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ORIGINALS

HIV infection-associated glomerulopathies: a spanish perspective

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SUMMARY

HIV nephropathy (HIVAN) is the most frequent cause of chronic renal failure in HIV-infected black patients. However, the prevalence of other glomerulopathies mediated by immunocomplexes has increased in the last years. We report on the glomerular diseases observed in HIV patients in our Hospital. Methods: A retrospective study of all patients with HIV infection and glomerular diseases diagnosed by renal biopsy. ***Results:*** *We found 27 patients with the following glomerular diseases: membranoproliferative glomerulonephritis (MPGN) in 8 patients, non-collapsing focal segmental glomerulosclerosis (FSGS) in 7, IgA nephropaty (IgA N) in 6, collapsing glomerulosclerosis in 4 (HIVAN, and membranous nephropaty (MN) in 2. Most of patients were young white men. A high prevalence of coinfection with hepatitis C virus (HCV) (77.8%) and hepatitis B virus (HBV) (37%) was found. At diagnosis, most of patients (90%) had proteinuria, with nephrotic syndrome in 52% of them; 59% presented with acute renal failure. Nine patients (33%) showed malignant hypertension at diagnosis: this complication was particularly common among IgA N patients (4/6, 66%).* ***Conclusion:*** *In our Hospital, immunocomplex-mediated glomerulonephritis were more frequent than HIVAN among HIV-infected patients. HCV-associated MPGN was the most frequently detected glomerular disease. A high prevalence of malignant hypertension was observed at diagnosis, particularly among patients with IgAN.*

Key words: ***HIV infection. Immunecomplex glomerulonephritis. HIV associated nephropaty. CHV infection. BHV infection.***

GLOMERULOPATÍAS ASOCIADAS A LA INFECCIÓN POR VIH UNA PERSPECTIVA ESPAÑOLA

RESUMEN

La nefropatía asociada al VIH (HIVAN) es la causa más común de insuficiencia renal crónica en los pacientes VIH de raza negra. Sin embargo, en los últimos años la prevalencia de otras glomerulopatías asociadas a inmunocomplejos ha ido en aumento. Nuestro estudio describe la patología glomerular en los pacientes VIH

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de nuestro centro. ***Material y métodos:*** *estudio retrospectivo de pacientes VIH con afectación glomerular confirmada mediante biopsia renal.* ***Resultados:*** *Se detectaron 27 pacientes en los que se habían diagnosticado las siguientes glomerulopatías: glomerulonefritis membranoproliferativa (GNMP) en 8, glomeruloesclerosis focal y segmentaria no colapsante (GSF) en 7, nefropatía mesangial IgA (GNIgA) en 6, glomeruloesclerosis colapsante (HIVAN) en 4 y glomerulonefritis membranosa (GNM) en 2. La mayoría de los casos eran varones jóvenes de raza blanca. Destaca una alta coinfección con el virus de la hepatitis C (VHC) (77,8%) y con el virus de la hepatitis B (VHB) (37%). En el momento del diagnóstico la mayoría de los pacientes presentaba proteinuria (96%), con síndrome nefrótico en el 52% de los casos, y un 59% presentaba un deterioro agudo de la función renal. Nueve pacientes (33%) presentaron HTA maligna al diagnóstico, siendo particularmente frecuente esta complicación entre los pacientes con GNIgA (4/6, 66%).* ***Conclusiones****: las glomerulopatías más frecuentes en nuestra población VIH son las asociadas a inmunocomplejos, sobre todo la GNMP asociada a la infección por el VHC. La HTA maligna tiene una alta incidencia en los pacientes VIH, más marcada en los pacientes con nefropatía mesangial IgA.*

Palabras clave: ***Infección VIH. Glomerulonefritis por inmunocomplejos. Nefropatía asociada al VIH. Infección por VHC. Infección por VHB.***

INTRODUCTION

The course and prognosis of HIV (human immunodeficiency virus)-infected patients is dramatically changing since the introduction of HAART (high activity antiretroviral therapy), with higher patient survival and decreased mortality. Renal diseases have a great impact on the course and prognosis of HIV-infected patients.[1] Secondary acute renal failure is common in these patients due to sepsis, hypotension, or drug-induced nephrotoxicity,[2] although there also exist renal impairment due to HIV itself. In 1984, Rao *et al*. described for the first time a pattern of sclerosing glomerulopathy that later on was called HIV-associated nephropathy (HIVAN), which is characterized by severe tubulointerstitial impairment.[3] It is the most common cause of glomerular collapse in HIV patients and is characterized by proteinuria, usually severe, and rapid progression to renal failure. HIVAN predominantly affects HIV patients of black ethnicity, who present a risk 18 times higher for developing this complication than HIV patients of Caucasian origin.[1,4]

After the description of HIVAN as a specific glomerular involvement in HIV-infected patients, further studies have described a wider spectrum of glomerular diseases that seem to be more frequent in HIV-positive patients: membranoproliferative glomerulonephritis (GN), IgA-mesangial nephropathy, «lupus-like» GN and other highly diverse types of glomerular involvement, all of them sharing a massive deposition of immunocomplexes at the glomerular level.[5] According to several studies, the incidence of glomerulopathies other than HIVAN is increasing in a number of countries, and in many of them their frequency clearly exceeds that of HIVAN. In spite of the fact that, according to the National Epidemiology Center, the number of newly HIV-infected patients annually is 2332 (54.7 new cases per million population), there are no studies on glomerular involvement in HIV-positive patients in our setting. In the present study we describe the experience of our Center with this pathology, confirming that immunocomplex-GNs are more frequent than HIVAN cases, presenting particular clinical and evolutionary characteristics and being closely related with common co-infections presented by HIV-positive patients.

MATERIAL AND METHODS

The «12 de Octubre» University Hospital is a tertiary hospital in southern Madrid assisting a population of 950,000 inhabitants. We may point out as relevant demographical data that the economic and socio-cultural levels and the unemployment rate are clearly below the average for the Community of Madrid. Besides, the percentage of immigrant population has shown a progressive increase in recent years.

For the present study, all HIV-positive patients having shown any kind of glomerular pathology demonstrated by renal biopsy were reviewed. The Registries from the Nephrology and Pathology Departments were used for patients identification. The following data were gathered from patients clinical charts: a) demographical data (age, gender, ethnicity, risk factor for infection, date of HIV detection), b) clinical data (type of presentation of glomerular disease, time elapsed since HIV-infection, infections history and concomitant infections, therapy received, extrarenal manifestations), c) biochemistry data (CD4 lymphocytes count and viral load, hematocrit and hemoglobin, platelets, leucocytes, percentage of eosinophils, creatinine and creatinine clearance, proteinuria, sediment, uric acid, cholesterol, triglycerides, total proteins, albumin, bilirubin, GOT, GPT, GGT, LDH, alkaline phosphatase, C3, C4, IgG, IgA, IgM, rheumatoid factor, ANA, anti-DNA, crioglobulinemia, proteinogram), obtained at the start of patient's follow-up. For the study, renal biopsies of the patients were reviewed: all of them were obtained percutaneously. We also registered the follow-up data of the patients until last follow-up visit, death or entry into chronic dialysis. Arterial hypertension (AHT) was defined as blood pressure values > 140 mmHg systolic BP and/or > 90 mmHg for diastolic BP. Malignant AHT was defined as severe AHT associated with grade III (defined as the existence of hemorrhages and/or fundus exudates) or grade IV (when papilledema was present) retinopathy. Nephrotic syndrome was defined as the presence of proteinuria > 3.5 g/day with hypoalbuminemia and hypoproteinemia. For final evolution of the patients, we analyzed the number of them having chronic renal failure, defined as serum creatinine (sCr) > 1.5 mg/dL, those having died, and those requiring chronic dialysis because of end-stage renal failure. Progression to renal failure was defined as a increase > 50% from baseline, improvement of renal failure as a decrease by 50% of initial creatinine, partial remission as proteinuria < 3.5 g/day but > 0.5 g/day with normal renal function, and complete remission as normal renal function with proteinuria < 0.5 g/day.

The data are expressed as mean and standard deviation and the corresponding range. Statistical

Table I. Demographic characteristics in different glomerulopathies

	MPGN (n = 8)	SFG (n = 7)	IgA GN (n = 6)	HIVAN (n = 4)	MGN (n = 2)	Total (n = 27)
Age (years)	35.5 ±4.9 (24-41)	39.29 ±5.02 (32-48)	41.17 ±6.7 (31-51)	37.5 ±7.7 (26-43)	39 ±5.66 (35-43)	**38.3 ±5.5 (24-51)**
Gender (M/F) %	7/1 (87.5%)	6/1 (87.5%)	6/0 (100%)	3/1 (75%)	1/1 (50%)	**23/4 (85.2%)**
Ethnicity (Caucasian/black) %	8/0 (100%)	5/2 (71.4%)	6/0 (100%)	3/1 (75%)	2/0 (100%)	**24/3 (88.9%)**
Risk factor (PDA/sexual) %	7/1 (87.5%)	5/2 (71.4%)	5/1 (83.3%)	2/2 (50%)	0/2	**19/8 (70.4%)**
HBV Infection %	2 (25%)	2 (28.5%)	4 (66.6%)	1 (25%)	1 (50%)	**10 (37%)**
HCV Infection %	8 (100%)	5 (71.4%)	6 (100%)	2 (50%)	2 (100%)	**21 (77.8%)**
Interval HIV infection-renal involvement (months)	85 ± 66.8 (0-180)	113 ± 68.54 (0-192)	70 ± 78.29 (0-192)	96 ± 48.99 (48-144)	90 ± 127 (0-180)	**91.1 ± 67.9 (0-192)**
Viral load (Copies/mL)	15761 ± 27053 (50-47000)	12606 ± 17300 (50-47800)	132569 ± 2156 (20-500000)	87366 ± 135976 (50-289417)	146170 ± 20667 (20-292320)	**65380 ± 13419 (20-500000)**
CD4 (cells/mm^3)	285.5 ± 131.2 (95-429)	233.4 ± 146 (49-423)	129.7 ± 245.2 (9-513)	2551 ± 169 (3-353)	192.5 ± 265.1 (5-380)	**468.4 ± 100.7 (3-513)**
Start of antiretroviral therapy	5 (62.5%)	4 (47.1%)	3 (50%)	2 (50%)	1 (50%)	**15 (55.5%)**
End of antiretroviral	7 (87.5%)	7 (100%)	3 (50%)	3 (75%)	2 (100%)	**22 (81.4%)**

Table II. Clinical presentation by type of glomerular involvement

	MPGN (n = 8)	SFG (n = 7)	IgA GN (n = 6)	HIVAN (n = 4)	MGN (n = 2)	Total (n = 27)
Malignant AHT	2 (25 %)	1 (14.2 %)	4 (66.6 %)	1 (25 %)	1 (50 %)	**9 (33.3 %)**
Acute renal failure	4 (50 %)	3 (42.8 %)	5 (83.3 %)	3 (75 %)	1 (50 %)	**16 (59.3 %)**
Nephrotic syndrome	5 (62.5 %)	5 (71.4 %)	0	3 (75 %)	1 (50 %)	**14 (51.9 %)**
Macroscopic hematuria	0	0	1 (16.6 %)	0	0	**1 (3.7 %)**
Non-nephrotic proteinuria	3 (37.5 %)	2 (28.5 %)	6 (100 %)	1 (25 %)	1 (50 %)	**13 (48.1 %)**
Microhematuria	5 (62.5 %)	3 (42.8 %)	4 (66.6 %)	3 (75 %)	2 (100 %)	**17 (62.9 %)**
AHT	3 (37.5 %)	4 (57.1 %)	4 (66.6 %)	3 (75 %)	1 (50 %)	**15 (55.6 %)**

analysis was done with SPSS software, version 11.0 for Windows. Inter-group comparisons were done by using the Student's t test and Mann-Whitney test. The chi-squared test was used for qualitative variables. Survival analysis was done with the Kaplan-Meier method and statistical comparisons by the log-rank test. Values with a p value < 0.05 were statistically significant.

RESULTS

Between 1992 and 2006 we found 27 HIV patients with glomerular involvement confirmed by renal biopsy. Of them, there were 8 (29.6%) membranoproliferative GN, seven (25.9%) non-collapsing segmentary and focal GN (FSG), six (22.2%) IgA mesangial GN (IgAGN), four (14.8%) collapsing focal and segmentary GN (HIVAN), and two (7.4%) membranous GN (MGN) (Tables 1, 2, and 3).

Our population is mainly of Caucasian origin (88.9%) and male gender (85.2%). The infection routes were PDA (parenteral drug abuse) (70.4%) and less commonly the sexual route (29.6%). Most of them present HCV (77.8%) and HBV (37%) co-infection and only 3 out of 27 patients presented only HIV infection without HCV or HBV co-infection. Mean time from HIV diagnosis to onset of renal impairment was 91.1 ± 67.9 (0-192) months and at that time 15 patients were receiving antiretroviral therapy (55.5%).

More than half of the patients, 16 patients (59.3%), presented with acute renal function. It is surprising that 9 patients (33.3%) had data suggesting malignant AHT at the time of presentation of renal pathology. All patients presented with proteinuria, 14 patients (51.9%) with nephrotic syndrome, and the remaining 13 had non-nephrotic proteinuria. Most of the patients (81.4%) received treatment with ACEI (angiotensin converting enzyme inhibitors) or ARA-II (angiotensin II receptor antagonists) and antiretroviral therapy (88.8%). At the end of the follow-up period three patients had died. Most of them remained with renal failure (59%) and 8 patients progressed to end-stage RF requiring dialysis.

Membranoproliferative GN (MPGN)

This is the most common pathology found in our patients (8 cases). Most of the patients are males, all of them Caucasian. We should point out in this entity that 100% of the patients have HCV co-infection. At clinical presentation, 50% had acute renal failure and 100% of the patients presented with proteinuria, in 62.5% of the cases with nephrotic syndrome, and 37.5% with non-nephrotic proteinuria. Patients received intensive medical therapy: ACEI or ARA-II in 62.5%, antiretroviral therapy in 87.5%, and steroids in 67.5%. Three out of 4 patients with renal failure progressed to end-stage renal failure, one of

Table III. Analytical data at the time of presentation of renal pathology

	MPGN (n = 8)	SFG (n = 7)	IgA GN (n = 6)	HIVAN (n = 4)	MGN (n = 2)	Total (n = 27)
Hemoglobin (g/dL)	13.2 ±1.9 (9.7-15)	12.2 ±2.2 (8.2-15)	9.8 ±1.8 (8.2-12.4)	9.7 ±1.5 (8-11.3)	8.6 ±4 (5.8-11.5)	11.3 ±2.5 (5.8-15)
Creatinine (mg/dL)	1.8 ±0.9 (0.8-3.2)	1.9 ±1.7 (0.5-5)	5.2 ±3.3 (2.3-9.9)	7.6 ±4.3 (2.1-12.4)	4.2±5.3 (0.5-8)	3.7 ±3.3 (0.5-12.8)
Proteinuria (g/día)	7 ±6.7 (0.3-20)	3.6 ±1.1 (1.2-4.5)	2.3 ±1.1 (0.9-4)	6.6 ±15.2 (2.1-12.4)	8.5 ±10.3 (1.2-15.9)	5.1 ±4.9 (0.3-20)
C3	89.9 ±22.4 (63-122)	115.3 ±51.5 (56-173)	11.8 ±32.2 (68-161)	122.6 ±37.1 (92-164)	103 ±15.5 (92-114)	106.2 ±34.5 (56-176)
C4	21.8 ±4.1 (16-27)	24.5 ±15.2 (12-49)	25.3 ±6.5 (18-34)	38.4 ±13.6 (23-49)	34 ±16.9 (22-46)	26.3 ±11 (12-49)

them with renal function recovering. None of the patients received therapy for HCV infection. The four patients that had pathology remission, either partial or complete, were receiving ACEI/ARA-II, but only received steroids.

Non-collapsing focal and segmentary GN (FSG)

This is the second most common presentation type (7 cases). Most of the patients are Caucasian males although 2 out of seven were of black ethnicity. The most common presentation type was proteinuria, with nephrotic syndrome being observed in 71.4% of the patients. It is surprising that 57.1% of the patients had AHT. All patients received ACEI/ARA-II and antiretroviral therapy. One patient received treatment with tacrolimus because of disease progression but it had to be discontinued due to severe adverse effects (neurological impairment with seizures secondary to thrombotic microangiopathy). At the end of the follow-up, 4 patients (57.1%) had renal failure but none of them required dialysis. None of the patients presenting complete remission had received steroids.

IgA mesangial GN (IgAGN)

This glomerulopathy was observed in 22.2% of our patients (6 cases). All of them were Caucasian males. HCV co-infection occurred in all patients and HBV co-infection in more than half of them (66.6%). Regarding clinical presentation, of note is that 66.6% of the patients had data suggesting malignant AHT, and in half of them it was associated with thrombotic microangiopathy. Five out of six patients had acute renal failure at the beginning of the follow-up and one of them CRF. Three of them had complete remission in spite of the fact that two of them had malignant AHT. These three cases were treated with ACEI/ARA-II from the beginning.

Collapsing glomerulopathy (HIVAN)

This entity affected four of the 27 patients. Only one patient was of black ethnicity. Its presentation form is aggressive, all of them had proteinuria, with nephrotic syndrome in 75% of the cases. Seventy-five percent present with acute renal failure, all of them (100%) progressing to chronic RF, and three of them (75%) requiring dialysis. We should highlight the high percentage (75%) of patients presenting with hypertension at the time of diagnosis. All patients received ACEI/ARA and three also received antiretroviral therapy.

Membranous GN (MGN)

This pathology occurred in just two patients, both presenting HCV co-infection and one of them with HBV co-infection. Both patients had proteinuria and one of them nephrotic syndrome and normal renal function. Both received ACEI and antiretroviral therapy.

Table IV. Treatment by renal pathology

	MPGN (n = 8)	SFG (n = 7)	IgA GN (n = 6)	HIVAN (n = 4)	MGN (n = 2)	Total (n = 27)
ACEI/ARA II	5 (62.5%)	7 (100%)	4 (66.6%)	4 (100%)	2 (100%)	**22 (81.4%)**
Antiretroviral therapy	7 (87.5%)	7 (100%)	5 (83.3%)	3 (75%)	2 (100%)	**24 (88.8%)**
Steroids	5 (62.5%)	1 (14.2%)	1 (16.6%)	1 (25%)	0	**8 (29.6%)**
Immunosuppressive therapy	0	1 (14.2%)	0	0	0	**1 (3.7%)**

DISCUSSION

HIV-associated CRF is the third most frequent cause of RF in black people aged 20-64 years.[6] The frequency of renal disease in HIV patients is difficult to estimate. American series of necropsies and renal biopsies establish a prevalence between 10%[7] in Miami series with a predominantly Afro-American population and 1% in San Francisco series[8] with Caucasian population. HIVAN disproportionately affects black people, with a likelihood 18 times higher for developing the pathology as compared with white individuals. In a series of 17 afro-American patients with renal biopsy or autopsy, Williams *et al*. observed that 41% suffered from HIVAN.[7]

In our series, only one out of four patients with HIVAN was of black ethnicity. However, there are other glomerulopathies, those associated with immunocomplexes, which mainly occur in Caucasian individuals. In a series of 27 Italian Caucasian patients, Casanova *et al*. did not find any patient with HIVAN; however, 65.5% presented immunocomplex-associated glomerulopathies.[9] This relationship between ethnicity and renal pathology has also been described by Nochy *et al*. that studied a series of 60 HIV patients with renal involvement confirmed by renal biopsy. They observed focal and segmentary glomerulosclerosis in 23/29 black people and only in 3/31 white people whereas IC (immunocomplexes)-associated GN was present in 16/31 whites and in 4/29 blacks.[10] Our series mainly comprises white people (23 out of 27 patients). Again, we confirm that IC-associated GNs are the most frequent type since only in 4 out of 27 patients HIVAN was present.

A high percentage of our patients present HCV co-infection (77.8%). This co-infection is due to the fact

Table V. Clinical course

	MPGN (n = 8)	SFG (n = 7)	IgA GN (n = 6)	HIVAN (n = 4)	MGN (n = 2)	Total (n = 27)
Exitus	2 (25 %)	0	1 (16.6 %)	0	0	**3 (11.1 %)**
Chronic dialysis	2 (25 %)	0	2 (33.3 %)	3 (75 %)	1 (50 %)	**8 (29.6 %)**
Renal failure	4 (50 %)	4 (57.1 %)	3 (50 %)	4 (100 %)	1 (50 %)	**16 (59.2 %)**
Partial remission	2 (25 %)	0	0	0	1 (50 %)	**3 (11.1 %)**
Complete remission	2 (25 %)	2 (28.5 %)	3 (50 %)	0	0	**7 (27.9 %)**

Table VI. Studies on HIV patients with renal disease

AUTHOR	City/Country	Núm. Pts.	Gender (M/F), HCV	Ethnicity	Diagnosis	Reference
Williams DI et al.	Londres	17	13 M, 4 F	47% black, 53% Caucasian	HIVAN 41%, Membranous GN 23%, hemolytic-uremic syndrome 12%, other 24 %	2
Rao TKS et al.	Nueva York	55	49 M, 6 F	100% black	HIVAN 90%, Mesangial GN 10%	3
Mazbar SA et al.	San Francisco	27	26 M, 1 F	63 % black, 37 % Caucasian	HIVAN 27%, Membranoproliferative GN 27%, interstitial fibrosis 9%, IgG7IgM neuropathy 9%, 28 % other	7
Nochy D et al.	Paris	60	51 M, 9 F	48 % black, 52% Caucasian	43 % HIVAN, IC-induced GN 37%, lupus-like nephritis 16%, HUS 11.5%	10
Casanova S et al.	Italia	26	21 M, 5 F	100% Caucasian	IC-induced GN 65.5%, Membranoproliferative GN 15.5%, lupus-like nephritis 11.5%, minimal changes 7.5%	9
Connolly JO et al.	Londres	34	25 M, 9 F	55.8% black, 41.1% Caucasian	50 % HIVAN, 14.5 % Membranous GN, 6% Membranoproliferative GN, 12 % HUS, 3% IC-induced GN, 14.5 % other	22
Shahinian V et al.	Texas	389	362 M, 27 F	54 % black, 35% Caucasian	26% w/o diagnosis, 7 % HIVAN, 7 % other glomerulopathy, 17 % ATN, 25% calcifications	6
Szczech La et al.	EEUU	89	73 M, 16 F	88 % black, 12 % other	47% HIVAN, 53 % no HIVAN	19
Cheng JT et al.	EEUU	14	8 M, 6 F, 100% HCV	93 % black, 7 % Caucasian	79% membranoproliferative GN, 21% Membranous GN	11
Stokes MB et al.	EEUU	12	11 M, 1 F, 100% HCV	58% black, 42% Caucasian	41% Membranoproliferative GN, 41 % Mesangial proliferative GN, 8% Membranous GN, 8 % Collapsing GN	12
Gutiérrez et al.	Madrid	27	23 M, 4 F, 77.8% HCV	11% black, 89% Caucasian	29.6% Membranoproliferative GN, 25.9% non-collapsing SFGS, 22.2% Mesangial GN, 14.8 HIVAN	

that in most of them PDA is the main infection route. This association has been previously described by others. Cheng *et al*. described 14 patients with HIV and HCV co-infection, all but one of black origin and all but one with PDA. Renal biopsy showed HIVAN in just one of them in spite of being a serried of Afro-American individuals. However, in 79% there was MPGN and in 21% MGN.[11] In their series of 12 patients (7 afro-Americans and 5 Latin-Americans), Stokes *et al*. describe, once again, that renal involvement is due to IC-associated GN. In 5 patients there is MPGN, GN mesangial in 5, and MGN in one patients and HIVAN in an additional one.[12]

In our patients, we also see how this association plays a determinant role in the occurrence of this renal pathology. In the case of MPGN, 100% of the patients present this co-infection.

A high percentage (33%) of our patients had malignant AHT at the time of presentation. This association is surprising in the case of IgA mesangial GN (66%). Although more frequent in IgAGN, malignant AHT was found in all other GN cases, including HIVAN where the occurrence of AHT is infrequent. Thus, 2 cases (25%) were detected in MPGN, one (14%) in FSG, one (25%) in HIVAN, and one (50%) in MGN. We believe that this complication in HIV patients with glomerular involvement is particularly important for its frequency, the severity of the clinical picture, and the impact on renal survival. However, there are no similar descriptions in the literature and its likely etiology is unknown. HIV patients present anti-cardiolipin antibodies in a higher percentage than that in the general population, reaching 65% of the patients.[13] These antibodies, that may or may not be associated to clinically detectable anti-phospholipid syndrome, may be related with this high incidence of malignant AHT since they

promote vascular thrombosis through systemic endothelial damage in which oxidative stress is involved. Although we unfortunately have not available anti-cardiolipin antibodies determination in our patients malignant AHT, we believe that it is important looking for them in those patients with HIV infection and glomerular involvement because of their potential therapeutic and preventive implications.

The indicated therapy varies according to the pathology. For HIVAN, improvement has been observed with antiretroviral therapy. A study done in 1995 describes the use of Zidovudine in 23 patients with HIVAN. Of the 15 patients adhering to the therapy, none of them progressed to end-stage RF. The eight patients not adhering to the therapy progressed to end-stage RF in an average time of 8 weeks.[14] A study from 1992 describes that Zidovudine therapy just slows down the progression to renal failure when it is started before renal failure is too advanced.[15] Similar results have been described with HAART, so that every patient diagnosed with HIVAN should be treated with this therapy.[16] In our series, three of the patients with HIVAN received antiretroviral therapy that did not prevented their progression to hemodialysis. The only patient having improved was the one of black ethnicity. This patient required hemodialysis recovering his renal function after treatment with ACEI.[17]

There are series describing renal function improvement in HIVAN cases with steroidal therapy. In a prospective study, Prednisone, 60 mg, was administered to 20 patients with HIVAN. Seventeen patients had improved renal function. In 12 out of 13 patients in whom proteinuria was determined, this parameter decreased. But this therapy is contraindicated or at least equivocal due to its strong association with severe infectious complications; 11 patients died during the follow-up and 6 developed severe infectious complications.[18] Only one of our patients with HIVAN received steroidal therapy with no renal function improvement.

There is no evidence showing that antiretroviral or steroidal therapy has an impact on the course of the different glomerulopathies other than HIVAN in HIV patients. In a study on 97 patients (42 with HIVAN and 47 with other lesions), Szczech *et al*. describe that antiretroviral therapy was not associated to lower rate of progression to renal failure in non-HIVAN lesions. In the case of the patients with HIVAN there is an association with better course.[19] About steroids, there are no data in the literature. In our experience, we cannot draw any conclusion about a likely beneficial role of this therapy in non-HIVAN glomerulopathies. Most of our cases received antiretroviral therapy but we did not observe that not treated patients had an especially unfavorable course. Eight patients were treated with steroids, five of them having MPGN: three improved (partial remission in 2 and complete remission in 1) whereas the remaining five had an unfavorable clinical course.

ACEI/ARA-II have shown in a number of studies to decrease proteinuria and progression to renal failure.[16] These medications are indicated in both HIVAN and non-HIVAN nephropathies. The only case of renal function improvement in our series with HIVAN is a patient that was receiving ACEI. Eighty-one percent of our patients received ACEI once the nephropathy was diagnosed.

Since HCV infection determines in many cases the onset of the nephropathy, besides being the first morbimortality cause in these patients, it is mandatory to plan for HCV therapy.[20] In 1994, Sánchez *et al*. already described the results of the therapy with interferon alpha 2b in 14 patients with HIV-HCV coinfection; 5 patients had a positive response to the therapy, in two of them a partial response. All patients responding had CD4 counts higher than 500/mm^3. These results have been improved with the association of Interferon and Ribavirin with sustained responses in about 20%. Currently the sustained response rate has gone up to 35% with the use of pegilated interferon plus ribavirin. The treatment is well tolerated. There is a mean withdrawal rate of 10-15%. The most common side effects are flu-like symptoms, anemia, and depression.[21] In spite of the fact that none of our patients received anti-HCV therapy, we believe that it is indicated because of the important role of this virus in the pathogenesis of renal disease and the acceptable treatment tolerability.

To conclude, in our HIV population, of mainly Caucasian origin, the most common glomerulopathies are those associated to immunocomplexes. The most frequent presentation type is membranoproliferative GN associated to HCV infection. We highlight the high frequency of occurrence of malignant AHT in these patients, especially in association with IgA-mesangial nephropathy.

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