Antonio Ríos[a,b,c,*], Beatríz Febrero[b], José Manuel Rodríguez[a,b,c]

[a] *Departamento de Cirugía Ginecología, Obstetricia y Pediatría, Universidad de Murcia, Murcia, Spain*
[b] *Servicio de Cirugía General y del Aparato Digestivo, Hospital Clínico Universitario Virgen de la Arrixaca, Servicio Murciano de Salud, El Palmar, Murcia, Spain*
[c] *Instituto Murciano de Investigación Bio-Sanitaria Virgen de la Arrixaca (IMIB-Arrixaca), El Pal, Murcia, Spain*

* Corresponding author.
E-mail address: arzrios@um.es (A. Ríos).
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Weil's disease and acute multifactorial hepatitis. About a case☆

Enfermedad de Weil y hepatitis aguda multifactorial. A propósito de un caso

Leptospirosis is a zoonosis characterised by outbreaks in South East Asia and Central and South America. In Europe, leptospirosis has been reported in Denmark, Greece, Portugal, France, Germany and the Netherlands. Incidence rates range from 10 to 100 cases per 100,000 people in endemic regions.[1] In Spain, the incidence was 0.86 cases per million inhabitants/year according to a study conducted between 2009 and 2012 by Domingo et al. The autonomous communities with the highest number of cases were the Canary Islands and the Basque Country, with no cases recorded in Aragon, La Rioja or Melilla.[2]

Factors contributing to higher levels of prevalence are local agricultural practices, close proximity to mammalian reservoirs (especially rodents, but also horses, sheep, goats, pigs and dogs), poor sanitation and high rainfall. The severest form of leptospirosis, known as Weil's disease, has mortality rates of up to 50%. Its non-specific clinical presentation makes it difficult to diagnose and distinguish from other infections and conditions involving acute liver failure and laboratory tests are therefore essential. According to a 2012 Cochrane review, the use of antibiotics seems to decrease the duration of symptoms by 2–4 days in mild forms, although their benefit in severe forms or Weil's disease is uncertain.[3]

The case considered in this article is unusual given the geographical area in which it occurred (the only case of leptospirosis reported since 1992 in La Rioja), the fact that it did not occur in summer, and the dominance of hepatic cytolysis in this patient. The patient was a 38-year-old Spanish man, who was a chef, with no medical or surgical history of interest. He occasionally smoked cocaine (at the weekend) with his last use one week prior to admission to hospital. He also drank 2 beers every weekend. He said he had not travelled abroad or taken any antibiotics or other herbal products recently. There was no evidence of contact with farm animals, sewage or rice fields.

He had a fever (39–40 °C), myalgia, vomiting, epigastric pain and jaundice, which started 7 days prior to admission. He had taken paracetamol 1 g and ibuprofen 600 mg 3 times a day from the onset of symptoms. His vital signs upon arrival at the emergency department were: temperature 38 °C, pulse 110 beats per minute and blood pressure 91/55 mm Hg. The patient was fully oriented. A physical examination revealed conjunctival jaundice and tenderness in the epigastric region upon palpation. Initial laboratory test results were as follows: urea 85 mg/dl, creatinine 3.94 mg/dl, AST 6788 U/l, ALT 3135 U/l and direct bilirubin 2.3 mg/dl, creatine kinase 3244 U/l, leukopenia (2300) and platelets 116,000. The peripheral blood film showed no evidence of schistocytes. The chest and abdominal X-rays, electrocardiogram, abdominal ultrasound and Doppler ultrasound of the liver were normal. Antibiotic treatment with ceftriaxone and piperacillin/tazobactam was commenced in the emergency department and piperacillin/tazobactam was continued throughout the patient's hospital stay. The patient was transferred to the intensive care unit. Serological tests were ordered for hepatotropic viruses, which were all negative (hepatitis A, B, C, D and E). Likewise, serological tests for cytomegalovirus, herpes virus and Epstein Bar virus and blood cultures were all negative. Paracetamol levels were normal and ethanol levels were below 10 mg/dl. Urine toxicology screening was also negative. Twenty-four hours after admission, the patient's renal failure, thrombocytopenia, anaemia and hyperbilirubinemia worsened, requiring a plasma transfusion (1000 ml), 2 units of packed red blood cells and one unit of platelet concentrate. After observing this deterioration, a serological test for leptospirosis was ordered.

The patient had an intermittent fever, bleeding from the mouth and atrial fibrillation, which was reverted with amiodarone. His level of consciousness gradually decreased, with neurological signs of hepatic encephalopathy (asterixis, myoclonia, seizures). He also has hypotension and signs of coagulopathy (petechiae and bruising). A brain CT scan showed no acute lesions. Renal replacement therapy and inotropic medication were started that day with no signs of response, resulting in the patient's death. The results of tests for antibodies to *Leptospira interrogans* were positive, with titres of 1:1280; however, the serotype was not identified. A liver biopsy was not possible but an autopsy was ordered; the results of this are not yet available.

Weil's disease is the severest form of leptospirosis. Symptoms include fever, jaundice, renal failure, hepatic necrosis,

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respiratory, neurological and cardiovascular disorders and bleeding diathesis. Acute renal failure is the most common complication and is caused by a combination of acute tubular injury and interstitial nephritis. Liver dysfunction tends to be mild and reversible, with mild transaminase increases (not usually greater than 200 U/l). However, this clinical course was not observed in our patient, leading us to believe that the patient's clinical and analytical decline was the result of a synergy of toxic factors (paracetamol, cocaine, leptospira infection). Given that our initial diagnosis was suspected hepatic necrosis due to cocaine, the patient was managed with a continuous N-acetylcysteine infusion. Due to its similarity to paracetamol-induced toxic injury, and due to the absence of a specific antidote, its use is described in the literature.[4–7]

With regard to leptospira infection, we do not know the epidemiological circumstances or features of the infection. The patient did not work or live in a rural environment and had no contact with sewage or stagnant water. However, since the patient was a chef, we can assume that the source of infection may have come from the store room of the restaurant where he worked. No other cases were diagnosed among his work colleagues or members of his family.

With regard to antibiotic treatment, penicillin, cephalosporins and doxycycline are the drugs of choice. None of these has proven superior to the other two.[8–11] Our patient was administered piperacillin and tazobactam during the 3 days of his hospital stay, with no change in outcome, and we therefore believe that this was the result of a synergy of multiple factors.

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Cristina Torres Vargas*, Ángela Martínez Herreros, Begoña Sacristán Terroba

Servicio de Aparato Digestivo, Hospital San Pedro de Logroño, Logroño, La Rioja, Spain

* Corresponding author.
E-mail address: cristinato@gmail.com (C. Torres Vargas).

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