CASE REPORT

Cavernous sinus thrombosis syndrome and brainstem involvement in patient with leptospirosis: Two rare complications of leptospirosis

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Leptospirosis is a bacterial disease that is caused by pathogenic spirochetes of the genus *Leptospira*. It can affect humans and animals. In humans, it can lead to a wide spectrum of symptoms. It is known as the most common zoonosis in the world. The typical presentation of the disease is an acute biphasic febrile illness with or without jaundice. Less common clinical manifestations may result from involvement of different human body systems. In many places, this disease may be under-diagnosed, especially when associated with neurological complications. Moreover, without treatment, leptospirosis can lead to organ damages, and even death. Neurological complications are uncommon and are reported in a few cases. Cavernous sinus thrombosis syndrome and brainstem involvement are rare complications of leptospirosis and are associated with a high mortality risk. To our knowledge, no such cases have been reported in the literature.

Key words: Brainstem involvement, cavernous sinus thrombosis, complication, leptospirosis

How to cite this article: Alian S, Taghipour M, Sharifian R, Fereydouni MA. Cavernous sinus thrombosis syndrome and brainstem involvement in patient with leptospirosis: Two rare complications of leptospirosis. J Res Med Sci 2014;19:907-10.

INTRODUCTION

Leptospirosis is the most widespread zoonosis worldwide and an important and possibly emerging infectious disease, which is caused by pathogenic spirochetes of the genus *Leptospira* and remains a challenge for public health officials and researchers, presenting significantly high rates of morbidity and mortality.[1] According to estimates from the World Health Organization, more than 500,000 severe cases occur every year worldwide. The reservoirs of *Leptospira* are rodents.[2] It is predominantly recognized as an occupational disease. The disease occurs where the sanitary infrastructure is precarious.[3] The leptospires are typically transmitted through direct or indirect contact with the urine of an infected animal. In general, clinical manifestation can be divided into two distinct clinical syndromes.[4] 90% of patients present with a mild anicteric febrile illness that may present as an influenza-like illness with headache and myalgia; 10% are severely ill with jaundice and other manifestations such as: Renal dysfunction, and hemorrhagic diathesis (Weil's disease). Some clinical presentations might be seen in this disorder which are: Sepsis, acute renal failure, hepatic dysfunction, electrolyte imbalance, pulmonary hemorrhage, cardiovascular collapse, thrombocytopenia, pancreatitis, myocarditis, rhabdomyolysis, acalculous cholecystitis, purpuric skin lesions, pericarditis, arthritis, and reproductive failure.[5,6] Involvement of the central nervous system is an important and serious complications, affecting children and adults alike, and can present as any of the following phenomena: cerebrovascular accident, cerebral venous thrombosis, cerebral arteritis, subarachnoid hemorrhage, blindness due to uveitis, optic neuritis, transverse myelitis, cranial nerve palsy, Guillain — Barré syndrome mononeuritis multiplex, peripheral nerve palsy, psychosis, suicidal behavior, cerebellitis, encephalitis, meningitis, chronic meningitis, and primary meningitis.[7-10] Here, in this manuscript, we report two rare presentations; brainstem involvement and cavernous sinus thrombosis (CST) syndrome in a patient with leptospirosis. To our knowledge and based on the literature review, this is the first such reported case.

CASE REPORT

In July 2013, a 63-year-old farm worker was admitted to an infection ward of Razi Hospital, Mazandaran, Iran complaining of weakness, headache, and fever. As a complicating aspect of the history, he had been working in a farm 1-week before admission following

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Received: 04-02-2014; **Revised:** 05-03-2014; **Accepted:** 10-06-2014

which he immediately developed generalized myalgia, malaise, and vomiting. There were no other constitutional symptoms such as abdominal pain, jaundice, etc. He denied any contact with animals. Past medical history was insignificant, but he has a positive surgical history. He had not any history of consumption of dairy products. He had not traveled to any special area recently such as some endemic areas of infectious diseases. On initial examination, the patient was alert and oriented. He was pyrexial, 39.5°C. There was conjunctival suffusion, but no scleral jaundice. Skin, heart, and lung were normal on physical examination. The bladder and liver were not felt, and rectal examination was normal. Neurological examination of cranial nerves was unremarkable, and kerning and brudzinski signs were negative. Headache increased permanently after 2 days. On the 5th day of hospitalization, hiccup, photophobia, diplopic vision, ptosis, and right site preorbital edema were noticed. At first, eye movement was normal, but at day sixth deviation of the right eye to the medial site was seen. After 1-day, sign of brainstem involvement presented in patient; our patient could not sit upright without the support and he was ataxic and dysarthric. Examination showed uvula deviated to the left site and lack of gag reflex. Right side facial paresis was significant. After the transportation of the patient to the Intensive Care Unit (ICU), his consciousness decreased then sensory symptoms was not reliable. In ICU, 1 time hemoptysis and gastrointestinal (GI) bleeding was reported. Abdominal sonography performed that its result not showed any abnormality. Based on the clinical suspicious to leptospirosis, the serum sample sent for laboratory evaluation. Results showed L. Serjoe hardjo equal to 1/1600. Other laboratory test results are summarized in Table 1. Furthermore, neurological consultation conducted for the patients neurologic deficits. Magnetic resonance imaging/magnetic resonance venography (MRV) prescribed which provide a probable existence of the CST syndrome in associated with brainstem involvement [Figures 1 and 2]. This sign could not be justified by only a neurological deficit and is more probable to be due to a systemic problem such as leptospirosis. The axial computed tomography (CT) scan showed increased intensity with conversity in right cavernous sinus. No focal lesions were seen, with normal cranial ventricles and cisterns. MRV showed a loss of flow in both sides of cavernous sinus with right cavernous sinus expansion and longitudinal filling defect in associated with parietal irregularities with superior sagittal sinus. Transverse, sigmoid, and internal jugular vein does not show any thrombosis [Figure 2].

Table 1: Laboratory exams of the patient admitted with the diagnosis of leptospirosis

Laboratory evaluations	Amount and units
WBC	$14.2\times10^3/\mu L$
RBC	$4.27\times10^6/\mu L$
HGB	11.7 g/dL
HCT	37.1% of RBCs
MCV	86.9 fl
MCH	27.4 pg/cell
PLT	$120\times10^3/\mu L$
PT	16.2 s
PTT	>120 s
INR	1.8
Fibrinogen	403 mg/dL (normal range=150-350)
D-dimer	>10,000 mg/L (normal value: <500)
FDP	>20 mg/mL (normal <5.0)
Antinuclear antibody (ELISA)	3.0 U/mL (positive >12)
Anti-ds-DNA (ELISA)	5.0 (positive >30)
P-ANCA (MPO)	2.9 U/mL (positive >18)
C-ANCA (PR3)	2.8 U/mL (positive >18)
CRP	1+
Bilirubin direct	1.1 mg/dL
Bilirubin total	1.9 mg/dL
FBS	115 mg/dL
Cholesterol, total	193 mg/dL
Triglycerides	100 mg/dL
HDL cholesterol	33 mg/dL
LDL cholesterol	140 mg/dL
SGOT (AST)	42 U/L
SGPT (ALT)	84 U/L
Alkaline phosphatase	191 U/L
LDH	404 U/L
CPK 1	49 IU/L
Amylase serum	41 U/L
Blood urea	30 mg/dL
Creatinine	0.8 mg/dL
Sodium (naterium) Na	135 mEq/L
Potassium (kalium) K	4 mmol/L
L. serjoe hardjo	1/1600 titer
Leptospira (IgG) EIA	0.65
Blood culture	No growth after 48 h
Wright agglutination test	Negative
2-ME	Negative
Coombs wright	Negative

WBC = White blood cell; RBC = Red blood cell; HGB = Hemoglobin; HCT = Hematocrit; MCV = Mean cell volume; MCH = Mean cell hemoglobin; PLT = Platelet; PT=Prothrombin time; PTT = Partial thrombin time; INR=International normalized ratio; FDP = Fibrin degradation product; MPO=Myeloperoxidase; ANCA = Antineutrophil cytoplasmic antibodies; CRP = C-reactive protein; FBS = Fasting blood sugar; HDL = High-density lipoprotein; LDL=Low density lipoprotein; SGOT = Serum glutamic oxaloacetic transaminase; AST = Aspartate aminotransferase; SGPT = Serum glutamic-pyruvic transaminase; ALT = Alanine aminotransferase; LDH = Lactate dehydrogenase; CPK = Creatine phospho kina; 2-ME = 2-mercaptoethanol

DISCUSSION

Leptospirosis is an infectious disease, which has a worldwide distribution. Human infection can occur either through direct contact with infected animals or, much more commonly through indirect contact with water or soil contaminated by the urine of infected rodents or animals.[2,6] Person-to-person transmission is extremely rare since man is a dead-end host for leptospiral dissemination. In contrast, leptospires

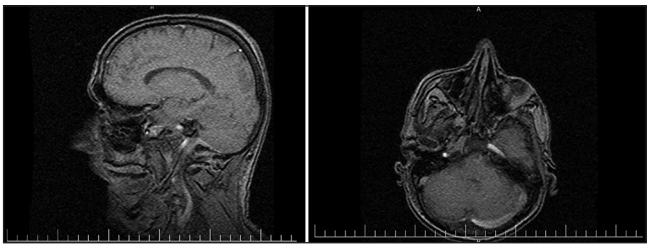

Figure 1: Magnetic resonance imaging

can survive for long periods in the renal tubules of infected animals without causing illness.[11] Most human infections occur in young adult men and children and result from occupational or environmental exposure. Epidemiological studies indicate that infection is commonly associated with certain occupational workers such as farmer, sewage worker, veterinarian, and animal handler.[12]

Leptospirosis present with different complications such as: Pulmonary, GI, neurologic, ophthalmic, cardiac, and musculoskeletal problems.[8]

Neurologic complications due to the leptospirosis are so rare. Among these uncommon cases, aseptic meningitis is the most frequent neurologic complication. As well as encephalitis, intracranial hemorrhage, cerebelitis, movement disorders, flaccid paraplegia includes: Julian bare such as presentation, mononeuritis, neurologia, facial nerve palsy, autonomic lability, and polymyositis are reported as a complication of the central and peripheral nervous system in leptospirosis.[1,9,13] Based on the review of literature, there is only one reported case similar to our case in the world. And also brainstem involvement followed by leptospirosis has not reported yet.

If so, we consider the etiology of the CST and brainstem involvement, the leptospirosis is not mentioned in any literature.

Here, in this study, we reported a case with CST and brainstem involvement simultaneously in a patient with leptospirosis, which could be the first such reported case in the world.

In this case, the interpretation is that; CST and brainstem involvement can occur due to the severe damage to the vessel wall, and given that TTP considered as a complication of leptospirosis, so the TTP could be the cause of CST and even the brainstem involvement.

After proofing of this association as soon as the diagnosis of TTP in patients with leptospirosis, the treatment should be started, in order not leading to serious complications

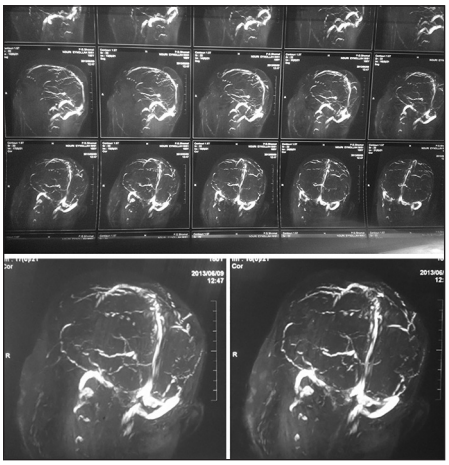

Figure 2: Magnetic resonance venography

such as CST and brainstem involvement, and minimize the mortality.

Early diagnosis of neurological manifestations and complications of leptospirosis is compulsory. It is magistral that physicians have a high suspicion of the disease in endemic areas to prevent false diagnosis. Moreover, suitable and effective treatment can reduce the neurological sequels. Thus, increasing medical community awareness about this disease and its associated complications is essential.

AUTHOR'S CONTRIBUTION

- ShA: Clinical aspect of the report and clinical management in hospital.
- MT: Writing and editing the manuscript and also managing the report process.
- RSh: Data collection.
- MAF: Help in searching thearticles and writing the manuscript.

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Source of Support: Nil, **Conflict of Interest:** None declared.