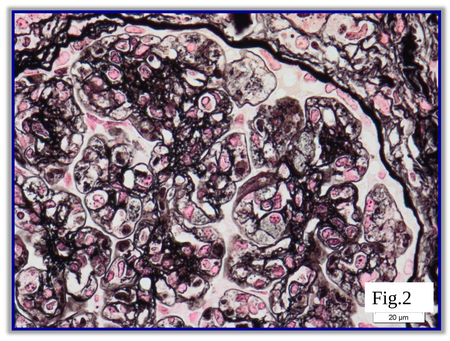


Fig.1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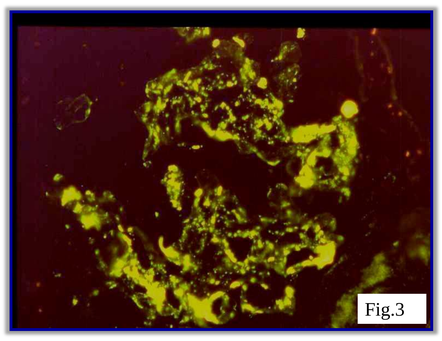
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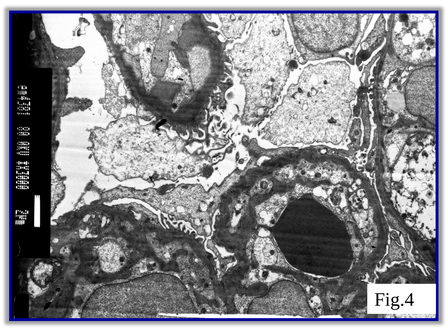
Fig.4

MPGN in a HCV infected patients with cryoglubolinemia: glomerulus with accentuated lobulation of tuft architecture, mesangial hipercellularity, some accumulation of eosinophilic material in capillary lumen and wall (fig.1 – haematoxylin-eosin, 20x), endothelial cell swelling with duplication of capillary basement membrane (fig.2 - methenamine silver, 40x). Mesangial and capillary wall deposition of C3 is demonstrated by immunofluorescence (fig.3) and on electron microscopy of formalin fixed sample (fig.4).

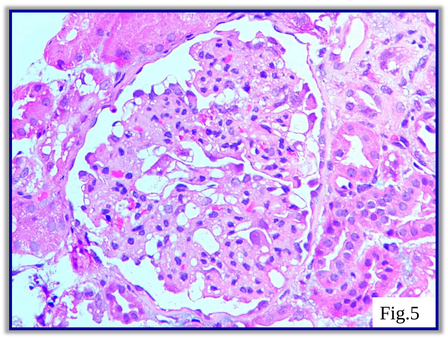
Fig.5

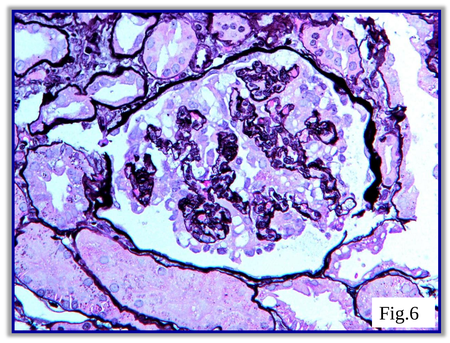
Fig.6

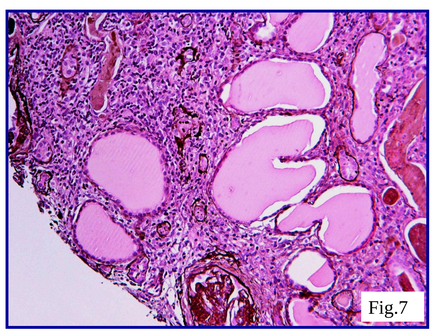
Fig.7

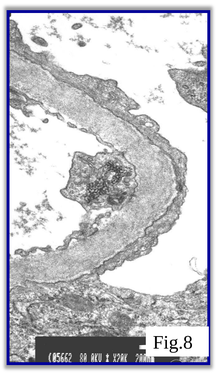
Fig.8

HIVAN in a HIV infected patient: a combined glomerular and tubular injury that is characterized by a collapsing glomerulopathy (fig.5- haematoxylin-eosin, 20x and fig.6- methenamine silver, 20x), microcystic transformation of renal tubules and concomitant interstitial inflammation and fibrosis (fig.7- methenamine silver, 10x). Some tubuloreticular inclusions were highlighted by electron microscopy. (fig8)

Clinical characteristics of infected patients

	HCV infected patients (n=19)	HIV infected patients (n=27)
Gender (%) Male Female	66.7%	77.8%
Race (%) Caucasian race Black race	72.2%	52.3%
Age	46.2 (+/-12.1)	49.5 (+/- 12.9)
Diabetes Mellitus (%)	16.7% (n=3)	18.5% (n=5)
HIV infection (%) HCV infection Hepatitis B virus infection HIV-HBV infection HBV-HCV infection	26.3% (n=5) 15,8% (n=3) 5.3% (n=1)	 18.5% (n=5) 7.4% (n=2) 3.7% (n=1)
Cryoglobulin (%)	26.3% (n=5)	-
Serum creatinine (mg/dl)	5.3 (SD4.6)	4.3 (SD 2.6)
Proteinuria (g)	15.86 (SD 49.2)	4.67 (SD 4.5)
Haematuria (%)	63.8%	74.1%
Renal replacement therapy (%,, $p<0.05$)	42.9%	55.6%

Histological features of infected patients

	HCV infected patients (n=14)	HIV infected patients (n=22)	HIV-HCV co-infected patients (n=5)
Mesangio-proliferative GN	1	1	1
Membranoproliferative GN	4 (28.6%)		1
GN proliferative extracapillary	1		
GN membranous		1	
FSGS/ HIVAN	3	12 (54.5%)	1
Chronic glomerulopathy n.o.s.		2	
Tubulointersticial nephritis	1	2	
Cast nephropathy	1		
Diabetic nephropathy	2	2	1
Amyloidosis			1
Lymphoma	1	2	
Intersticial fibrosis and tubular atrphy none/mild/moderate	4 / 4/ 6	3 / 7 / 12	0 / 2 / 3

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Conflict of interest statement: None declared