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Acute kidney disease related to leptospirosis[☆]

Fracaso renal agudo asociado a leptospirosis

Dear Editor,

Leptospirosis is a zoonotic disease, which occurs all over the world and is related to direct or indirect contact of humans with the urine of infected animals.¹ The clinical manifestations are highly variable, from flu-like symptoms to very serious forms (Weil's disease with liver, kidney and meningeal involvement and alterations in haemostasis).^{1–3} Leptospirosis causes acute interstitial nephritis which often presents either as asymptomatic urinary abnormalities (mild proteinuria, microhaematuria); acute kidney injury (AKI), which is typically non-oliguric and hypokalaemic, like a haemolytic uraemic syndrome (HUS); or chronic kidney disease (CKD) of unknown aetiology.⁴ Although the diagnosis of leptospirosis is not common, severe cases with AKI are the main reason for requiring nephrology treatment. For that reason, we carried out a retrospective descriptive study of all the cases of leptospirosis diagnosed in our hospital in the period 2007–2017. Our study had the approval of the Continuing Education, Teaching and Research Commission. The immunodiagnostic techniques used for the screening were serum detection of total antibodies by indirect haemagglutination and/or IgM antibodies by ELISA, with positive cases confirmed by microscopic agglutination test (MAT) in serum and/or detection of *Leptospira* sp. DNA in urine by real-time PCR. We used the diagnostic criteria of the Centers for Disease Control and Prevention (CDC), classifying the cases as confirmed or probable. In total, 10 cases of leptospirosis were diagnosed (8 men and 2 women). **Table 1** shows the clinical-analytical data of the patients studied, the possible sources of infection and the form of presentation. Six of the eight males had AKI. Of these, only two required haemodialysis; both were transferred to intensive care for inotropic support and assisted ventilation, these two being the cases with the highest levels of serum bilirubin. All patients survived. Eight patients had suggestive epidemiological factors (some more than one factor) and in two cases they were

not known. In terms of clinical presentation, two presented with flu-like symptoms, two with Weil's disease and six with atypical manifestations. **Table 2** shows the microbiological diagnostic techniques used and the titres of the different varieties. Of the 10 patients studied, four met diagnostic criteria, with an antibody titre by MAT >1:800 and/or detection of *Leptospira* DNA in urine by real-time PCR. The remaining six patients had positive screening for indirect haemagglutination and/or IgM ELISA without diagnostic confirmation criteria. MAT is the “gold standard” in the immunodiagnosis of leptospirosis due to its specificity (serovariety/serogroup). As MAT requires isolation of the microorganism by culture and experience in the isolation, it is performed in reference laboratories and is therefore not always available. The serovarieties was *icterohaemorrhagiae* (rats) in three of the cases determined by MAT. Leptospirosis-associated AKI occurs in 44–66% of affected patients,⁵ and our series was 60% which is in the same line with that range with developing AKI. According to the KDIGO (Kidney Disease: Improving Global Outcomes) guidelines for AKI,⁶ four had stage 3 and two, stage 2. As in this series, most cases of AKI are associated with jaundice.⁴ Although the most common is non-oliguric AKI, in cases associated with jaundice and/or hypotension, oliguric or anuric AKI can occur and if necessary, both haemodialysis and peritoneal dialysis can be given. Most patients recover renal function, but in some patients a degree of renal failure may persist and progress to CKD. In a recent article in which renal biopsy was performed after recovery of the patient with antibiotics, inflammatory infiltration was demonstrated in both the tubules and in the interstitium, where most of the cells were monocytes or CD68-positive macrophages predominantly of the M1 phenotype.⁷ After treatment with oral corticosteroids, the patient recovered renal function, which is why the authors suggest that corticosteroids may be a therapeutic option for some patients with sustained tubulointerstitial nephritis after surviving severe leptospirosis.⁷

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Table 1 – Clinical, analytical and epidemiological data and clinical presentation for the patients infected with leptospirosis.

Patient	Date of diagnosis	Gender	Age (years)	TB (mg/dl)	Platelets (No./ μ l)	Inotropic support/assisted ventilation	AKI	KDIGO stages	HD	Epidemiological data	Symptom onset
1	02/10/07	M	66	16.0	35,000	No/No	Yes	2	No	c	Flu-like symptoms
2	01/03/10	M	47	9.2	72,000	Yes/No	Yes	2	No	a (rats) c	Atypical presentation (jaundice)
3	09/07/10	F	46	2.8	475,000	Yes/Yes	No	–	No	e	Atypical presentation (acute mesenteric ischaemia)
4	02/05/13	M	68	7.9	4000	Yes/Yes	Yes	3	No	a (goats, hens, rabbits) c	Atypical presentation (epistaxis not contained with tamponade)
5	04/09/14	M	20	1.8	127,000	No/No	No	–	No	a (iguana) d	Atypical presentation (abdominal pain)
6	19/02/15	M	49	26.3	67,000	Yes/Yes	Yes	3	Yes	a (dogs, cats, horses, goats)	Flu-like symptoms
7	07/09/15	F	19	0.6	482,000	No/No	No	–	No	e	Atypical presentation (fever, weight loss, polyarthritis and severe anaemia)
8	23/09/16	M	45	3.4	259,000	No/No	Yes	3	No	b	Weil syndrome
9	05/01/17	M	71	0.8	424,000	No/No	No	–	No	a (cows, sheep, dogs, cats, pigs) b	Atypical presentation (night fever, diffuse abdominal pain)
10	02/06/17	M	53	37.8	15,000	Yes/Yes	Yes	3	Yes	a (goats)	Weil syndrome

AKI: acute kidney injury; Creat (s): serum creatinine; F: female; HD: haemodialysis; M: male; TB: total bilirubin.

Epidemiological data: a: contact with mammals; b: fresh water bathing; c: unpasteurised food intake; d: trips abroad; e: unknown.

Table 2 – Microbiological results of patients diagnosed with leptospirosis.

Patient	Year	ELISA IgM	HAI ^a	Microagglutination (serovar and titre)	PCR (urine)	Case classification ^b
1	2007	–	Titre 1:128	–	–	Probable
2	2010	Positive	Titre 1:2 ^b Titre 1:64 Titre 1:128	–	–	Probable
3	2010	Positive	Titre 1:2	–	–	Probable
4	2013	Positive	–	<i>Icterohaemorrhagiae</i> 1:800 <i>Sarmini</i> 1:400 <i>Copenhageni</i> 1:100	–	Confirmed
5	2014	–	Titre 1:640	–	–	Probable
6	2015	Positive	Titre 1:1280	<i>Icterohaemorrhagiae</i> 1:200	Positive	Confirmed
7	2015	Positive	Titre 1:320 ^c	<i>Hurstbridge</i> 1:100	–	Probable
8	2016	Positive	–	<i>Sejroe</i> 1:3200 <i>Hebdomanis</i> T1:3200 <i>Hardjo</i> 1:400 <i>Wolfii</i> 1:400 <i>Copenhageni</i> 1:200 <i>Icterohaemorrhagiae</i> 1:200 <i>Hurstbridge</i> 1:200 <i>Shermani</i> 1:100	Positive	Confirmed
9	2017	Positive	–	<i>Icterohaemorrhagiae</i> 1:800 <i>Hardjo</i> 1:400 <i>Castellonis</i> 1:400 <i>Shermani</i> 1:400 <i>Hurstbridge</i> 1:400 <i>Sejroe</i> 1:200 <i>Ballum</i> 1:200 <i>Pyrogenes</i> 1:200 <i>Bataviae</i> 1:200 <i>Canicola</i> 1:100	–	Confirmed
10	2017	Positive	–	–	–	Probable

^a Haemagglutination.
^b Centers for Disease Control and Prevention (CDC) diagnostic criteria.
^c Results of successive samples.

In summary, leptospirosis causes acute interstitial nephritis which can simply result in asymptomatic urinary alterations, but may also lead to typically non-oliguric AKI. In cases associated with jaundice and hypotension (hypovolaemic or associated with myocarditis), the patient could develop oliguric or anuric AKI, which may require dialysis. Although these patients generally recover renal function, some may go on to develop CKD. In certain cases, if a patient presents with CKD of unknown or unidentified aetiology, depending on their medical history, it could be useful to test for anti-*Leptospira* antibodies or *Leptospira* in urine by PCR.^{8–10} In view of the fact that 60% of our patients had atypical presentation of a disease which is uncommon in our environment (10 cases in 10 years), we felt it necessary to highlight the importance of diagnosing and treating this condition in patients who have had contact with untreated waters.

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Use HFR-supra for porphyria cutanea tarda treatment in hemodialysis patient[☆]

Uso de HFR-supra para el tratamiento de porfiria cutánea tarda en paciente en hemodiálisis crónica

Dear Editor,

We present the case of a 53-year-old man on long-term hemodialysis since July 2008 secondary to diabetic nephropathy. His previous medical history included type 2 diabetes with poor metabolic control, morbid obesity, hypertension (HTN), severe mixed dyslipidaemia, secondary hyperparathyroidism, hyperuricaemia and Child-Pugh B7 chronic alcoholic liver disease. In August 2016, he developed erosive, vesicular, painful lesions on his upper limbs, abdomen and lower limbs which became worse when exposed to the sun. Tests for faecal protoporphyrins were positive (53 µg/g) and skin biopsy was compatible with the diagnosis of porphyria cutanea tarda (PCT). The patient began joint follow-up with dermatology. However, his lesions became worse (especially on his upper limbs) and were associated with severe joint pain. In July 2017, it was decided to start treatment with chloroquine, with improvement of the lesions and pain until he became asymptomatic.

After three months of treatment without modifying his life habits or his usual treatment, he had a new flare-up of very painful skin lesions associated with arthralgia and limited mobility in the interphalangeal joints of both hands (Figs. 1-4). After consultation with dermatology, it was decided



Fig. 1 – Lesions on the back of the left hand.

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