Primary neuroleptospirosis

J N Panicker, R Mammachan, R V Jayakumar

Abstract
Leptospirosis is an important zoonosis of worldwide distribution. It is uncommon for leptospirosis to present as a primary neurological disease. In this study of patients who presented with an acute neurological disease, and who were subsequently found to have leptospirosis, aseptic meningitis was the commonest manifestation. The other presentations were myeloradiculopathy, myelopathy, Guillain-Barré syndrome-like presentation, meningoencephalitis, intracerebral bleed, cerebellar dysfunction, iridocyclitis, and tremor/rigidity. Treatment consists of antibiotics, crystalline penicillin being the drug of choice, which reduces the course of illness if given early. The role of steroids is controversial. The prognosis after primary neuroleptospirosis is generally good but altered sensorium and seizures herald a worse prognosis. (Postgrad Med J 2001;77:589–590)

Keywords: neuroleptospirosis; aseptic meningitis; Weil's disease

Leptospirosis is an important zoonosis caused by pathogenic leptospires and is characterised by a broad spectrum of clinical manifestations ranging from inapparent infection to fulminant and fatal disease. The spirochetes are transmitted after direct contact with urine, blood, or tissue from infected rodents. The pathogenic form, Leptospira interrogans, consists of 23 serogroups such as icterohaemorrhagiae, canicola, and pomona which are in turn comprised of nearly 200 serovars.1 After an incubation period of one to two weeks, leptospirosis manifests as a biphasic illness consisting of an initial leptospiroemic phase lasting three to seven days followed by an immune phase lasting four to 30 days.2 The clinical spectrum of the disease ranges from the mild anicteric leptospirosis manifesting as an influenza-like presentation of fever and myalgia to the far more serious Weil's syndrome, comprising jaundice, renal dysfunction, and bleeding diathesis.3 It is a disease of worldwide distribution, predominantly involving tropical and rural areas. Epidemics may be associated with periods of flooding. Cases in developed countries are related more to recreational activities such as swimming. Cases of leptospirosis are underreported, with 1500–2000 cases being reported globally every year.4 While the annual incidence was 150 cases in Australia. From Barbados (Caribbean) 31 cases were reported while from Polynesia 153. The incidence at this hospital is around 800 cases per year and constitutes 3.5% of admissions in the medicine wards.

This study aims to delineate the neurological manifestations of leptospirosis and reports on patients with leptospirosis who presented initially with a neurological disease.

Patients and methods
Patients admitted to the general medicine wards of our hospital during the period of 1996 to 1999 for acute neurological disease and who were found to have leptospirosis were included. Enzyme linked immunosorbent assay (ELISA) for leptospira antibody (Serion ELISA classic for leptospira IgM, IgG/quantitative; associated with 100% sensitivity and 94% specificity) was used to identify such patients.

Results
Forty patients presenting with an acute neurological disease were found to have leptospirosis. The various neurological manifestations are given in box 1.

In 13 patients, the initial manifestations were fever, headache, and neck stiffness and analysis of the cerebrospinal fluid (CSF) established the diagnosis of aseptic meningitis. The mean CSF protein concentration was 1.1 g/l and CSF glucose 2.5 mmol/l. The highest cell count noted was 150 × 10^3/l, predominantly lymphocytes.

Paraparesis was the initial presentation in 17 patients. Initial flaccidity followed by hyper-reflexia and extensor plantar response was seen in 14 patients and seven of these patients showed radicular involvement as well. Three patients had a lower motor neuron paraparesis. Thus the diagnosis of myelopathy was made in seven patients, myeloradiculopathy in seven, and Guillain-Barré syndrome-like presentation in three.

Box 1: Cases of primary neuroleptospirosis
Aseptic meningitis: 13
Myeloradiculopathy: 7
Myelopathy: 7
Guillain-Barré syndrome-like presentation: 3
Meningoencephalitis: 3
Intracerebral bleed: 2
Cerebellar dysfunction: 2
Iridocyclitis: 2
Tremor/rigidity: 1

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Phocytic pleocytosis less than 500 raised to 0.4–3.0 g/l, normal glucose, and lymphocytic pleocytosis less than 500 × 10⁹/l. While antibodies may be detected during this phase, leptospira cannot be isolated.

**Discussion**

It is uncommon for leptospirosis to present as a primary neurological disease. The progression of neurological manifestations in patients with leptospirosis follows a pattern: the first phase is dominated by clouded sensorium and meningism while the second phase is characterised by classical neurological features (box 2). Leptospires reach the CSF and brain as early as 48 hours after inoculation. The differential diagnosis of neuroleptospirosis is given in box 3.

**Aseptic meningitis**

Leptospirosis is responsible for 5%–13% of all cases of aseptic meningitis. The commonest manifestation of neuroleptospirosis is aseptic meningitis. While 50%–90% of patients have CSF pleocytosis, only half of these patients have clinical features. The common serotypes implicated are canicola, icterohaemorrhagiae, and pomona. During the leptospiraemic phase, signs of meningeal irritation are uncommon, opening CSF pressure is usually raised and leptospira can be isolated from the CSF, while cytology and biochemistry of the CSF are usually normal. The immune phase is mediated by immune complexes and is characterised by the classical manifestation of headache, vomiting, and meningeal irritation. Examination of the CSF reveals raised opening pressure, proteins raised to 0.4–3.0 g/l, normal glucose, and lymphocytic pleocytosis less than 500 × 10⁹/l. While antibodies may be detected during this phase, leptospira cannot be isolated.

**Intracranial bleed**

An intracranial bleed arises as a result of thrombocytopenia, hypoprophosphominaemia, and vasculitis and commonly manifests as subarachnoid bleed and extradural haematoma.

**Ocular manifestations**

During the leptospiraemic phase, leptospira seed the aqueous humour and infection persists long after the illness disappears. Uveitis is the commonest manifestation. Chorioretinitis, papilloedema, papillitis, optic neuritis, retinal bleed, and cotton wool spots are other manifestations of leptospirosis in the eyes.

**Pathology**

Most of the clinical features are due to capillary endothelial damage and vasculitis. Nervous system involvement is essentially immune mediated and gross changes include exudates, leptomeningeal oedema, brain and spinal cord congestion, and haemorrhage. Microscopically, perivascular round cell infiltration of small and medium sized blood vessels along with patchy demyelination are the prominent features.

**Prognosis**

Prognosis of neuroleptospirosis is generally good. Meningitis usually resolves by 3–6 weeks. Encephalomyelitis resolves after a few weeks to months, mononeuritis multiplex cranialis within 1–2 months, and Guillain-Barré syndrome-like presentation by 6–8 weeks. Altered sensorium and seizures herald a worse prognosis. Rarely, sequelae can occur including uveitis, deafness, and chronic meningitis.


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