

Case Report

Acute encephalitis as initial presentation of leptospirosis

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Abstract

Encephalitis is an acute inflammation of the brain matter, very often associated with viral infections, but it can also be caused by non-viral pathogens such as leptospirosis. Leptospirosis is a systemic disease caused by bacteria of the *Leptospira* genus. Leptospiral infection has a broad spectrum of clinical manifestations ranging from subclinical or mild illness to a fulminant life-threatening illness. In this case report we describe a young patient from Southern Albania with isolated encephalitis caused by *Leptospira*, where acute encephalitis was the initial presentation of the disease.

Key words: leptospirosis; encephalitis; CSF.

J Infect Dev Ctries 2017; 11(4):361-363. doi:10.3855/jidc.8613

(Received 25 April 2016 – Accepted 13 August 2016)

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Case Report

The patient, an 18 years old female from Saranda, a city in southern Albania, was referred from another hospital and admitted to the emergency room (University Hospital Center “Mother Teresa”) in September 2016 with temperature of 38.2°C, headaches, nausea and vomiting, photophobia, and generalized myalgias. The symptoms had started 4-5 days prior to admission with fever and disorientation. At the time of admission the patient was alert but not well oriented, her communication was poor and was unable to tolerate any noise. She denied having had any bleeding phenomena, melena or rash. She lived in a village and helped her family with farmer's work. She was not able to provide any further history due to her mental status. Upon initial evaluation, her blood pressure was 115/60 mm Hg, heart rate of 86 beats per minute and respiratory rate of 20 per minute. The patient was alert but oriented to self only, she had no focal neurologic deficits and the rest of the neurological exams were normal. She had no nuchal rigidity and her cardiac, pulmonary and abdominal exams were unremarkable. The skin was without any rashes, and there were no petechiae or jaundice. The initial laboratory workup and imaging studies revealed no abnormalities except from increased creatinine phosphokinase (CPK) levels of 395 U/L. A lumbar puncture was done immediately for diagnostic purpose.

Cerebrospinal fluid (CSF) was clear, with slightly elevated opening pressure. CSF analysis showed 22 WBCs/mm³, all of which were lymphocytes. CSF glucose and protein levels were within normal limits. Serum samples tested for West Nile virus, rickettsiae, tick-borne encephalitis, influenza and brucellosis yielded negative results. On day 4 of hospitalization, taking into account the epidemiological data and the other negative results, it was decided to test for leptospirosis through ELISA testing. Patient's serum samples were tested ELISA-IgM positive and ELISA-IgG negative confirming diagnosis for leptospirosis. Since admission the patient had been treated with ampicillin 6 gram/day, steroids and mannitol against edema. Ampicillin was continued once serological findings were indicative of Leptospirosis. There was a good response to therapy and her condition improved substantially. She was discharged from the hospital seven days after admission. When the patient visited our outpatient clinic for follow-up after 4 weeks, another ELISA test for leptospirosis was performed. This serological examination was negative for IgM and positive for IgG antibodies. Unfortunately we were not able to determine the antibody titer by microscopic agglutination test (MAT), since this test is not available in our country.

The purpose of this report is to present a rare manifestation of leptospirosis, where acute encephalitis was the initial presentation of the disease.

Discussion

Encephalitis is an acute inflammation of the brain matter. The most common infectious agents associated with encephalitis are viruses such as Influenza, herpes simplex, West Nile virus, measles, mumps, rubella, rabies, chickenpox, and arboviruses [1]. Less frequently, acute encephalitis can be caused by bacterial pathogens, including *Leptospira* species. The latter is a widespread zoonosis, especially in regions of tropical climate. Leptospirosis is transmitted through direct contact with the urine of infected animals and can be an important epidemiological problem in these countries. Clinical manifestations of this disease are diverse, making appropriate and timely diagnosis challenging. Leptospirosis can be asymptomatic, present as a flu-like disease or could manifest as a severe form with systemic involvement of kidneys, liver, lungs, heart, pancreas, eyes. The more severe form of the disease is known as Weil's disease, and can carry significant mortality risk [2–6].

Leptospirosis is not uncommon in Albania. The Mediterranean-tropical climate with humid summer and fall favors spreading of leptospirosis. The majority of cases are seen between April-September [6]. In general, rainfall, flooding, urbanization, and outdoor recreation are important emerging risk factors [2]. Symptoms suggesting leptospirosis are non-specific but usually include fever, headache and myalgia, skin rashes and petechiae, sometimes with hemorrhages [4]. Both the literature and our own experience suggest that it is highly uncommon for leptospirosis to present with neurological symptoms as the primary complaint that the patient brings to medical attention. Moderate forms of leptospirosis are very hard to differentiate from viral diseases associated with encephalopathy especially in tropical regions [3]. Even though physicians working in endemic areas for leptospirosis are well aware of the clinical presentation of the disease, challenges still exist, especially when leptospirosis presents with atypical clinical pictures, such as isolated neurological manifestations. Neurological manifestations are seen in 10%-15% of cases and are often missed. *Leptospira* species usually enter the bloodstream through overt or unnoticed skin damage, and then gain access to different tissues or organs through blood stream. Central nervous system (CNS) can be affected directly because of parenchymal infection with *Leptospira* or secondary due to hepatorenal involvement [4].

Panickers *et al* reported that *Leptospira* is able to penetrate into the CSF 48 hours after the inoculation [5]. Our patient presented a classical form of encephalitis, and the challenge was to establish the diagnosis with the causative agent. As stated above, the patient was serologically tested for West Nile virus, rickettsia, tick-borne encephalitis, influenza, brucellosis and EBV in accordance with epidemiological factors of our country. Admittedly, the patient did not have any rashes, which makes some of these agents less likely and actually not many cases of Influenza are seen in September. On the other hand, early fall is the time of the year when most of leptospirosis cases are seen in Albania [6]. Our patient comes from the region of Saranda, which is not one of the endemic areas, but has been the origin of some reported cases. She was involved in farming at her family's farm, and she had reportedly noticed rodents in their property. As we know, rodents are the main reservoirs of *Leptospira* bacteria capable of infecting humans and other animals.

In its classical form of systemic leptospirosis (Weil's disease), involvement of CNS [7] presenting as encephalitis [8], meningitis [9], primary meningitis [10], cerebral venous thrombosis [11], and cerebellitis [12] is well documented. Meningitis can be a significant feature of the clinical profile of leptospirosis, principally in the milder, anicteric forms of the disease. Compared to other cases described in the literature, what makes our case more unique is the initial presentation of the disease as acute encephalitis. The patient's condition had started 4-5 days before being hospitalized with signs and symptoms typical of encephalitis. Through this article we want to emphasize the importance of leptospirosis presenting initially as encephalitis. For example, according to Khan *et al* neurological involvement is usually seen in very severe forms [3]. This was clearly not the case for our patient, as there was no evidence of hepatorenal injury or other end-organ damage. We believe that leptospirosis should be part of the differential diagnosis of isolated encephalitis, especially in endemic areas during the respective typical time of the year. Obviously multiple different diagnostic challenges exist and there are many factors that can delay or impede the appropriate diagnosis of neuroleptospirosis. The clinical presentation is often confused with viral meningitis and many facilities lack diagnostic capabilities, or have difficulties using them in a timely fashion. Sometimes, early empiric use of antibiotics might mask the clinical presentation of the disease and make appropriate diagnosis even more challenging [12]. We believe that,

for patients coming from an area endemic for leptospirosis, this pathogen should be taken into consideration as a possible causative agent of encephalitis. High level of clinical suspicion is crucial for appropriate and timely diagnosis and treatment.

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Conflict of interests: No conflict of interests is declared.