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Case Report

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A Case Report of Autoimmune Haemolytic Anaemia in Leptospirosis, a Rare Presentation

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ABSTRACT

Leptospirosis is a zoonotic illness caused by pathogenic spirochetes of the genus Leptospira, which causes diverse clinical manifestations and complications. Infection is biphasic, with a bacteraemic phase and an immune-mediated phase. A small number of patients will develop multiorgan failure. Transient thrombocytopenia is the most common haematological manifestation, while immune-mediated haemolytic anaemia is a very rare manifestation observed in humans. A 22-year-old previously healthy male presented with high-grade fever, body aches, and a background history of exposure to muddy water. He was managed for leptospirosis complicated with multiorgan failure. He developed a gradual drop of haemoglobin during the immune phase, clinical features and investigations were in favour of cold-type autoimmune haemolytic anaemia (AIHA), highlighting the importance of considering the occurrence and identifying the type of AIHA among patients with leptospirosis with multiorgan involvement.

Keywords: Leptospirosis, autoimmune haemolytic anaemia

INTRODUCTION

Leptospirosis is a zoonotic illness caused by pathogenic spirochetes of the genus Leptospira, which causes diverse clinical manifestations and complications. Infection is biphasic, with a bacteraemic phase and an immune-mediated phase (1). A small number of patients will develop multiorgan failure. Transient thrombocytopenia is the most common haematological manifestation, while immune-mediated haemolytic anaemia is a very rare manifestation observed in humans (3). Here we present a case of a 22-year-old previously healthy male who was managed for leptospirosis complicated with multiorgan failure and transient cold-type AIHA during the immune phase. This case highlights the importance of considering the occurrence of AIHA and identifying the type of AIHA by immunohaematological testing in patients with leptospirosis with multiorgan involvement, for further management, to avoid unnecessary blood transfusions.

CASE REPORT

We report a case regarding a 22-year-old previously healthy male who presented with high grade, intermittent fever for 4 days with severe myalgia,

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headache, back pain, and history of exposure to muddy water one week prior. His examination was unremarkable except for bilateral conjunctival suffusions and tender calf muscles. Towards the day 6 of illness, he developed cardiovascular instability requiring inotropic support, along with reduced urine output and rising serum creatinine. He was also observed to have progressive jaundice, right hypochondriac pain, deranged liver function tests. However, there were no bleeding manifestations or shortness of breathing. He was managed for complicated leptospirosis with intravenous (IV) ceftriaxone, IV methylprednisolone pulses, and oral doxycycline. ICU care was given for close monitoring of haemodynamic status, acute liver and kidney injuries, although he didn't require hemodialysis or ventilatory support.

Daily monitoring of full blood counts showed gradual decline of haemoglobin. Blood film showed evidence of haemolysis along with positive haemolytic markers including elevated reticulocyte count and significantly increased lactate dehydrogenase (LDH) levels. Positive direct antiglobulin test (DAT) was suggestive of immune mediated haemolysis. Further DAT profile showed C3d only positivity with probable diagnosis of cold AIHA. Table 1 further summaries the investigations. His lowest recorded haemoglobin level was 7.9g/dl, and he was managed with supportive care, including folic acid supplements.

DISCUSSION

Leptospirosis is a zoonotic illness caused by pathogenic spirochetes of the genus Leptospira, which results in diverse clinical manifestations and complications. In Sri Lanka, approximately 3,000-5,000 suspected cases are reported each year, with a case fatality rate of 1-2% in the recent past (1). High-risk populations include farmers, animal handlers, and individuals exposed to potentially contaminated water.

Spirochetes colonize the renal tubules of the carriers including both wild and domestic farm animals like rodents, cattle, dogs, and pigs and are excreted in urine. Transmission to humans occurs either direct contamination of infected animal tissue, body fluid or indirectly by contaminated moist soil, lakes, streams, rivers through damaged skin, or mucosal surfaces. The incubation period is 5-14 days with biphasic disease patterns including bacteraemic and immune phases.

In the initial bacteraemic phase, leptospira proliferates and disseminates throughout the body, causing tissue damage resulting in acute fever with chills and rigors, headache, myalgia, nausea, and vomiting. Characteristic conjunctival suffusion appeared on the 3rd day of illness. After production of IgM antibodies, leptospira is cleared from the body, but the tissue damage continues due to immune mechanisms in the later immune phase. Most infections will be asymptomatic or show transient febrile illness. However, a small number of cases will develop severe forms of illness with multiorgan failure, affecting the kidney, liver, lungs, heart, and blood cells.

Thrombocytopenia is the most common hematological manifestation, while disseminated intravascular coagulation (DIC) is among the most severe. Anaemia is commonly seen due to non-immune haemolysis, blood loss, and bone marrow suppression due to acute infection(2). Although immune-mediated haemolysis is well-documented in animal leptospirosis, it is a very rare presentation in humans, with only five cases reported in the medical literature (3).

Our patient had a normal haemoglobin level at the presentation and it gradually declined during the immune phase. Also, he has no previous history of sensitising events that lead to development of red cell antibodies such as blood product transfusions and haemopoietic stem cell transplants. His blood picture revealed spherocytes with polychromasia, without red cell fragmentations indicating haemolysis. Elevated reticulocyte count, reticulocyte index, and lactate dehydrogenase (LDH) levels confirmed the ongoing haemolysis. Positive DAT with C3d only positivity confirmed the immune-mediated haemolysis, more in favor of cold AIHA.

The mainstay of treatment of cold AIHA includes supportive care with folic acid supplements, avoidance of triggers, and symptomatic blood transfusions while warm AIHA needs concomitant steroids. Immunomodulating agents like rituximab are indicated in cold AIHA if the patient developed

Table 1: Summary of investigation

Test	Reference values	Results on admission (D4)	D6	D10	D14	D30
Full blood count						
White cell count 10^3 /ųl	4-11	6.4	18	16	9.4	6.2
Neutrophils 10^3 /ųl	2-7	5.1	12	13	7.4	5.1
Lymphocytes 10^3 /ųl	1-5	1.1	4.8	2.1	1.8	1.4
Esoinophils 10^3 /ųl	<0.5	0.1	0.5	0.4	0.4	0.3
Monocytes 10^3 /ųl	0.2-0.8	0.1	1.0	0.5	0.2	0.1
Platelets 10^3 /ųl	150-400	33	5	11	154	370
Haemoglobin g/dl	12-15	12.3	8.5	7.9	8.2	12.1
MCV fl	80-100	88	90	98	96	86
CRP mg/dl	<5	290.8			10.8	
ESR mm/hr	<22	90				
Serum creatinine ųmol/l	65-120	100.4	154.3	67		
Serum Na mmol/l	135-145	138	132		138	
Serum K mmol/l	3.5-5.5	4.1	3.9		4.7	
AST U/L	<30	27	223	181	30.3	
ALT U/L	<30	38	57.9	118		
ALP U/L	40-130		85.9			118
Gamma-glutamyl transferase U/L	<55	43.6	152			94
Total protein g/dl	6.6-8.8	7.2				7.6
Serum albumin g/dl	3.5-5.5	4.1	3.3			4.4
Total bilirubin ųmol/l	5-19	14.6	367	194	134	15.6
Direct bilirubin ųmol/l	1.7-6.8	5.6	216	114	103	10.2
Indirect bilirubin ųmol/l		9.0	101	80	29	5.4
Ultrasound abdomen		Bilateral acute kidney injury with acute liver parenchymal disease				
ECG		Sinus rhythm				
Chest X-ray		Normal				
2D echocardiogram		Normal				
Blood culture		Negative				
Urine culture		Negative				
Hep B s antigen		Not detected				
Hep antibodies IgM		Not detected				
Blood picture		Infection/inflammation with evidence of haemolysis with spherocytes and polychromatic cells				
Leptospirosis MAT			1:2560			
Reticulocyte count %	0.3-2	0.5	9.52			
Retic index	0.3-2		7.5			
Lactate dehydrogenase U/L	140-280			717		
Direct antiglobulin test				C3d (2+) positive IgG-negative		
UFR; pus cells	<10	1-2				
UFR; red cells	Nil	Nil				
UFR; protein	Nil	Nil				

symptomatic anaemia, transfusion dependence, or severe circulatory symptoms (4). We administered three IV methylprednisolone pulses beginning on D7 of the illness, and his lowest haemoglobin level was noticed on D10, indicating the poor response to steroids. This is because the overall response of cold AIHA to steroids is often partial and unsustainable with a response rate of 14-69% in larger series (4). Considering his symptoms and the transient nature of the immune phase, we opted for close monitoring of our patient and folic acid supplements were continued. Since his lowest haemoglobin was 7.9g/dl, blood transfusions were not given and it subsequently normalized after one month of settling the infection further confirming the diagnosis of cold AIHA associated with Leptospirosis.

Conclusion

Leptospirosis is a common zoonotic infection seen in Sri Lanka, occasionally resulting in multiorgan failure. Even though thrombocytopenia and mild anaemia are commonly seen during the infection, AIHA is a very rare manifestation. It is crucial to perform immunohaematological testing including DAT and DAT profile to identify the type of AIHA to determine the treatment options. Since the immune phase is transient, anaemia can be managed with supportive care, but severe anaemia may need transfusional support with immunomodulatory agents, or steroids depending on the subtype of AIHA.

Author declaration

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All data generated during the study are included

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