Research Article

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WEIL'S DISEASE WITH A PATHOGNOMONIC CONJUNCTIVAL SUFFUSION AND RASHES: A CASE REPORT

Vaishnavi K [1], Channaraya V [2], Ramakrishna Prudhivi *[3], Monika K A [1], Charitha K S [1], Ramana Reddy M [1]

[1]Department of Pharmacy Practice, Dayananda Sagar College of Pharmacy, Bengaluru, India

[2]Senior Consultant Physician, Sagar Hospitals, Kumarswamy layout, Bengaluru-560078. Retired professor HOD medicine, KIMS, Basavangudi, Bengaluru, India

[3]Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananada Sagar University, Bengaluru, India

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***Corresponding author**
E-mail: ramakrishna.prudhivi@gmail.com

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ABSTRACT

Leptospirosis is an emerging infectious disease, as illustrated by recent large outbreaks in Asia, Central and South America, and the United States. Severe form of leptospirosis, characterized by jaundice, renal dysfunction, and haemorrhagic diathesis, is referred to as Weil's disease. The outbreak of Weil's disease in India has increased in past couple of years due to worst floods. A 39year old male admitted to the hospital with fever, uniform rashes, chills, and weakness. Initially the dengue and malaria rapid tests were negative with elevated GRBS, serum creatinine, bilirubin levels, SGOT/SGPT and decreased platelets. Patient was put on antibiotics in view of sepsis with UTI, AKI and thrombocytopenia. The next day Leptospirosis was confirmed with leptospira IgM and ELISA. The patient developed conjunctival suffusion, jerky movements and pedal oedema during hospitalisation which was decreased within 2days with the antibiotics. The hepatic and renal function improved on 6th day of admission and slowly the patient improved biochemically and symptomatically. The patient recovered and discharged after 9days of hospitalisation. The above case of Weil's disease presented was initially misinterpreted as Dengue this should serve to alert healthcare providers and the general public as leptospirosis is often overlooked and under diagnosed due to its non-specific symptoms. The physicians should be alerted to consider leptospirosis in the differential diagnosis so that early empirical treatment can be given.

Key words: Weil's disease, leptospirosis, acute kidney injury (AKI), conjunctival suffusion.

INTRODUCTION

The Weil's disease is a severe form of leptospirosis. It is an infection caused by spirochete bacteria called *Leptospira* which belongs to the genus called Leptospirosis. It is one of the most wide spread zoonotic diseases in the world.[1]

Leptospira is further divided into two classification systems. The traditional classification is based on phenotypic characteristics, classified into two main species: *Leptospira interrorgans* and *L.biflexa*. The second classification system is characterised on DNA-DNA hybridisation and The most common pathogenic species seen in human include *L.weilii, L.autumnalis, L.canicola, L.hardjo,* and *L.hebdomadis*.[2]

Leptospirosis is transmitted by the urine or blood of affected animals and is contagious as long as the urine is moist. Rats, mice, moles are important primary hosts but a wide range of other mammals including dogs, cows, sheep, rabbits and certain marine mammals carry and transmit the disease as secondary hosts.[3]Human infection results from contact with contaminated food, water, soil or through cutaneous exposure with these infected animals.[4] The people who are at risk include veterinarians, slaughterhouse workers, farmers, sailors, sewer maintenance workers and countryside rangers. The incubation period of leptospirosis is 7-12 days. It can also range from 2-20 days. The disease occurs as a two clinically recognizable syndromes called Anicteric leptospirosis (85-90%) and Icteric leptospirosis (10-15%).

Anicteric leptospirosis is characterised with fever, severe myalgia, headache, chills and rigors. The septicemic phase (1st phase) for 3-7 days with intense fever, headache, nausea, vomiting, maculopapular skin rashes, lymphadenopathy, splenomegaly and most common conjunctival suffusion. The second stage is immune stage which is asymptomatic that lasts for 1-3 days and has less severe headache, vomiting than first stage. Uveitis, iritis, congenital congestion and chorioretinitis may also appear during the immune stage. This stage is characterised with appearance of IgM antibodies cleared from cerebrospinal fluid (CSF) results in aseptic meningitis after few days of this stage.

Icteric leptospirosis or Weil's syndrome is characterised by hepatic, renal and vascular impairment. Patients with this stage probably have jaundice, thrombocytopenia, hypotension, haemorrhage, Congestive Heart failure(CHF) with non-specific ECG changes, increased creatinine phosphokinase (CPK) and death can occur due to heart, liver and respiratory failure therefore it is considered as a most severe form of disease.[5]

The Weil's disease has varied clinical manifestations which is a challenging task in order to confirm the diagnosis. The conventional tests include microscopic agglutination test (MAT) which is a gold standard and enzyme -linked immunosorbent assay (ELISA) which detects antibodies against leptospirosis. Molecular tests, like polymerase chain reaction (PCR) is Successful in detecting Leptospira DNA in serum and urine samples of patients.[6]Organ specific like kidney function tests, liver function tests(LFT) can be done to identify severity.

Leptospira is identified in blood and CSF for first 7-10days and then in urine after 2 weeks.

Leptospirosis in all its forms is susceptible to treatment with antibiotics, so far there are no such reports are published against resistance to antibiotics. The most usually recommended antibiotics are high dose of penicillin G, amoxicillin, ampicillin, and doxycycline. Penicillin is used unless the patient is hypersensitive to it, in such case erythromycin is used. In more severe cases cefotaxime or ceftriaxone are preferred and corticosteroids (prednisolone) in gradually reduced doses for 7-10 days in case of severe haemorrhagic effects. Organ specific care and treatment are required in case of kidney, liver, and heart involvement. Glucose and salt solution infusions are preferred in serious cases. Hyperkalaemia can be treated by using potassium binders and calcium carbonate for hyperphosphatemia.[7]

The epidemiology of leptospirosis is complex and dynamic. Since leptospirosis resulted in underdiagnosed, underreported and ignored due to its vast clinical manifestations that makes diagnosis difficult. Leptospirosis is among the most neglected infectious diseases and even is lacking on many lists of neglected infectious diseases.

It is estimated that 7-10 million people are infected by leptospirosis annually out of which one million cases of severe leptospirosis occur annually with 58900 deaths[8]

According to occupational groups involved and the nature of disease different names has been used like seven-day fever in Japan, cane cutter's disease in Australia, rice field leptospirosis Indonesia, Fort Bragg fever in USA and weil's disease which is one of the severe forms occurs in many countries including India, china, continental Europe, England and south-east Asian countries.[9]
Kerala, the southern Indian state had severe attack of leptospirosis in 2018 due to worst floods, around 200 cases were confirmed with the disease and nearly 30 deaths were reported.[10.] Thus there is a great significance in detecting the disease in early stage to initiate the treatment at right time here one case report was discussed.

Study is carried out as per International conference of Harmonization-Good Clinical Practices Guidelines (ICH-GCP) or as per Declaration of Helsinki guidelines.

CASE REPORT

A 39-year-old male patient was admitted to the hospital on emergency basis with 6days history of fever, chills, pain in abdomen, generalised weakness, and headache. Relevant vital signs and investigations are noted with high grade fever (101^0F), pulse of 126 beats/min, BP-110/70mmhg, local examination had uniform erythematous rashes (figure1) and per abdomen showed hepatomegaly with mild ascites. Initially laboratory parameters are noted which showed elevated GRBS (227mg/dl), thrombocytopenia (70,000/µl), deranged Serum Creatinine (2.1mg/dl), Total Bilirubin (4.43mg/dl), Direct Bilirubin (3.59mg/dl), Serum Urea (55.64mmol/l) and mildly increased SGPT/SGOT (55/74IU), dengue rapid profile showed IgG weakly positive and IgM negative.

The patient was admitted to the high dependency unit for sepsis with UTI, fever with thrombocytopenia, acute kidney injury (AKI) and was initiated with intravenous fluids (100ml/hr), paracetamol (1gm SOS), Tablet Doxycycline (100mg BD), Injection ceftriaxone (2g BD).

On the second day fever spikes were appeared (104^0F), with deranged platelet count (78000/µl), serum creatinine (1.8mg/dl), and worsened total and direct bilirubin levels (5.03mg/dl, 4.06mg/dl). The patient was investigated for malaria parasite which was negative, leptospira IgM and ELISA showed positive therefore the patient diagnosed with leptospirosis/weil's fever. With the confirmation of Weil's disease the patient was put on crystalline penicillin (20lakhs units for every 6hours).

Reference was given to nephrology department in view of acute kidney injury, dose adjustments are made based on creatinine clearance and advised to monitor input/output (I/O), and Creatinine phosphokinase (69U/C) levels were within the normal limits.

On the following day the patient was observed to have involuntary movement of head with fever and jerky movement. Reference was given to neurology department in view of above complaints and advised for MRI brain as it did not showed any significant abnormalities the jerks are considered as likely tremor due to fever.

On the 4th day the laboratory investigations slightly improved but the patient complained bilateral pedal oedema, rashes and congenital congestion. The physician stopped crystalline penicillin and started with methyl prednisolone (40mg for every 8 hours).

On the 5th day of hospitalisation the fever continued with rashes, eye congestion and reduced involuntary movements. In view of elevated GRBS (243mg/dl) the patient was given with 6units of insulin human mixtard and monitored.

On the 6th day the patient was symptomatically better. EEG showed mildly abnormal with diffuse theta range slowing indicating non-specific diffuse cortical dysfunction and with the increased GRBS levels a fixed insulin dose (20units of Human mixtard) was given.
Next 2days the patient had no fever, rashes and no fresh complaints were seen, the leptospira PCR test was negative and conjunctivitis also decreased.

As shown in figure 2 the platelet count was improvedfrom 70000/µl to 150000/µl. The kidney chemistry profile (figure 3) showed progressive improvement during hospitalisation and as such the liver chemistry profile(figure4) also showed improvement. Patient improved symptomatically and biochemically hence discharged after 9days of admission with discharge medications as follows Tab-Cefixime+Clavulanic acid 200mg BD(5days), Tab-Doxycycline 100mg BD(5days), Tab-Pantoprazole 40mg OD(1wk), Multivitamin capsule OD(1wk) and Tab-Paracetamol 650mg SOS.

DISCUSSION

We followed the ICMR ethical guidelines to collect the data and carry out this research work. Leptospirosis is a zoonosis of wide clinical spectrum ranging from asymptomatic cases to severe Weil's disease. Leptospirosis classically presents as a biphasic illness. In symptomatic cases of leptospirosis, clinical manifestations vary from mild to serious or even fatal. More than 90% of symptomatic persons have the relatively mild and usually anicteric form of leptospirosis, with or without meningitis.

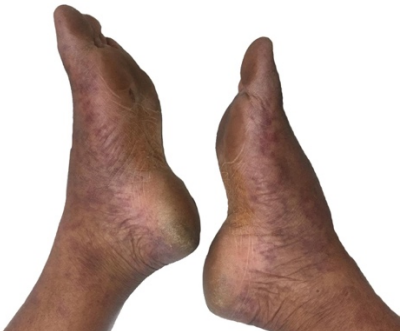

Figure 1: uniform erythematous rashes

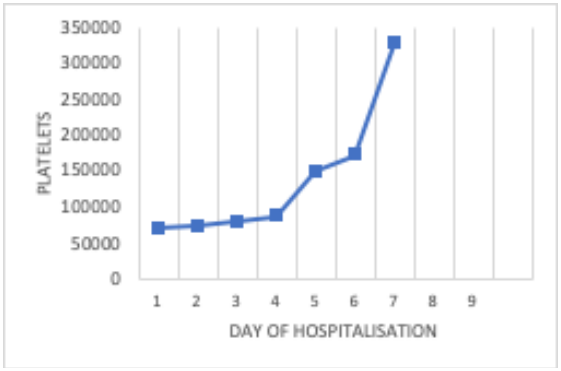

Figure 2: platelet profile

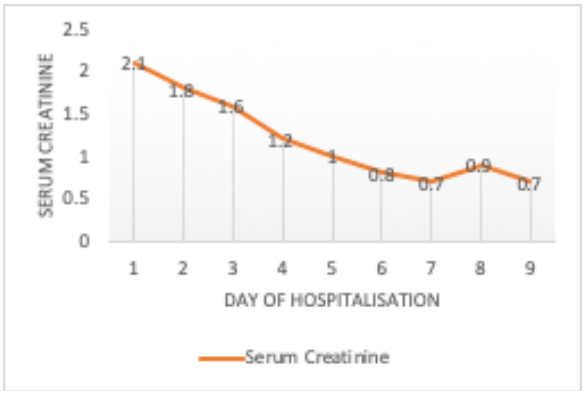

Figure 3: kidney chemistry profile

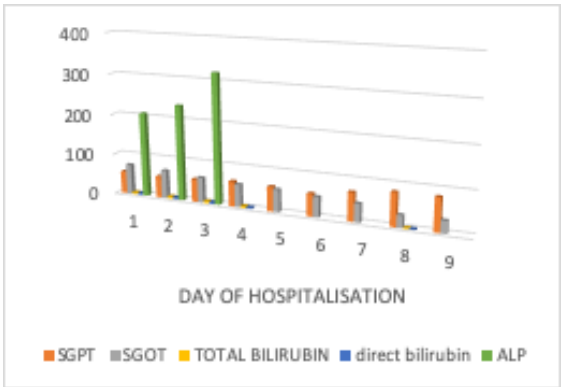

Figure 4: liver chemistry profile

Severe leptospirosis with profound jaundice (Weil's syndrome) develops in 5 to 10% of infected individuals. The incubation is usually 1 to 2 weeks, the symptoms can be of two distinct phases namely anicteric and icteric. Anicteric or septicaemia phase includes general flu like symptoms like fever, headache, chills, muscle pain and vomiting. The most common finding on physical examination is fever with conjunctival suffusion and rashes can be seen which may be maculopapular or erythematous. In this phase the bacteria can be isolated from blood cultures and cerebrospinal fluid (CSF). The second phase is an icteric or immune phase where circulating antibodies and the bacteria can be isolated from the urine. A specific organ damage can be noticed like meningitis, renal symptoms, pulmonary manifestations, respiratory distress, jaundice, pancreatitis and myocarditis.[11]

In this case, patient was admitted with high grade fever, chills, abdomen pain, uniform erythematous rashes and thrombocytopenia. The systemic uniform rashes all over the body with idiopathic fever are the anicteric symptoms noticed initially. Here patient diagnosis is not initially considered because of differential diagnosis and suspected to have sepsis with acute kidney injury. The diagnostic test like ELISA, leptospira IgM confirmed the presence of the disease.

According to WHO modified Faine's criteria which is a system of scoring for the diagnosis of leptospirosis, where a diagnostic score is obtained based on clinical data, epidemiological factors, bacteriological and laboratory findings. A score between 20 and 25 suggests leptospirosis as a possible diagnosis and this patient showed a strong presumption of the disease with a diagnostic score of 32 similarly same recommendations are followed in the intensive case report with multiorgan failure by Turkam Togal study.[12]

The presence of acute kidney injury in this case might be due to various factors like direct nephrotoxicity, hypovolemia, acute tubular necrosis, rhabdomyolysis and endotoxin associated vasoconstriction. Neurological involvement occurred on third day of hospitalisation where patient experienced involuntary jerky movements and are considered to be likely tremors due to fever. Raise of direct and total bilirubin in this patient may be due to haemolysis or extra vascular red blood cell destruction.

In a case report of Weil's disease by Venkata Krishna pothukuchi et.al, the patient was seen with conjunctival haemorrhages, icterus, mucosal bleed and pedal oedema,[1] our patient was also seen with a pathognomonic conjunctival suffusion and pedal oedema which was noticed on fourth day of hospitalisation suggested as one of the confirmatory physical findings of leptospirosis. Increased liver enzymes and ultrasound of abdomen showed presence of Hepatitis, hepatomegaly with fatty liver and grade 1 nephropathy. There was remarked increase in GRBS levels from 5th day was due to impaired hepatic metabolism. Which further effected glycogenolysis hence the blood glucose levels are increased and here the patient was treated with insulin Human Mixtard. EEG showed mildly abnormal with diffuse theta range slowing indicating non-specific diffuse cortical dysfunction and tachycardia.

The majority of infections in leptospirosis are self-limiting and the effectiveness of antimicrobial therapy for the mild febrile form of leptospirosis is controversial, but such treatment is indicated for more severe forms. Treatment should be initiated as early as possible; nevertheless, contrary to previous reports, treatment started after the first 4 days of illness was predominant. The current choices of treatment for mild leptospirosis is oral form of doxycycline, tetracycline, amoxicillin, and ampicillin. Although several other antibiotics, including newer class of

cephalosporin's, are highly active against leptospires. In severe leptospirosis intravenous high dose of Penicillin G is considered, if patient is allergic then erythromycin is recommended.[13] According to standard pattern of treatment this patient was treated with oral doxycycline, cephalosporin and parenteral penicillin G. and experienced beneficial effects in improving conjunctival suffusion, rashes, pedal oedema, hepatic and renal function with the use of corticosteroids. Similarly In a case of fulminant leptospirosis by Elias Maroon et.al, use of corticosteroids improved patient's renal dysfunction, thrombocytopenia, and haemoptysis.[5]

Leptospirosis with multi-organ dysfunction is very severe and considered as Weil's syndrome which can be reversible with early diagnosis and initiation of treatment. Mortality is highest among patients who are elderly and those who have Weil's syndrome. Leptospirosis during pregnancy is associated with high foetal mortality.[14] Long-term follow-up of patients with renal failure and hepatic dysfunction has documented good recovery of renal and hepatic function. In this case patient had multi-organ involvement who was diagnosed with Weil's disease and the standard treatment regimen was followed for early recovery.

CONCLUSION

In India due to lack of awareness of the disease and lack of appropriate laboratory diagnostic facilities, leptospirosis has been often underdiagnosed and under reported. The clinicians have to put together their experience and awareness about the disease in order to achieve the early detection of patients with leptospirosis. The above case report highlights the importance of creating awareness about early diagnosis of leptospirosis which would enable physicians to start the treatment as early as possible and helps for reducing morbidity and mortality.

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ABBREVATIONS

Acute Kidney Injury (AKI), Electroencephalogram (EEG), Enzyme linked immune sorbent Assay(ELISA), Congestive Heart Failure(CHF), Creatinine Phosphokinase(CPK), Gross Random Blood Sugar (GRBS), Liver Function Tests(LFTs), Polymerase Chain Reaction (PCR),Urinary Tract Infection (UTI).

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