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Diagnóstico tradicional versus diagnóstico en un solo paso del virus de la hepatitis C. Estudio piloto en 2 centros asistenciales[☆]



A pilot study on the implementation of reflex testing for the diagnosis of active hepatitis C virus infection at two healthcare centres

Hepatitis C treatment with direct-acting antiviral agents successfully cures over 95% of patients.¹ Providing access to treatment for all patients with chronic hepatitis C virus (HCV) is a priority in all plans to eliminate hepatitis C. To this end, suitable strategies are required for the diagnosis of active HCV infection.

The diagnostic algorithm for hepatitis C starts with the detection of antibodies. However, antibody detection techniques do not distinguish an active infection from a resolved infection.² The detection of HCV RNA indicates viral replication, which is why it is the most commonly used marker to diagnose and confirm active HCV infection. Patients with positive HCV RNA are candidates to be assessed for antiviral therapy. HCV core antigen forms part of the internal structure of HCV. As with HCV RNA, its detection indicates viral replication.³

During the period from 2015 to 2017, at the *Hospital Universitario San Cecilio in Granada* and the *Complejo Hospitalario Universitario de Santiago*, we performed an ambispective and observational pilot study to evaluate the impact of the joint implementation of reflex testing, accompanied by the implementation of alerts for the requesting physician, on the referral of patients to be assessed for treatment.

In the retrospective phase (January–December 2015), 204 new patients diagnosed with HCV were identified (108 from the *Hospital Universitario San Cecilio*, 96 from the *Complejo Hospitalario Universitario de Santiago*, 69.6% males, with a mean age of 54.0 ± 13.28 years) by means of the traditional system (HCV serology and, in positive tests, confirmation with immunoblotting techniques and issuance of a report to the requesting physician). Following consultation of the electronic medical records and data in the laboratory information systems, and after one year of follow-up since diagnosis, we determined that 65% (133 patients) visited an infectious/gastrointestinal diseases specialist for a treatment assessment, after a median of 83 days (IQR: 46–164). Of these 133 patients, 68% were referred from Primary Care. The remaining 71 patients (35%) were not seen for a treatment assessment. A total of 65% of the patients had been diagnosed by Primary Care. Of all the patients who were assessed for treatment, 88% were viraemic.

The prospective phase was performed in the period from March to December 2016 and consisted in implementing reflex testing, by incorporating the detection of viraemia using core antigen testing (Architect HCV Core Ag Assay[®], Abbott Diagnostics, Germany) on the same sample in which the positive serology result was obtained for all new diagnoses, so that patients with previous positive serological tests were excluded. In addition, a comment was included systematically in the reports, in which it was advised to refer patients with active infections to the specialist in order for them to be assessed for treatment. In this period, we analysed 116 new HCV diagnoses in Primary Care (87 from the *Hospital San Cecilio*, 29 from the *Complejo Hospitalario Universitario de Santiago*, 67% males, with a mean age of 56 ± 14 years). There were no differences in terms

Table 1
Characteristics of patient referrals in the retrospective and prospective phases of the study.

	Retrospective phase						Prospective phase					
	Overall (n = 204)		HUSC (n = 108)		CHUS (n = 96)		Overall (n = 116)		HUSC (n = 87)		CHUS (n = 29)	
Referral rate (%)	12 m	65	12 m	68	12 m	61	12 m	84	12 m	86	12 m	79
	6 m	51	6 m	50	6 m	36	6 m	77	6 m	78	6 m	72
Time to referral (median in days, IQR)	12 m	83 (46–164)	12 m	96 (57–194)	12 m	73 (36–113)	12 m	69 (25–102)	12 m	65 (24–99)	12 m	72 (29–123)
	6 m	67 (36–102)	6 m	70 (47–108)	6 m	59 (32–96)	6 m	63 (22–91)	6 m	62 (22–91)	6 m	70 (26–91)

CHUS: Complejo Hospitalario Universitario Santiago de Compostela; HC: hospital care; HUSC: Hospital Universitario San Cecilio; m: months; PC: primary care.

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of age and gender at the two centres included in the study, neither in the retrospective nor prospective phase, although a greater number of patients included from the *Hospital Universitario San Cecilio* came from Primary Care. After one year of follow-up, 84% of the patients were assessed to start treatment, after a median of 69 days (IQR: 25–102) from diagnosis to the consultation with the specialist. Only 18 patients (16%) were not seen by the specialist. Table 1 summarises the frequency and times to referral in both phases of the study, with the details of the referral at one year and at six months from diagnosis. These data reveal that reflex testing is an alternative which improves the traditional diagnosis, as it allows a greater number of losses in referral to be avoided.^{4–6} Furthermore, reflex testing avoids overloading specialist consultations with patients whose infections have already resolved spontaneously.^{7,8}

In conclusion, our study shows how the implementation of reflex testing has a real impact on the treatment cascade for hepatitis C, by allowing a greater number of patients to be assessed for treatment. We believe that these diagnostic strategies should be incorporated by Microbiology Departments, to help eliminate hepatitis C.

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Autochthonous Weil's disease: A case report[☆]



Enfermedad de Weil autóctona: a propósito de un caso

Leptospirosis is a zoonotic disease with worldwide distribution caused by spirochetes of the genus *Leptospira*.^{1–5} Transmission to humans occurs through direct contact with the urine, blood or tissue of an infected animal or exposure to contaminated environments, such as standing water.^{1–5} It can cause a wide variety of clinical manifestations, ranging from a mild form to severe disease, and may even be life-threatening.^{1–3} It appears to be mainly linked to occupational activity, individuals with unfavourable socio-economic conditions, recreational activities or individuals living with pets.^{1–3,5}

Below, we describe the case of a 30-year-old man, with no history of interest, referred to our centre for symptoms of multi-organ failure. Three days prior to admission, the patient had consulted his primary care physician due to flu-like symptoms, general malaise with dysthermia, odynophagia and myalgia. He was admitted to a regional hospital due to fever along with significant laboratory test abnormalities: anaemia; intrahepatic cholestasis; rhabdomyolysis and leukocytosis with thrombocytopenia. As regards his relevant medical history, a recent 20-day trip to the province of Guipuzcoa in the Basque Country is highlighted, during which he bathed in ponds and may have swallowed poor-quality water. He did not mention

insect bites, contact with animals or travel to tropical countries. The patient was initially stable, but his condition worsened, with hypotension and desaturation in the context of a spiking fever. In the control laboratory tests (6 h later), his analytical parameters were seen to have worsened. He passed various bloody stools containing fresh blood. That same day he was referred to our centre, where he was admitted to the ICU due to rapid progression of bilateral pulmonary infiltrates which led to acute hypoxaemic respiratory failure, requiring him to undergo orotracheal intubation and mechanical ventilation. His clinical picture was interpreted as septic shock of unknown origin with rapid progression to multiple organ dysfunction syndrome. Intensive support measures were initiated. Given the symptoms of icterohaemorrhagic fever together with the history of bathing in ponds and the possible ingestion of poor-quality water, infection due to *Leptospira* was suspected and treatment with meropenem (1 g/8 h), linezolid (600 mg/12 h) and doxycycline (100 mg/12 h) started. Blood cultures and respiratory, urine and serum samples were collected to rule out hepatotropic viruses, HIV, Lyme disease, *Leptospira* and atypical pneumonia. 32 h after his admission, *Leptospira* infection was confirmed by means of a PCR on urine and plasma (negative serology). Targeted treatment was started with ceftriaxone (2 g/12 h). While in hospital, the patient's clinical course was unfavourable, with life-threatening progression as a result of refractory hypoxaemia due to pulmonary haemorrhage and multi-organ failure, eventually leading to his death seven days after admission.

In Spain, leptospirosis is mainly diagnosed by serological testing through the detection of IgM antibodies against *Leptospira* or seroconversion (ELISA, ICT or MAT).^{1–5} The isolation of *Leptospira*

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