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Caution with the use of the new direct acting antivirals in the hepatitis C virus related renal disease☆

Precaución con el uso de los nuevos antivirales de acción directa para el tratamiento del virus de la hepatitis C en pacientes con enfermedad renal asociada

Dear Editor,

Hepatitis C virus (HCV) and chronic kidney disease (CKD) are often linked prompting a significant increase in morbimortality. New direct acting antivirals (DAA) against HCV achieve rapid response in short period of time.[1] However, their use in HCV related renal disease (HCVRRD) is pretty scarce. We present 5 patients with CKD and HCV treated with them (Table 1). All subjects were males (52–57 years old) with impaired renal function and different degrees of proteinuria and microhematuria. Renal biopsy was performed in 1 patient (membranoproliferative glomerulonephritis secondary to cryoglobulinemic vasculitis) being avoided in others due to high risk of bleeding (thrombocytopenia and antiplatelet therapy). Four subjects started on sofosbuvir (SOF) and daclastavir (DAC) and one received DAC with simeprevir (SIM). While HCV viral load achieved negativization (14–30 days), a decline in renal function and a dramatic increase in proteinuria were observed in those SOF with DAC. The only biopsied patient received corticosteroids and Rituximab (375 mg/m^2, 4 doses) 4 weeks after starting therapy with renal recovery and proteinuria decrease. Patient receiving DAC and SIM finally died of gastrointestinal bleeding 3 months later. Three individuals were admitted during antiviral therapy: severe cellulitis in one case; 2 heart failure episodes in other; last subject required different admissions and finally started chronic hemodialysis.

In our patients, CKD is related with HCV infection, confirmed at least in one case and high suspicion in the others. Treatment of HCV becomes the mainstay 1–2, not only for the infection itself but also for the kidney. In our experience, new DAA achieved a rapid decrease in viral load with an important increase of microhematuria, proteinuria and a notable worsening of renal function in 4 of these 5 patients, one of them finally requiring hemodialysis. The explanation for this disturbing phenomenon could be either an emergent acute intersticial nephritis, but the rapid increase and the amount of proteinuria and microhematuria did not support this possibility, or the exacerbation of HCVRRD, most firmly supported for the same reasons. As suggested by the favorable outcome of the only confirmed HCVRRD patient treated according to published recommendations,[2] this situation could be due to an amplification of the immunological processes involved. The lack of diagnostic confirmation made us to avoid using rituximab in the others.

In our experience, the new DAA are very potent and effective drugs, but with a paradoxical worsening of the HCVRRD, mainly when sofosbuvir is used, an aspect that should be studied.

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Table 1 – Patient evolution after the start of HCV treatment.

	Gender age	HBV	HIV (yes–no/ viral load)	Pre-treatment HCV viral load (IU/ml)/ Genotype	Cryoglobulins	Treatment	HCV negativisation time (days)	Renal biopsy	Diagnosis		Pre	1m	2m	3m	4m
1	M	No	No	990 670	Positive	DAC 60 mg/24 h SOF 400 mg/24 h	24	Yes	MPGN secondary to CV	PCr	1.54	1.51	1.36	1.36	1.1
										CKD-EPI	50	51	58	58	84
	54			1b						P/CR ratio	3100	11 378[a]	3244	–	194
2	M	No	Yes	1 404 259	Negative	DAC 60 mg/24 h SOF 400 mg/24 h	14	No	No	PCr	1.12	1.39	1.4	1.67	–
										CKD-EPI	64	58	–	52	–
	52		< 1.57 log	1a						UP/CR ratio	1351	2819	–	3260	–
3	M	No	Yes	1 593 228	Negative	DAC 60 mg/24 h SOF 400 mg/24 h	30	No	No	PCr	1.9	2.48	2.55	2.91	2.86
										CKD-EPI	32	25	24	17	20
	54		<1.57log	1b						P/CR ratio	3532	–	12 995	7572	10 170
4	M	No	No	24 976	Positive	DAC 60 mg/24 h SIM 150 mg/24 h	14	No	No	PCr	3.12	2.51	2.71	3.1	–
										CKD-EPI	15	28	25	–	–
	54			1b						UP/CR ratio	148	423	219	–	–
5	M	No	Yes	15 240 836	Positive	DAC 60 mg/24 h SOF 400 mg/24 h	15	No	No	PCr	2.03	3.03	2.51	4.1	5.77
										CKD-EPI	31	21	27	16	6
	57		< 1.57 log	4						P/CR ratio	–	4297	2110	5557	6142

HBV: Hepatitis B virus; HIV: human immunodeficiency virus; HCV: Hepatitis C virus; DAC: daclatasvir; SOF: sofosbuvir; SIM: simeprevir; MPGN: membranoproliferative glomerulonephritis; CV: cryoglobulinaemic vasculitis; PCr: plasma creatinine (mg/dl); CKD-EPI: chronic kidney disease epidemiology creatinine equation (ml/min/1.73 m^2); UP/CR ratio: urine protein to creatinine ratio (mg/g); pre: pre-treatment; 1m: 1 month post-treatment; 2m: 2 months post-treatment; 3m: 3 months post-treatment; 4m: 4 months post-treatment.

[a] Start of treatment with rituximab.

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Dialysis catheter related bacteriemia by *Gordonia rubropertincta* and *Sputi* in two hemodialysis patients

Bacteriemia relacionada por *Gordonia rubropertincta* y *Sputi* en 2 pacientes en hemodiálisis

Dear Editor,

Here we present two cases of bacteremia related to catheter infection by this organism.

Patient 1: 85-year-old man with end-stage renal disease on hemodyalisis via permanent tunelled catheter, was hospitalised in Nephrology for study something similar than a constitutional syndrome. He related a period of two months characterised by weakness, fever lower than 38 °C without shivering, and hyporexia with a lost of 10 kg.

The blood test showed leukocytosis (10,850/>L, normal formula), hemoglobin 12.1 g/dL, C-reactive protein 10 mg/L. The rest of analyzed parameters were normal range. Other studies, including blood cultures, tumor markers and computed topographies, were conducted without any positive result.

As the patient remained with fever, daptomycin and meropenem were initiated. After 8 days of empiric antibiotic treatment, blood cultures revealed a gram positive bacillus, which was finally identified as a *Gordonia rubropertincta*. Meropenem was stopped after a 14-day treatment, and at the time of the discharge medical, the patient was completely asymptomatic, and blood cultures were negative.

Two weeks later, the patient came back with the same symptoms, and new blood cultures revealed *G. rubropertincta* again. Meronem was administrated, and then, the tunneled catheter was removed.

Although cultures drawn from the dialysis catheter were all negative, antibiotic treatment was given for 3 weeks more and a transesophageal echocardiography was performed being negative for endocarditis.

Patient 2: A 91-year- old man, on hemodyalisis via permanent tunelled catheter, presented well-tolerated fever intradialysis with no other symptoms associated. Blood test showed leukocytes 5890 (neutrophils 79.85) and PCR 1, with the remaining results normal.

Empiric antibiotic treatment with vancomycin was initiated, and blood cultures isolated *Gordonia sputi*. After 3 weeks treatment, the patient was asymptomatic, but a new control blood culture revealed *G. sputi* again. Then, we administrated ciprofloxacin and the tunneled catheter was removed. The last blood sample test was negative.

This is the first report of catheter related bacteraemia caused by *G. rubropertincta* and *Sputti*, confirming its pathogenic potential in dialysis patients.

Gordonia species are aerobic actinomycetes, Gram-positive, catalase-positive and weakly acid-fast bacilli.[1] They are isolated from the environment, useful properties in biotechnology, but they also have been reported to cause infections. Their identification by conventional methods is difficult, so it is believed that a number of *Gordonia* spp. infections are undetected.[2] Recently, Ramanan et al. reported 5 cases of Gordonia bacteremia colleted between 1999 and 2013. In three cases the infection was related to a Hickman catheter, and another was considered a contamination from a tunneled dialysis catheter. Interestingly, none of these species were *G. rubropertincta*, and in addition, the infection in the hemodialysis patient was considered as a contaminant.[3]

Our case report other specie, *G. rubropertincta*, that was previously known as *Rhodoccoccus rubropertinctus* until 1989. It is a rare pathogen that could cause a variety of infections in humans, not only immunocompromised even immunocompetent hosts.[3,4]

Although there is no standardized treatment due to the small number of cases reported, it seems that *Gordonia* spp. is usually susceptible to several antibiotic treatments, and it has good response rates. In our case, antibiotic treatment with daptomycin and meropenem was not enough even long-term, and removing the intravascular catheter was needed to get negative blood cultures.

In conclusion, improvement in laboratory techniques will allow identifying ubiquitous microorganisms as *Gordonia* spp.,

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