Weil syndrome causing autoimmune haemolytic anaemia

RAHUL SAI GANGULA, M. MUKHYAPRANA PRABHU, WEENA STANLEY

ABSTRACT

Weil syndrome is a fulminant form of leptospirosis, usually caused by spirochetal organism *Leptospira interrogans*. It is characterized by icterus, petechial rashes over the body, signs of renal failure and hepatic failure. Anaemia is a usual manifestation of *Leptospira* infection, but autoimmune haemolytic anaemia is rare. We report a patient with autoimmune haemolytic anaemia following *Leptospira* infection, which was responsive to high-dose steroid therapy.

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INTRODUCTION

Weil disease-associated, autoimmune-mediated vasculitis is a well-documented phenomenon. However, autoimmune-mediated anaemia is rarely documented or under-recognized. We report a patient with autoimmune haemolytic anaemia in Weil syndrome, which has previously been reported in only four cases in the medical literature.

THE CASE

A 50-year-old farmer came to our hospital with complaints of yellowish discolouration of his eyes for 10–15 days, fever and abdominal pain for 2 days, and breathlessness for 1 day. He described the fever as intermittent, low grade, and associated with chills and rigors. The abdominal pain was localized to the right lower quadrant and he had one episode of vomiting. The patient started having breathing difficulty for 1 day, even at rest. He had no previous illness and used to consume 90 ml of whisky daily for 3 years, which he had stopped 1 year ago.

At the time of admission, examination revealed—pulse rate 90/minute, blood pressure 130/80 mmHg in the right arm supine position, temperature 98.6 °F and respiratory rate 24/minute. He had icterus, bilateral crepitations in the infrascapular area, no use of his accessory muscles, tenderness over the right iliac fossa and no organomegaly. A provisional diagnosis of leptospirosis was made as the patient came from an area endemic for *Leptospira* infection. His laboratory investigations are shown in Table I.

He was empirically started on piperacillin and tazobactam, ceftriaxone and doxycycline. As there was progressive renal failure with septic acute tubular necrosis and rhabdomyolysis, haemodialysis was started. Doxycycline was stopped on day 4 as his liver function tests deteriorated. Despite 5 days of antibiotics, the patient was deteriorating clinically and due to poor oxygenation was intubated and connected to a mechanical ventilator. Meropenem was added and ceftriaxone was continued. He started improving clinically, his oxygenation improved, his ventilatory assistance was decreased and weaning trial was conducted after the rapid shallow breathing index was calculated. He was then extubated and continued on oxygen supplementation. His *Leptospira* serology was positive for immunoglobulin M (IgM) antibodies.

The patient developed anaemia, which progressed slowly during his hospital stay with the haemoglobin decreasing from 12.7 g/dl to 5.5 g/dl. His peripheral smear was suggestive of spherocytes and evidence of haemolysis with fragmented red blood cells; lactate dehydrogenase (LDH) was elevated and the direct Coombs test was positive—suggestive of autoimmune haemolytic anaemia. Drug-induced haemolytic anaemia was unlikely as he was not on any drugs which would have caused it (antibiotics had been stopped about 10 days after admission). A vasculitis work-up was negative and there were no other manifestations of vasculitis. A cold agglutination test was not done as the patient was deteriorating. He was started on injectable corticosteroids following which his haemoglobin started improving. He was then changed to oral high-dose steroids. The patient improved with no further complications and no decrease in haemoglobin till his next follow-up after 1 month. The steroids were tapered over the following 6 weeks and patient has had no further relapses.

DISCUSSION

Leptospirosis is a zoonotic disease, caused by genus *Leptospira* spirochetal infection.[1] The most common species causing Weil disease in humans is *Leptospira interrogans*.[1] The clinical spectrum of *Leptospira* infection includes asymptomatic mild illness through fulminant Weil syndrome causing bleeding, renal and hepatic failure.[1,2] Rhabdomyolysis, pulmonary haemorrhage, myocarditis, thrombotic microangiopathy, meningitis and cerebellitis are rare manifestations of leptospirosis.[1,2]

Autoimmune haemolytic anaemia associated with leptospirosis is a well-documented phenomenon in animals.[3–7] However, human *Leptospira* infection triggering immune-mediated haemolytic anaemia is rare and only four case reports are available in the medical literature.[8–11]

Anaemia is also an important usual manifestation in *Leptospira* infection. Initial studies led to the belief that suppression of erythropoiesis was the primary mechanism involved.[12] However, studies, which did sternal biopsy, indicate that there was moderate activation of erythropoiesis, which contradicted the traditional belief.[13–15] These studies proved that anaemia in leptospirosis did not impair functional ability of the bone marrow, but it was hyperproliferative normoblastic haematopoiesis.[13] They concluded that low glucose-6-phosphate dehydrogenase might be a prognostic criterion for developing an anaemic syndrome.[14] They also concluded that anaemia in the acute phase of illness was primarily due to erythrocyte haemolysis, while anaemia in the latter part of the illness was mostly due to renal failure.[15] There is some evidence that plasmapheresis improves the outcome, supporting evidence of an immune-mediated pathology.[16,17]

Our patient developed Weil syndrome acutely and so it was unlikely that renal failure was causing anaemia.[15] In addition to the evidence of haemolysis in the peripheral smear, there was elevated LDH, spherocytes in the peripheral smear, positive direct Coombs test and elevated reticulocyte count and index, which were suggestive of autoimmune-mediated haemolysis. The patient was initially started on a high dose of steroids (1 mg/kg/day) and he responded well. Hence, intravenous immunoglobulin (IvIg) was

Kasturba Medical College, Sharada Madhava Pai OPD Block, Manipal, Karnataka, India
RAHUL SAI GANGULA, M. MUKHYAPRANA PRABHU, WEENA STANLEY Department of Medicine

Correspondence to M. MUKHYAPRANA PRABHU; *mm.prabhu@manipal.edu*

TABLE I. Laboratory investigations during the patient's hospital stay

Investigation	Day of admission	Day 6	Day 12	Day 18	Day of discharge
Haemoglobin (g/dl)	12.7	10	8.8	5.5	8.9
Total white cell count (cmm)	14 300	31 100	23 600	25 900	10 500
Platelet count (cmm)	15 000/ml	156 000/ml	237 000/ml	295 000	392 000
Serum urea (mg/dl)	95	75	175	181	127
Serum creatinine (mg/dl)	5.0	4.1	8.2	8.3	3.2
Serum sodium (mmol/L)	130	146	136	140	132
Serum potassium (mmol/L)	3.7	3.9	4.3	3.2	4.2
Total bilirubin (mg/dl)	20.8	29.8	8.4	4.3	3.8
Direct bilirubin (mg/dl)	15.6	23.1	6.1	3.6	2.8
Aspartate aminotransferase (i.u./L)	290	265	56	46	24
Alanine aminotransferase (i.u./L)	137	173	29	12	12
Alkaline phosphatase (U/L)	216	170	287	228	146
PT (seconds)/INR	11.4/1.06	–	11.9/1.10	–	13.9/1.29
APTT (seconds)	31.8	–	32.2	–	37.7
Peripheral smear	Reduced platelets	Spherocytes, fragmented RBC, occasional nRBC	Few spherocytes +, fragmented RBC normocytic normochromic to microcytic hypochromic, multiple small platelet clumps +	Spherocytes +, platelet clumps +	
Leptospira serology	IgM antibodies for *Leptospira* detected				
Haemodialysis (HD)	HD started		HD catheter removed		

INR international normalized ratio PT prothrombin time APTT activated partial thromboplastin time RBC red blood cells nRBC nucleated red blood cells

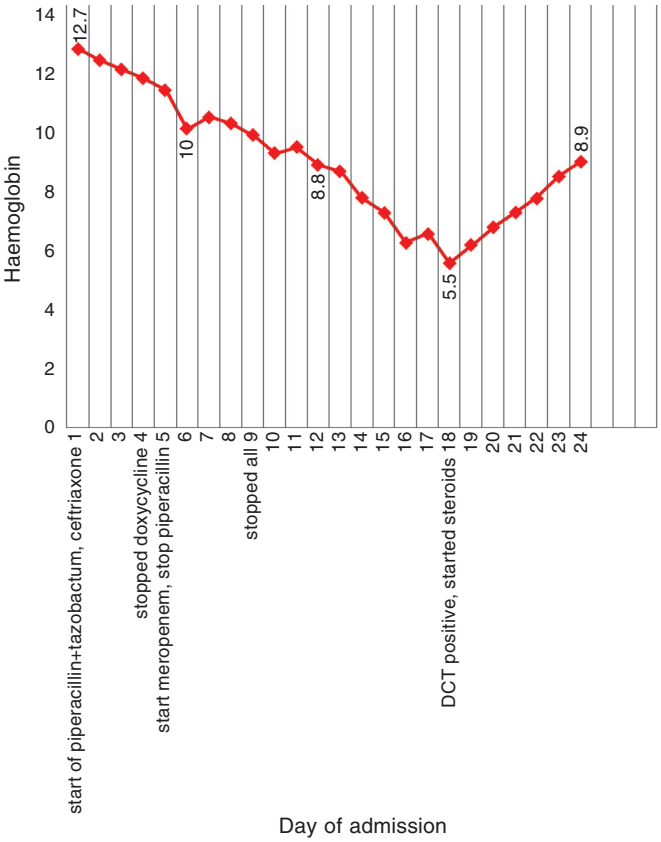

FIG 1. Graphical table with haemoglobin on the Y-axis and important events and time on the X-axis DCT direct Coombs test

not started, as done in some previous studies.[8] Patients might develop immune-mediated haemolysis in some leptospiral infections for which immunosuppressants, IvIg or plasmapheresis may be the ideal choice.[18]

Conflicts of interest. None declared

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