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Weil disease in a traveller visiting friends and relatives returning from Cuba to Spain

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Dear Sir.

Due to the increase in international travel and migration, imported leptospirosis has become a public health problem. Clinical suspicion of this infection can be challenging due to its non-specific clinical picture very similar to other infections such as malaria, typhoid fever, dengue and hantavirus [1,2]. Laboratory diagnosis depends on two methods: detection of antibodies against the organism, and detection of *Leptospira* spp. DNA by molecular techniques. However, the sensitivity of PCR may vary depending on sample collection timing or infection stage, so the diagnosis of leptospirosis mainly relies on serology [2]. We described a case of imported leptospirosis in a VFR traveller returning to Spain after two-month trip to Cuba.

A 55 years-old man from Cuba, resident in Spain for 14 years, attended the emergency department of the Hospital Universitario Marqués de Valdecilla (HUMV), Santander, Spain, after returning from a two-month trip to his country of origin. The patient reported onset of fever, general malaise, dry cough, headache since 8 days before his return, with oliguria and progressive jaundice in the last three days. During his stay in Cuba, the patient reported several mosquito bites.

Medical examination revealed conjunctival and cutaneous jaundice with no fever or purpuric lesions. Laboratory findings showed impairment-renal function (Cr 3,1 mg/dl) and liver function with increased direct and indirect bilirubin (total serum bilirubin 4,8 mg/dl, direct serum bilirubin 2,9 mg/dl), leukocytosis (21.4 × 10*3/μL), thrombocytopenia and progressive anaemia with Hb of 9.4 mg/dl.

With a recent travel history, investigations to rule out malaria were performed using a rapid antigen detection test and microscopic examination. PCR results for dengue, chikungunya, zika, West Nile and yellow fever viruses were negative, and serological results revealed previous dengue infection with positive IgG and negative IgM. Acute or active viral hepatitis infections were also ruled out, and bacteriological cultures for blood and urine were negative.

During admission, the patient presented general malaise with fever peaks up to 38,8 °C and episodes of haemoptysis. He was diagnosed with acute renal failure requiring fluid and electrolyte support to recover renal function, and antibiotic therapy was started with aztreonam 1g + tigecycline 50mg/IV since he was allergic to penicillin.

On day 4, tests yielded positive results for Leptospira IgM by indirect chemiluminescent immunoassay (Leptospira VirClia®, Vircell, Spain) with an index value of 4.74. The diagnosis of leptospirosis was established, and doxicicline 100 mg every 12h was initiated. The serum sample was sent to the National Microbiology Centre (NMC) for confirmation along with a urine sample for PCR. The NMC confirmed IgM results by ELISA technique with an index value of 3.76, while the urine PCR results were negative. Additionally, hantavirus infection was ruled out by negative PCR result at NMC. The patient was discharged on day 8 in stable condition and fully recovered within two weeks.

Imported leptospirosis is often underdiagnosed making it difficult to estimate the true global burden of the disease [3]. This case underscores the diagnostic challenges in a patient with compatible symptoms and a recent history of travel to an endemic area.

Although it should be considered in the differential diagnosis of tropical fever, very few cases of imported leptospirosis have been reported in our country, especially in visiting friends and relatives (VFR) [3]. Between 2009 and 2018, +Redivi network, a Spanish national collaborative network, documented ten cases, mostly associated to Southeast Asia trips, with only one from a VFR migrant [3,4].

In returning travellers from the Americas, dengue is the leading cause of fever, followed notably by leptospirosis when returning specifically from Central America and the Caribbean [5]. Given the strong suspicion of leptospirosis in our patient and after excluding malaria, dengue, and other arboviruses, further investigations were conducted, including serological tests and PCR. Finally, the diagnosis was established through a positive IgM result.

PCR is a reliable diagnostic tool for leptospirosis but spirochete DNA is rarely found in blood more than a few days after onset of fever, making urine the appropriate sample, with a detection window of up to 21 days [4]. However, in cases where PCR results are negative, serology plays a crucial role in diagnosing leptospirosis. IgM detection has been shown to be more sensitive and detectable from the first week of symptoms, providing strong evidence of infection as observed in our clinical case. Previous studies have also highlighted the limitations of relying solely on molecular techniques, with reports of negative PCR results but positive serology [3,6].

Leptospirosis is an emerging zoonotic infection that requires rapid

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recognition and accurate diagnosis. Established migrants returning to their home countries to visit friends and family, defined as VFRs, have been shown to be at increased risk for travel-related infectious diseases [7]. The presented case underlines the significance of a comprehensive diagnostic approach, involving microbiological methods, along with a careful evaluation of clinical presentation, and travel history. The combined utilization of PCR and serology improves diagnostic yield, reducing the risk of underdiagnosis and facilitating to initiate appropriate treatment to prevent potential complications.

Author contributions

FAR and CA managed the case. ZMG drafted the manuscript and approved final version; FAR, EC, IL, CA and JCM revised the final version of the manuscript.

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Patient consent

Informed consent was obtained from the patient and reflected in the medical record.

Declaration of competing interest

The authors have declared no conflicts of interest.

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Zaira Moure *
Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

Francisco Arnáiz-de Las Revillas
Servicio de Enfermedades Infecciosas, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain
Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Spain

Elena Cantón, Isabel Lara
Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

Carlos Armiñanzas
Servicio de Enfermedades Infecciosas, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

Jorge Calvo-Montes
Servicio de Microbiología, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain
Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Spain

* Corresponding author. Marqués de Valdecilla University Hospital, Microbiology Department, Av. Valdecilla s/n, 39008, Santander, ES, Spain.
E-mail addresses: zaira_moure@hotmail.com, zaira.moure@scsalud.es (Z. Moure).