CLINICAL CASE PRESENTATION

TEL AVIV SOURASKY MEDICAL CENTER

Dr. Zaid Dana

A-69 -year -old woman was admitted to ER in Sourasky medical center in Tel Aviv because of delirium and a new onset jaundice.

On arrival her vital signs were: BP 127/75 mm Hg, pulse 96 beats/min, temperature 36.3°C, normal respiratory rate with saturation 96% while breathing ambient air.

On examination the patient's skin,subglossal mucosa and sclera were jaundiced, there were telangiectasias ,pruritus signs and maculopapular rash on the limbs and trunk (with palms and soles sparing).The abdomen was soft and not tender, w/o HSM. On neurologic examination-no meningeal signs, disoriented to time and place, muscle strength and reflexes and the remainder of the examination were normal.

Lab Tests	On admission	On release
Hemoglobin (1.7-15.5 g/dL)	13.6	9.4
MCH (26-34 pg)	30.2	
MCV (80-96 fL)	86.8	
RDW (0-15 %)	15.3	
Reticulocytes (0-2%)	0.56	
Reticulocytes No.	0.02	
WBC (4-11 $10^3/\mu L$)	33.9	9.1
PLT (150-450 $10^3/\mu L$)	163	560
Glucose (70-110 mg/dL)	203	
BUN (5-25 mg/dL)	155	15
Creatinine (0.6-1.1 mg/dL)	3.83	0.93
K+ (3.5-5.3 mmol/L)	2.51	4.36
ALT (5-35 U/L)	61	90
AST (7-40 U/L)	53	44
GGT(6-28 U/L)	99	33
Alk.Phosph. (25-100 U/L)	151	145
Bilirubin (0.1-1.2 mg/dl)	19.8	1.9
Direct bilirubin (0-0.3 mg/dL)	14.9	
LDH (208-378 U/l)	702	
CRP (0-5 mg/L)	20.5	1.9
PT (10.03-12.43 sec)	10.7	
PTT (25-34 sec)	24.9	
Fibrinogen (180-470 mg/dL)	621	
D dimer (0-0.49 FEU mg)	1.2	

ABG- normal PH, lactate within a normal range.

Amonia level-14 mcg/dL(20-85)

Haptoglobin 1580 mg/L (387-2108)

Blood smear- no schistiocytes or blasts; toxic granulation 89% neutrophills

Urinalysis revealed 25 WBC/µL, BLD 1 mg/dL, bilirubin 1 mg/dl

Urinary sediment- granular casts, few WBC and RBC

Chest X ray showed no opacities or pleural effusions

Electrocardiogram-normal sinus rate

Urinary catheter was inserted- 400 cc rest.

Ceftriaxon, ampicillin and fluids were administered after obtaining blood and urinary cultures.

The patients son, who lives abroad was reached on phone and the following information was obtained:

The patient had a history of : hypertension, dislipidemia, anemia, erythrocytosis, depression, s/p right THR

Medications list: aspirin, enalapril, omepradex, simvastatin, clomipramine, NSAIDs

She’s been well until two days before admission, when she sounded confused while talking with her son on the phone.

On the day of admission her neighbours found her confused and called an ambulance. She had no domestic animals and hadn’t travel abroad recently.

The patient was admitted to ICU.

Doxycyclin was administered upon admission.

After 4 days the patient was transferred to our department .

CT of the head without the administration of contrast material – hadn't reveal any pathological findings.

Lumbar puncture was performed one day after admission: xantochromia, protein -195 mg/dl (12-60) glucose 72 mg/dL (50-70), 147 WBC, 82% PMN, 12800 RBC. Gram stain reveald no bacteria, aerobic and anerobic cultures were sterile.

RENAL FAILURE

+

JAUNDICE

+

ASEPTIC MENINGITIS

Differential diagnosis:

1.Neoplastic/ paraneoplastic:

*MM

*Stauffer's syndrome (associated with a number of malignancies: Hodgkin lymphoma' medullary thyroid cancer, hypernephroma, renal sarcoma, T cell lymphoma, gastrointestinal malignancies.

2. Infection

*Viruses: CMV, EBV, HIV

*Q fever, rickettsial disease (Meditteranian spotted fever), leptospirosis, Lyme disease, syphilis

*Malaria, dengue fever- no recent travel

3. Drugs:

*NSAIDs

*clomipramine- can cause confusion and cholestatic hepatitis

5. Autoimmune diseases:

*SLE- would’nt explain leukocytosis

*Sarcoidosis- rare without pulmonary involvement

The following diagnostic tests were performed:

1. Blood work up:

* Rheumatological panel including C3, C4, RF, ANA, ANCA

*Serology for HBV, HCV, CMV, EBV, HIV, Q fever, leptospira, rickettsia conorii and typhi; Brucella melitensis, Bartonella henselae, Borelia

*Tumor markers: CEA, CA19-9, CA15-3, CA125, α fetoprotein.

*SPEP+IF

2. LP: xantochromia, protein -195 mg/dl (12-60) glucose 72 mg/dL (50-70), 147 WBC, 82% PMN, 12800 RBC. PCR for HSV 1+2 , WNV and leptospira was sent to the laboratory.

3. EEG- focal left frontotemporal slowing

4. TTE+ TEE-no evidence of vegetations

5. Imaging studies:

*Total body CT- no pathologic fidings

*Abdominal US- normal gallblader w/o stones, no biliary dilatation

*CT of the head without the administration of contrast material – hadn’t reveal any pathological findings

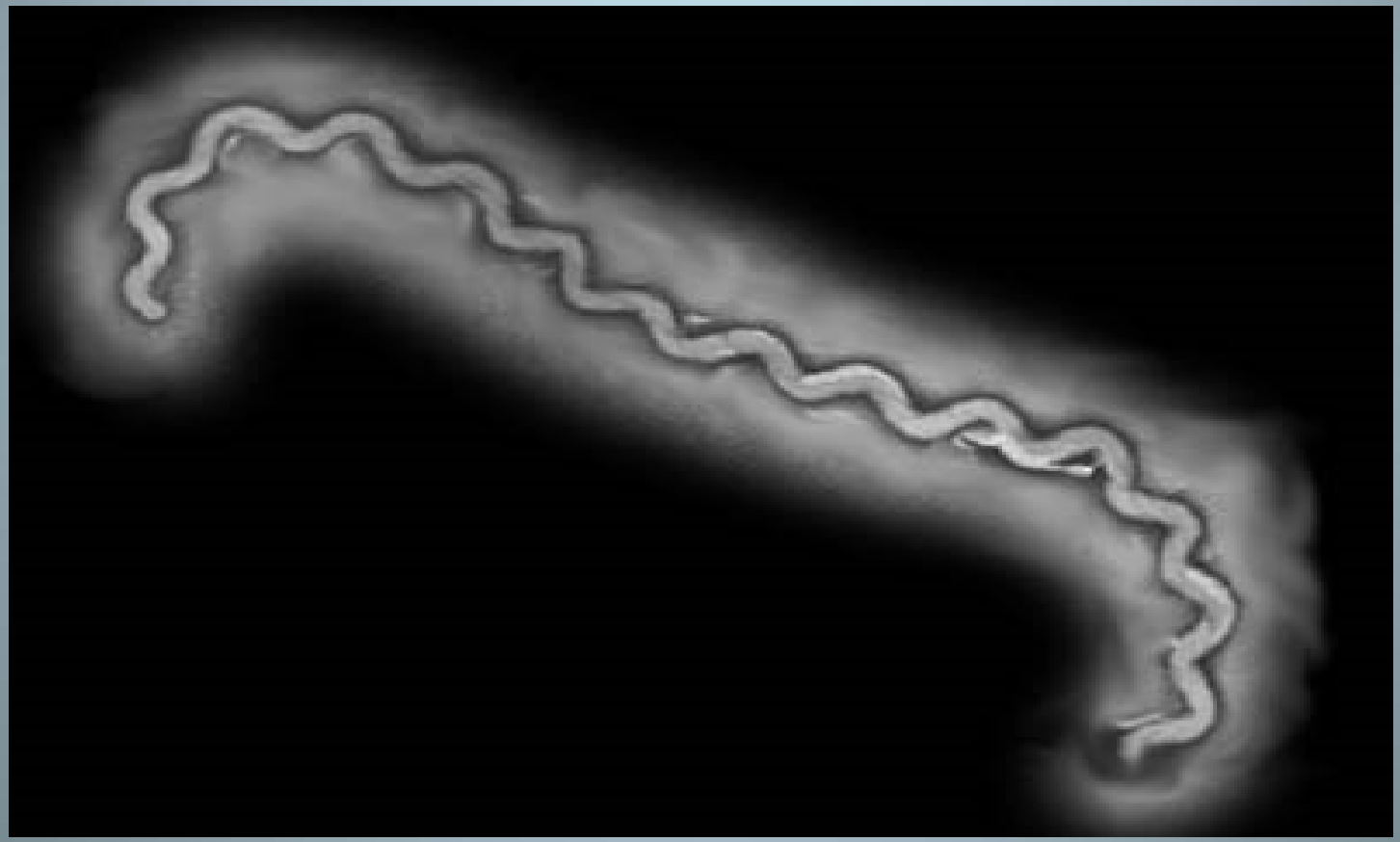
*MRI of the head-Minimal periventricular hyperintensity.

Because of the temporal focalisation on EEG and pleocytosis acyclovir was administered until negative PCR for HSV returned.

All the tests returned negative except for…

Serology for leptospira!

(PCR negative from blood, urine and CSF)



LEPTOSPIROSIS

Leptospirosis is a zoonosis caused by the spirochete, Leptospira interrogans.

Humans most often become infected after exposure to environmental sources, such as animal urine, contaminated water or soil, or infected animal tissue.

Portals of entry include cuts or abraded skin, mucous membranes or conjunctiva. The infection is rarely acquired by ingestion of food contaminated with urine or via aerosols.

Leptospirosis is associated with a variable clinical course.

The disease may manifest as a subclinical illness followed by seroconversion, a self-limited systemic infection, or a severe, potentially fatal illness accompanied by multiorgan failure.

Leptospirosis presents with the abrupt onset of fever, rigors, myalgias and headache in 75- 100 % of patients, after an incubation period of 2- 26 days (average 10 days).

25 - 35 % have an associated nonproductive cough and approximately 50 % experience nausea, vomiting and diarrhea.

Other less common symptoms include arthralgias, bone pain, sore throat, and abdominal pain; acalculous cholecystitis can occur in children .

While leptospirosis has classically been described as a biphasic illness, fewer than 50 % of cases exhibit a biphasic course

Physical examination is often unrevealing.

An important, but frequently overlooked sign, is conjunctival suffusion. This is not a common finding in other infectious diseases, and its presence in a patient with a nonspecific febrile illness should raise the diagnosis of leptospirosis.

7 - 40 % of patients can have muscle tenderness, splenomegaly, lymphadenopathy, pharyngitis, hepatomegaly, muscle rigidity, abnormal respiratory auscultation, or skin rash.

Aseptic meningitis can be documented in 50 - 85% of patients if CSF is examined after seven days of illness. The meningitis is thought to be secondary to a host immune response to the organism rather than to direct infection.

While most cases of leptospirosis are mild to moderate, the course may be complicated by renal failure, uveitis, hemorrhage, acute respiratory distress syndrome, myocarditis and rhabdomyolysis .

Liver failure is generally reversible and not a cause of death in leptospirosis.

Dyspnea, oliguria, WBC counts above 12,900/mm3, repolarization abnormalities on electrocardiograms, and alveolar infiltrates on chest radiography have been associated with adverse outcomes.

Vasculitis with necrosis of extremities may be seen in severe cases.

LABORATORY FINDINGS

Leptospirosis is a nonspecific clinical illness, and routine laboratory tests are similarly nondiagnostic.

WBC counts are generally< 10,000/mm3 but may range between 3,000 and 26,000/microL; a shift to the left is seen in about two-thirds of patients.

Urinalysis frequently shows proteinuria, pyuria, granular casts and occasionally microscopic hematuria .

Elevated CPK is found in 50 % of patients and may be a useful clue for the diagnosis

Approximately 40 % of patients have minimal to moderate elevations of transaminases (usually <200 IU/L).

Hyponatremia is common in severe leptospirosis.

Jaundice is only observed in patients with Weil's syndrome, the most severe form of leptospirosis. Patients with this syndrome can develop hepatic and renal dysfunction and hemorrhage. In occasional patients, the serum bilirubin concentration reaches 60 to 80 mg/dL (1026 to 1368 mmol/L).

Thrombocytopenia is uncommon, but a poorly understood hemorrhagic diathesis may occur in the absence of demonstrable coagulation defects or severe thrombocytopenia. Pancytopenia has been reported as the presenting manifestation in case reports with complete resolution following treatment with penicillin.

The CSF may show a neutrophilic or lymphocytic pleocytosis with minimal to moderately elevated protein concentrations and normal glucose.

DIAGNOSIS

Culture — leptospirosis can be confirmed by culture of the organism from clinical specimens in appropriate media. Blood and CSF specimens are positive during the first 3-10 days of the illness. Isolation of the organism from the blood is successful in approximately 50 % of cases. Urine cultures become positive during the second week of the illness and remain so for up to 30 days after the resolution of symptoms.

Serology — serological tests are most often used for confirmation. A number of serologic tests are employed, including the microscopic agglutination test (MAT), macroscopic agglutination test, indirect hemagglutination, and ELISA.

The gold standard is considered to be the MAT .Unfortunately, this test requires live organisms, considerable expertise, and is performed only by reference laboratories such as the CDC. The MAT is most specific when a fourfold or greater rise in titer is detected between acute and convalescent serum specimens. However, a single titer of >1:800 is strong evidence of current or recent infection with leptospira. Cross reactive antibodies have been associated with syphilis, relapsing fever, Lyme disease, and legionellosis.

Since the MAT is not readily available, another assay typically is performed first in suspected cases of leptospirosis. Two commercially available rapid tests, the microplate IgM ELISA and an IgM dot-ELISA dipstick test, performed well in studies conducted in the United States and Thailand that used MAT as the comparator .If one of these assays is positive, sera for MAT can then be sent to the CDC.

Molecular techniques — Molecular techniques, such as PCR, are being explored to assist in the diagnosis of leptospirosis. These techniques are not widely available but are promise tools for quick, accurate diagnosis.

TREATMENT

Antimicrobial treatment — Human leptospirosis is often self-limited and requires no antibiotic treatment. Symptomatic patients presenting for medical care should be treated to shorten the illness and decrease shedding of the organism in the urine.

For outpatients the suggestet treatment is oral doxycycline because it is also effective for rickettsial disease, which can be confused with leptospirosis (100 mg orally twice daily)

For hospitalized adults with severe disease, the options are intravenous therapy with penicillin (6 million units daily), doxycycline (100 mg twice daily), ceftriaxone (1 g every 24 hours), or cefotaxime (1 g every six hours).

THANK YOU