Rate of leptospiral meningitis and meningoencephalitis in Tehran

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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.

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
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 meningial 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 leptospirosis. For confirmation, more specific tests including detection of leptospiral DNA in CSF by PCR should be performed. Our study suggests that leptospirosis 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).
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.

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

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

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REFERENCES


