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Published in:
The Netherlands Journal of Medicine

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2017

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Wiegersma, J. S., Franssen, C. F. M., & Diepstra, A. (2017). Nephrotic syndrome due to lupus-like glomerulonephritis in an HIV-positive patient. *The Netherlands Journal of Medicine*, 75(9), 412-414. <http://www.njmonline.nl/getpdf.php?id=1912>

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Nephrotic syndrome due to lupus-like glomerulonephritis in an HIV-positive patient

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ABSTRACT

Lupus nephritis, a well-known complication in systemic lupus erythematosus, is characterised by a proliferative glomerulonephritis or membranous nephropathy along with a full-house immunofluorescence pattern on renal biopsy. There are very few exceptions in which similar histopathological findings are present, but case reports show that an increasing number of HIV-positive patients (mostly black Africans, but also white patients) have HIV-immune complex disease (HIVICK), which can mimic lupus nephritis. Lupus-like HIVICK is treated differently than 'true' lupus nephritis, so distinction is warranted.

KEYWORDS

HIV immune complex kidney disease, HIV-associated nephropathy, HIVAN, HIVICK, lupus-like glomerulonephritis

CASE REPORT

A 26-year-old Caucasian female was referred to our centre for a second opinion. A few weeks earlier, she was admitted to another hospital with malaise, generalised weakness and peripheral oedema of the lower extremities. Medical history included perinatal asphyxia and pulmonary embolism without an apparent cause (at the age of 24 years).

On physical examination, she was hypertensive (blood pressure 150/114 mmHg) and had severe oedema in both legs. Physical examination was otherwise unremarkable. Serum creatinine was elevated (*table 1*) and urinalysis showed glomerular erythrocyturia with 30-50 erythrocytes per high power field with < 1% acanthocytes and a few erythrocyte casts. Proteinuria was 13.1 g/24 hours. The differential diagnosis consisted of membranous

What was known on this topic?

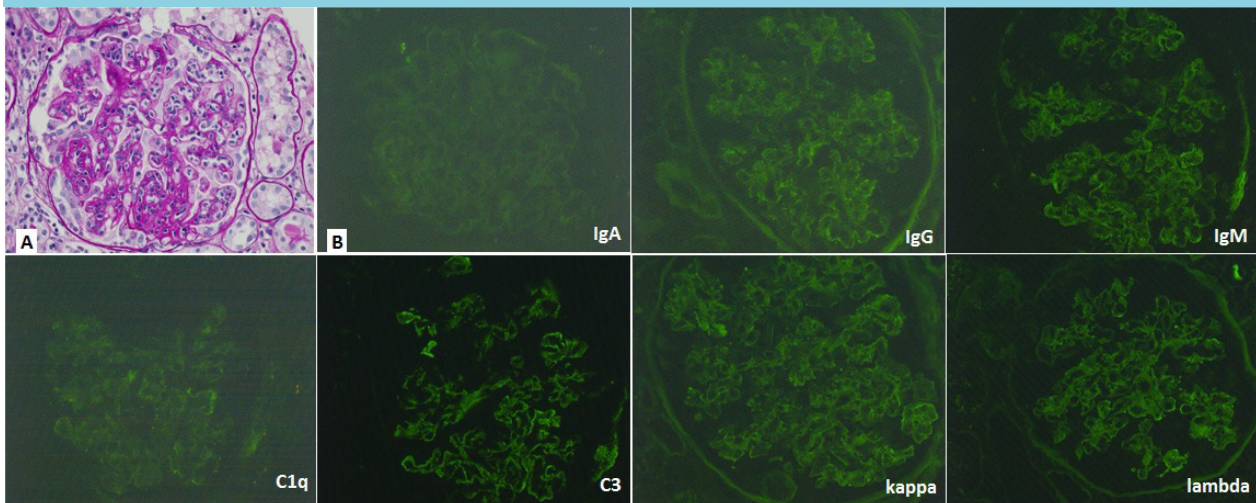
HIV infection is associated with various nephropathies, with HIV-associated nephropathy (HIVAN) being the most common. After introduction of combination antiretroviral therapy, the epidemiological spectrum of HIV-associated renal pathology has changed with a relative decrease of HIVAN and an increase of drug-induced tubular disease, HIV-immune complex kidney disease and HIV-associated comorbidities such as hepatitis C, diabetes mellitus and hypertension.

What does the case add?

Although nephrotic syndrome is a well-known manifestation in HIV-positive patients, it is mostly associated with HIVAN. Nephrotic syndrome due to lupus-like glomerulonephritis is far less common. Furthermore, this is the first case where lupus-like glomerulonephritis was the presenting manifestation of HIV infection. This case report also shows that antiretroviral treatment, together with antiproteinuric medication, may have a marked favourable effect on proteinuria and renal function.

nephropathy (including lupus), membranoproliferative glomerulonephritis or IgA nephropathy. A kidney biopsy showed active, diffuse and global lupus nephritis class 4/5 with endocapillary and mesangial proliferation and few sclerotic lesions. Immunofluorescence staining was positive for IgA, IgG, IgM, light chain type lambda and kappa and C1q/C3 (*figure 1*), Congo red was negative. Electron microscopy was not performed. Additional screening for ANA, ENA, and anti-DNA was negative; a weak cryoglobulin type 3 was detected along with a low complement factor C3 (0.69 g/l; normal 0.90-1.8 g/l) and normal C4 (0.21 g/l; normal 0.10-0.40 g/l). Except for a dubious facial rash and pancytopenia (without haemolysis) there were no other criteria for systemic lupus

Figure 1. a) PAS staining of a representative glomerulus. Endocapillary proliferation consists of the presence of neutrophils and lymphocytes and endothelial cell enlargement. There is mesangial proliferation and a small sclerotic lesion. b) Immunofluorescence studies demonstrate mesangial and membranous staining in the characteristic 'full house' pattern, i.e. positive staining for all immune reactants (IgA, IgG, IgM, C1q, C3, kappa and lambda light chains)



erythematosis. The negative ANA and anti-DNA was also inconsistent with lupus disease, so another underlying disease was sought. Additional investigation revealed an HIV-1 infection with a viral load of 1.52×10^6 copies/ml and CD4 count $0.13 \times 10^9/l$ (reference range $0.4-1.3 \times 10^9/l$). Serology for hepatitis B and C was negative. Antiviral therapy was started (dolutegravir, abacavir and lamivudine) in combination with antiproteinuric drugs (furosemide and enalapril). Along with a favourable virological response, renal function improved and the nephrotic syndrome went into partial remission (table 1).

DISCUSSION

The most common HIV-associated nephropathy is focal segmental glomerulosclerosis (known as HIV-associated nephropathy, HIVAN), which was first reported in the USA in 1984. It is characterised by nephrotic range proteinuria, renal dysfunction and collapsing focal segmental glomerulosclerosis, due to direct viral infection of renal cells or the action of viral proteins.¹ Without combination antiretroviral therapy (cART) renal function often rapidly progresses to end-stage renal disease. Treatment with cART is therefore considered mandatory.² Due to the introduction of antiretroviral treatment, the incidence of HIVAN has decreased. This has changed the epidemiological spectrum of renal pathology associated with HIV, with a relative increase in other nephropathies such as HIV-immune complex kidney disease, cART-induced tubulotoxicity and HIV-associated

comorbidities such as hepatitis C virus infection, diabetic nephropathy and nephrosclerosis.^{1,3-5} Thrombotic microangiopathy and amyloid A amyloidosis are less frequently seen, but are also associated with HIV and kidney disease.

HIVICK is characterised by the presence of glomerular and mesangial immune deposits and consists of a broad spectrum of histopathological entities such as membranous nephropathy and lupus-like nephritis.⁵ According to the literature, patients with HIVICK generally have less advanced HIV infection, usually have only mild proteinuria and less frequently progress to end-stage renal disease compared with HIVAN.^{5,6} In retrospective case series of HIV-positive patients, HIVICK is found in about 4-30% in renal biopsies (mostly reported as membranous nephropathy, and only rare cases described as lupus-like nephritis).^{1,4,6} However, selection bias may have underestimated the true incidence of HIVICK. The pathogenesis of HIV infection in immune complex renal disease is poorly understood, and treatment is also less obvious. Most patients with immune complex kidney disease are already treated with cART, but for those who have not yet received antiretroviral therapy, such as this patient, treatment may have beneficial effects on renal outcome.^{1,5-10} Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are often prescribed in order to control blood pressure and proteinuria, with a few case reports that report prescribing immunosuppressive therapy.^{5,10-12} More literature on pathogenesis, treatment and outcome is warranted in this upcoming renal disease.

Table 1. Laboratory results

	At presentation	After 1 year	Normal range
Serum			
Haemoglobin (mmol/l)	6.0	9.2	7.5-9.9
Leucocytes (10 ⁹ /l)	3.3	10.3	4.0-11.0
Lymphocytes (10 ⁹ /l)	0.99	NA	0.8-3.2
Thrombocytes (10 ⁹ /l)	110	348	150-350
Haptoglobin (g/l)	1.4		0.3-2.0
CRP (mg/l)	16	NA	< 10
Albumin (g/l)	13	43	35-50
Creatinine (μmol/l)	152	90	60-110
eGFR (ml/min/1.73 m ²)	40	76	> 90
ANA	Neg	NA	
AntiDNA (IU/ml)	1	NA	0-15
ANCA	Neg	NA	
Cryoglobulin	Weak*	NA	
Complement C ₃ (g/l)	0.69	NA	0.75-1.40
Complement C ₄ (g/l)	0.21	NA	0.10-0.34
Urine			
Protein (g/24h)	13.1	0.9	
Creatine clearance (mL/min)	40	118	
Selectivity index	37%	NA	

CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; ANA = antinuclear antibodies; AntiDNA = anti double stranded DNA; ANCA = Anti-neutrophil cytoplasmic antibodies; NA = not applicable. *a weak mixed cryoglobulin was detected (type III; polyclonal IgG).

DISCLOSURES

The authors declare no conflict of interest. No funding or financial support was received.

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