

Rate of leptospiral meningitis and meningoencephalitis in Tehran

Ebrahim Kheirandish, Mahmood Nabavi*, Mostafa Tahaminia

Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University, M.C., Tehran, Iran

ABSTRACT

Background: Leptospirosis is an endemic zoonosis in Iran. One of the most important forms of its presentations is meningoencephalitis. The present study was designed to evaluate leptospiral infection in patients with aseptic meningitis or meningoencephalitis in tertiary care hospitals in Tehran.

Patients and methods: A study was conducted on 20 patients admitted with aseptic meningitis or meningoencephalitis in Imam Hossein Hospital in Tehran. Leptospiral antibodies were detected in acute and convalescent sera and in CSF of infected patients.

Results: Fifteen percent of cases (3 cases) were seropositive for leptospiral antibodies by ELISA. All of these cases presented with meningoencephalitis.

Conclusion: This study suggests that leptospiral infection can be associated with aseptic meningitis or meningoencephalitis, thus, physicians should consider leptospirosis in differential diagnosis of patients presenting with meningoencephalitis.

Keywords: *Aseptic meningitis, Meningoencephalitis, Leptospirosis.*
(Iranian Journal of Clinical Infectious Diseases 2009;4(4):233-236).

INTRODUCTION

Leptospirosis is an endemic zoonosis in Iran. Seroepidemiologic studies in Iran revealed 3.3% seropositivity in humans. Human seropositivity in Tehran was around 3.6% (1). *Leptospira* is excreted in environment by urine of reservoir animals, and transmitted to humans by direct or indirect contact with urine or tissues of infected animals. The disease may have two distinct phases; an initial septicemic stage and an immune phase (2,3). One of the most important presentations in immune phase is aseptic meningitis and

meningoencephalitis; and in 10% of cases, it can be the only manifestation of leptospirosis. In endemic area, leptospiral meningitis accounts for 5 to 40 percent of all cases of aseptic meningitis (4).

Most cases of leptospirosis are diagnosed by serology. Microagglutination test (MAT) is standard but a complex test. Therefore more rapid, simple and sensitive tests including ELISA and IFA have been applied (3). High titer IgM in appropriate clinical setting or fourfold rising titers of IgM or IgG in paired samples is diagnostic of leptospirosis (5,6). Detection of IgM antibodies in CSF can be used in leptospiral meningitis (3,7,8).

Importance of leptospiral meningitis has been noticed in many reports and studies in some

Received: 19 January 2009 Accepted: 12 July 2009

Reprint or Correspondence: Mahmood Nabavi, MD.
Infectious Diseases and Tropical Medicine Research Center,
Shahid Beheshti University, M.C., Tehran, Iran.

E-mail: mahmoodnabavi53@yahoo.com

countries, but it has not been determined in Iran. This study was conducted to evaluate leptospiral infection rate in these patients, for the first time in Iran.

PATIENTS and METHODS

Twenty patients with aseptic meningitis or meningoencephalitis admitted in Imam Hossein General Hospital were evaluated between 2006 and 2008, including 13 men and 7 women. They aged 15 to 78 years. Mean duration of symptoms before admission was 3.7 days.

Diagnosis of meningitis was verified based on CSF pleocytosis in patients with signs and symptoms of meningeal irritation (neck stiffness, headache, nausea and vomiting). If signs and symptoms of encephalitis (alteration in level of consciousness, restlessness, convulsion and others) were present in addition to meningitis, diagnosis of meningoencephalitis was made. In presence of negative smear and routine cultures of CSF, it was referred as aseptic meningitis or meningoencephalitis that usually is associated with lymphocytic pleocytosis and normal CSF glucose level.

Acute serum samples of all patients, and convalescent serum samples and CSF samples of some patients were examined for anti-leptospiral antibodies by ELISA or IFA in two local laboratories. IgM titer greater than 1:20 in IFA method or greater than 1:80 in ELISA method in acute serum, fourfold rising in convalescent serum or detection of IgM in CSF were considered as positive results.

RESULTS

Of 20 patients, 3 were seropositive for leptospiral antibodies by ELISA suggestive of leptospiral infection. Two cases had IgM antibody titers of 1:100 and 1:200 and the other case had fourfold rising in IgG titer. None of these cases

underwent CSF testing for anti-leptospiral IgM. All 3 cases were men, presented with meningoencephalitis, and admitted in summer. None of the cases had risk factors for leptospiral infection including exposure with recreational water or reservoir animals, consumption of contaminated food or water, travel to endemic regions or occupational exposure. Two patients had headache and myalgia. Fever detected in two cases. Pulmonary manifestations, conjunctival suffusion, muscle tenderness, lymphadenopathy, hepatosplenomegaly and jaundice were not present. Renal function tests were normal, but mildly elevated liver aminotransferases was detected in all. Leukocytes were within normal range. CSF analysis did not differ with others, except for lower leukocyte counts. No significant difference was found in age, mean duration of symptoms onset before admission and epidemiologic factors with other patients. Characteristics of 3 cases are shown in table 1. Appropriate antibiotic therapy was commenced in these patients.

DISCUSSION

Aseptic meningitis and meningoencephalitis are illnesses characterized by signs and symptoms of meningitis and/or encephalitis, CSF analysis usually showing lymphocytic pleocytosis and negative smear and routine cultures for bacteria. One of their causes is leptospirosis.

In a study in Salvador, leptospiral infection was detected by MAT in 7.12% of 112 patients with aseptic meningitis (9). Positive serology in 3 patients in our study is suggestive of leptospiral infection; but for confirmation, more specific tests including detection of leptospiral DNA in CSF by PCR should be performed. Our study suggests that leptospiral infection can be a cause of aseptic meningitis or meningoencephalitis in 15 percent of cases. That is in agreement with Silva MV study, in which IgM antibody was demonstrated in 14.6% of CSF samples from 171 patients with meningitis (7).

Table 1. Characteristics of 3 patients with meningoencephalitis and positive serology for leptospiral infection

	Case 1	Case 2	Case 3
Sex	Male	Male	Male
Age (years)	29	72	36
Onset of symptoms before admission	7 days	3 days	10 days
Symptoms and signs	Headache, Nausea and vomiting, Myalgia, Agitation, Neck stiffness	Fever, Nausea, Delirium, Neck stiffness	Headache, Fever, Myalgia, Delirium, Seizure, Neck stiffness
CSF			
WBC	32	11	10
PMN	10%	10%	---
Lymph.	90%	90%	---
Glucose	39	50	100
Protein	80	10	28
RBC	---	---	1380
Blood sugar (mg/dl)	---	132	130
WBC	8400	7600	6700
PMN	76%	67%	69%
Lymph	13.5%	16%	14%
U/A	Normal	Normal	Normal
BUN/Cr	Normal	Normal	Normal
ESR (mm/hr)	---	82	12
AST(u/l)	35	47	65
ALT(u/l)	47	20	101
Bilirubin(mg/dl)	Normal	Normal	Normal
Received treatment	Ceftriaxone	Ceftriaxone	Ceftriaxone

In a study in Philippines, 100 patients with aseptic meningoencephalitis were screened for leptospirosis. With MAT assay the diagnosis was made in five cases. None of the cases was complicated by renal dysfunction or jaundice (10). In our study, epidemiologic factors, clinical presentations or laboratory values suggestive of leptospirosis were not present. However, in our study mildly elevated liver aminotransferases and admission in summer may be predictors of leptospiral infection. All 3 cases in our study presented with meningoencephalitis, which is comparable with one report that described an outbreak in children who bathed in a channel. Six cases were reported, of which four had meningoencephalitis appearance (11).

Our study had some limitations. Sample size was quite small. Evaluation of IgM antibodies in CSF was not achieved in all patients due to ethical concerns of re-LP; and of convalescent serology due to lack of patients adherence. Unavailability of CSF-PCR was another limitation. Other causes of aseptic meningitis or meningoencephalitis and elevated liver aminotransferases were not ruled out.

In conclusion, this study suggests that leptospiral infection can be considered a cause of aseptic meningitis and especially meningoencephalitis in Iran, hence, physicians should consider leptospirosis in differential diagnosis of patients presenting with meningoencephalitis. Further studies are strongly recommended to evaluate leptospiral infection rate

in patients with aseptic meningitis or meningoencephalitis in Iran with greater sample size, in other age groups and with more reliable, sensitive and specific methods including CSF-PCR test.

ACKNOWLEDGEMENT

The authors would like to thank the Infectious Diseases and Tropical Medicine Research Center for providing the scientific support for this study and from Dr. M.Asmar, Professor of Parasitology for his expert recommendations.

REFERENCES

1. Sebek Z, Bashiribod H, Chaffari M, Sepasi F, Sixl W. The occurrence of leptospirosis in Iran. *J Hyg Epidemiol Microbiol Immunol*. 1987;31(4 Suppl):498-503.
2. Center for food security and public health. Leptospirosis. 2005; [7 screens]. Available at: URL: <http://www.cfsph.iastate.edu/factsheets/pdfs/leptospirosis.pdf>. Accessed 20 Oct 2007.
3. Levett PN. Leptospirosis. *Clin Microbiol Rev*. 2001;15(2):296–326.
4. de Souza AL. Neuroleptospirosis: unexplored and overlooked. *Indian J Med Res*. 2006;124:125-28.
5. Ahmad SN, Shah S, Ahmad FMH. Laboratory diagnosis of leptospirosis. *J Postgrad Med*. 2005;51:195-200.
6. Terpstra WJ, et al. Human leptospirosis: guidance for diagnosis, surveillance and control. WHO, ILS. 2007. Available at URL: <http://www.emedicine.com/neuro/topic 697.htm>. accessed 10 Dec. 2007.
7. Silva MV, Camargo ED, Batista L, Vaz AJ, Ferreira AW, Barbosa PR. Application of anti-leptospiral ELISA-IgM for the etiologic elucidation of meningitis. *Rev Inst Med Trop Sao Paulo*. 1996;38(2):153-6.
8. Romero EC, Billerbeck AE, Lando VS, Camargo ED, Souza CC, Yasuda PH. Detection of leptospiral DNA in patients with aseptic meningitis by PCR. *J Clin Microbiol*. 1998;36(5):1553-5.
9. Silva HR, Tanajura GM, Tavares-Neto J, Gomes Md Mde L, Linhares Ad Ada C, et al. Aseptic meningitis syndrome due to enterovirus and *Leptospira* spp. in children of Salvador, Bahia. *Rev Soc Bras Med Trop*. 2002;35(2):159-65.
10. Watt G, Manaloto C, Hayes CG. Central nervous system leptospirosis in the Philippines. *Southeast Asian J Trop Med Public Health*. 1989;20(2):265-9.
11. Suárez Hernández M, Bustelo Aguila J, Pérez González L, Gorgoy González V. Outbreak of leptospirosis, predominantly meningoencephalitic, among children in the municipality of Morón. *Rev Cubana Med Trop*. 1991;43(2):136-9.