

# Acute Disseminated Encephalomyelitis Following Leptospirosis

SR Chandra\*, D Kalpana\*\*, TV Anilkumar\*\*, KA Kabeer\*\*\*, P Chithra\*\*\*, Rani Bhaskaran\*\*\*\*

## Abstract

Acute disseminated encephalomyelitis is very rare following leptospirosis. Here we describe a patient who developed the condition after leptospiral infection, which responded to intravenous immunoglobulin only. ©

## INTRODUCTION

Leptospirosis is a spirochetal infection with a clinical spectrum ranging from asymptomatic to a life-threatening disease called Weil's syndrome. On the other hand, postinfectious or postvaccinal acute disseminated encephalomyelitis (ADEM) typically occurs 1-4 weeks after an inciting febrile or exanthematous illness or an immunization. To date, only a few cases of ADEM associated with leptospiral infection have been reported.<sup>1</sup> Here we report a case of severe ADEM in a patient with leptospirosis, which was only partially responsive to methyl prednisolone that recovered completely after treatment with intravenous immunoglobulin.

## CASE REPORT

A 47-year-old lady, working as an office assistant, was admitted to our critical care unit with history of worsening of sensorium. She was going to office and doing all the household jobs till one-week back. She developed low-grade fever and severe myalgia lasting for 3 days. Following that she complained of general weakness, and dimness of vision. The next day she was unable to walk, there was dragging of right foot and she had difficulty in making a bolus of food with the right hand. She became drowsy 2 days before admission to our unit and was receiving treatment from the nearby hospital. She did not have seizures at anytime. There was no history of diabetes, hypertension, arthralgia, arthritis or skin rash.

At the time of admission, she was febrile (temp-100°F), the vitals were stable; there was no icterus, pallor, skin rashes or lymphadenopathy. Eyes showed bilateral bulbar conjunctivitis with subconjunctival hemorrhages. She was stuporous, responding to painful stimuli only (Glasgow Coma Scale -7); the pupils were equal and reacting to light.

The right upper limb was kept in a decorticate posture and there was decreased spontaneous movement of right upper and lower limbs. Fundus examination was normal; there was no evidence of optic neuritis or papilloedema. She had no neck stiffness; Kernig's sign was negative.

As she had a rapidly progressive encephalopathy following a febrile illness with severe myalgia, conjunctivitis with subconjunctival hemorrhages, leptospirosis with encephalitis was considered the first possibility and viral encephalitis or acute disseminated encephalomyelitis were considered as the differential diagnoses.

The investigations showed a normal CBC and ESR. The blood sugar, urea, electrolytes and creatinine were normal. She had a serum bilirubin of 0.8 mg%, SGOT-94 and SGPT-125. The creatine phosphokinase was elevated (522 IU). ANA, LE cell, rheumatoid factor, and anticardiolipin antibodies were negative.

The lumbar puncture yielded clear cerebrospinal fluid under normal tension. The cell count was 10 cells/cmm and all the cells were lymphocytes. Proteins -45 mg% and sugar 80 mg%. The CSF culture showed no growth of bacteria. The herpes simplex antibody (IgM) was negative. Oligoclonal bands were negative in CSF.

She underwent a CT scan of brain on the second day after admission, which showed small ill-defined areas of hypodensity in basal ganglia, thalamus and subcortical white matter. A magnetic resonance imaging of brain was done on the following day, which showed multiple well circumscribed lesions in the subcortical white matter, corpus callosum, both thalami, and basal ganglia and upper brainstem (Figs. 1,2). There were no lesions in the infratentorial compartment. The lesions were hypointense on T1 and hyperintense on T2 with minimal contrast enhancement. The possibilities thought of were a primary demyelinating disease like multiple sclerosis or acute disseminated encephalomyelitis.

The leptospira antibody titer was positive at the time of admission and there was a four-fold rise in titer when repeated

\*Professor; \*\*Resident; \*\*\*Senior; \*\*\*\*Head of Department, Department of Neurology, Medical College, Thiruvananthapuram, Kerala.

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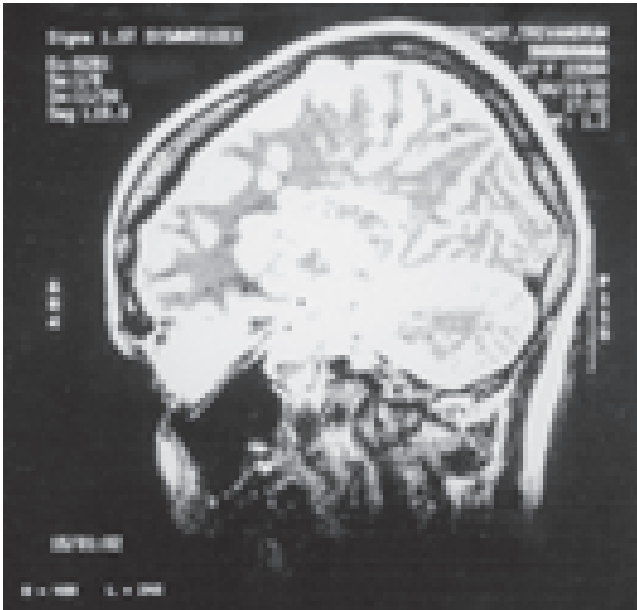


Fig. 1 : MRI T2 weighted image, sagittal section. Note multiple plaques in subcortical region and corpus callosum.

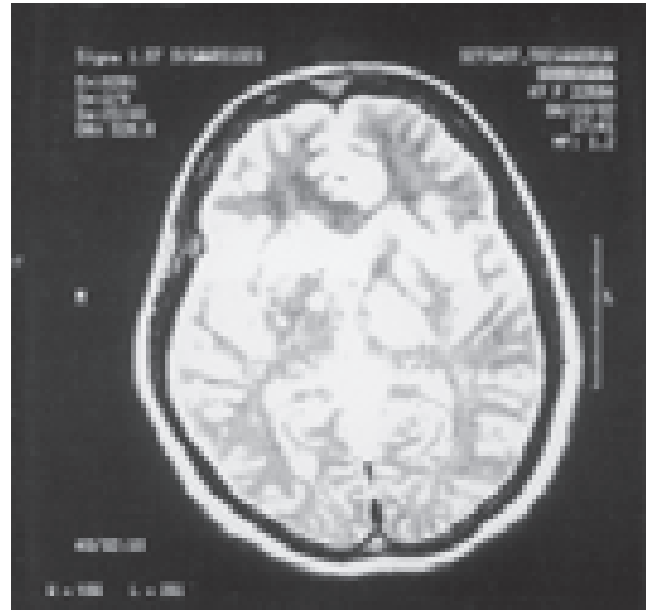


Fig. 2 : MRI T2 weighted image, multiple plaques in the white matter, both thalami (left more than right) and basal ganglia.

after 2 weeks (Quantitative IgM haemagglutination test).

She was started on high dose crystalline penicillin, acyclovir and methyl prednisolone -1 gm IV daily for five days. She became afebrile, the sensorium improved, there was spontaneous eye opening, she was withdrawing limbs in response to pain and was obeying one step commands. She was put on oral steroids after the five-day course of methyl prednisolone. Within three days the sensorium deteriorated, the upper limbs went into decerebrate posturing in response to pain. There was no response to calls or painful stimuli. She remained in this state for four days.

Intravenous gamma globulin was started as a last resort (20 gm daily for 5 days). She showed signs of improvement from the third day of immunoglobulin treatment. She started responding to pain, and later to calls. She could move the limbs in response to painful stimuli, even though there was scarcity of movements on the right side. There was hypertonia of the right upper and lower limbs. Bedside physiotherapy was started and supportive measures continued. After a week she opened the eyes, and started to talk a few words. The speech was slurred. By this time, she could identify her relatives and was taking food orally.

She was put on oral steroids for 8 weeks, which was tapered and stopped in a month. Physiotherapy was continued and by about 6 weeks she was able to walk without support. She was able to look after the household activities and rejoined duty after three months. There was no relapse of symptoms for the last 9 months. She has no residual neurologic deficits at present.

MRI brain was repeated 6 months after the first imaging. (Figs. 3,4) Most of the hyperintense lesions in the T2 weighted imaging had disappeared by now and no new lesions had appeared confirming the clinical diagnosis of acute disseminated encephalomyelitis.

## DISCUSSION

Here the patient presented with a rapidly progressive encephalopathy following a one-week history of fever myalgia, conjunctivitis and a raised antileptospiral antibody titer. The cerebrospinal fluid examination ruled out an intracranial infection. All the investigations for vasculitidae were negative. The MR imaging suggested a demyelinating process. The presence of thalamic, basal ganglionic and brainstem lesions and the strong history of preceding infection favored ADEM. The almost complete disappearance of lesion without the development of new lesion in the follow up MRI after 6 months confirmed the diagnosis.

Leptospirosis is a zoonotic disease caused by the spirochete, *Leptospira interrogans*. The severity varies from asymptomatic infection to the hepatorenal syndrome (Weil's disease). *Leptospira* can affect the central nervous system frequently.<sup>2</sup> The manifestations include aseptic meningitis, encephalitis, Guillain Barre syndrome, cerebellar ataxia etc. Acute disseminated encephalomyelitis has been described following leptospira,<sup>1</sup> even though the incidence is rare. In the large series of 40 patients of neuroleptospirosis, no patient had ADEM.<sup>2</sup> Our patient presented with features of encephalopathy, one week after the onset of fever, myalgia and conjunctivitis and had a high titer of antileptospira antibodies at admission, corresponding to the immune phase of the disease. The serum level of CPK was raised; however she had normal liver and renal function. Weil's syndrome (fulminant hepatorenal syndrome) need not be present in all cases of neuroleptospirosis.<sup>2</sup> In the only case report of ADEM after leptospira infection also the liver function tests were normal. (Alonso-Valle H, *et al*).<sup>1</sup>

ADEM is an autoimmune disease with formation of antibodies cross-reacting with myelin. The disease had a bad prognosis with a mortality of 20-30%, till the efficacy of methyl

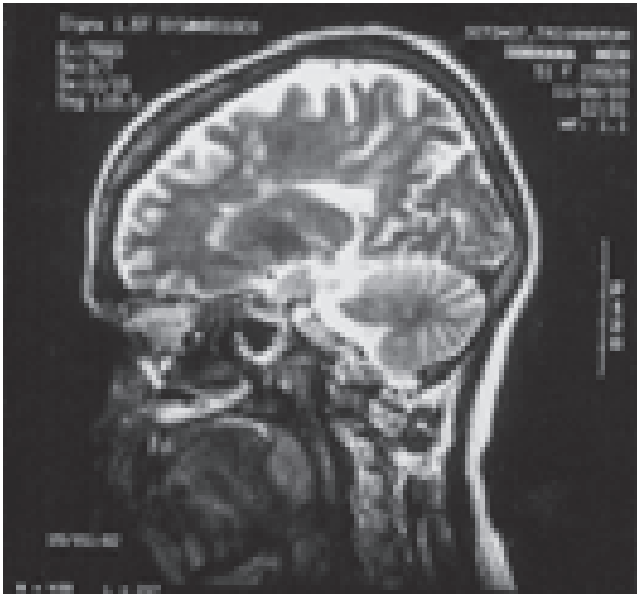


Fig. 3 : MRI T2 sagittal image after 6 months - most of the lesions have disappeared and there are no new lesions.

prednisolone was established beyond doubt. Recent case series shows a better prognosis with only 5% mortality and 20% disability among survivors,<sup>3</sup> but a significant proportion develops multiple sclerosis later. The presence of multiple lesions, especially periventricular and those involving corpus callosum and variable degree of enhancement suggesting different age of lesions increase the probability of progression to multiple sclerosis. The development of new lesions in follow up MRI also predicts development of multiple sclerosis later. The initial MRI showed multiple lesions involving the corpus callosum in our patient and multiple sclerosis was one of the differential diagnoses given by the radiologists. There were lesions in both thalami, basal ganglia and brainstem, which are more common in ADEM. The follow up scan after 6 months showed disappearance of most of lesions and no new lesions were demonstrable strongly favoring a monophasic illness like ADEM.

As ADEM is an autoimmune disease various immunosuppressive modalities have been tried against it. Methyl prednisolone treatment has improved the prognosis of this condition.<sup>4,6</sup> In patients not responding to steroids, plasmapheresis and immunoglobulin were tried. Pradhan *et al*<sup>6</sup> and Sahlas *et al*<sup>5</sup> reported significant improvement with intravenous immunoglobulin when the patients deteriorated

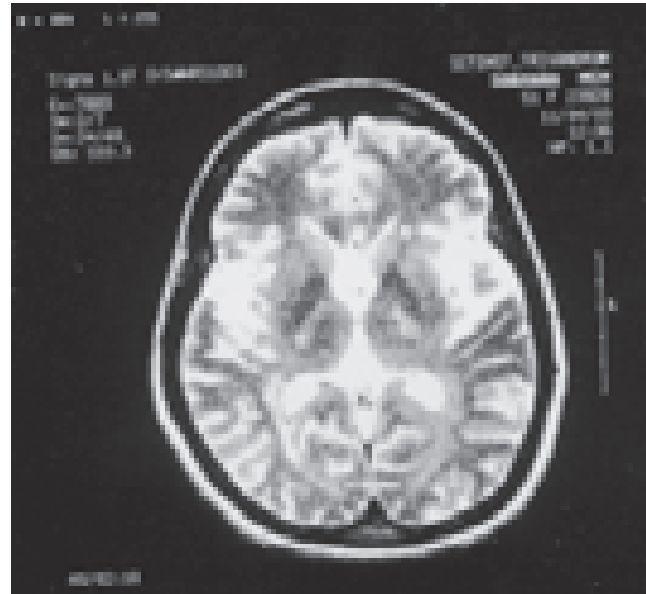


Fig. 4 : MRI T2 axial image after six months - most of the lesions have disappeared and there are no new lesions.

on methyl prednisolone. Pradhan *et al*<sup>6</sup> recommends IVIG in fulminant cases of ADEM not responding to methyl prednisolone. Use of gamma-globulin may help in saving lives in patients not responding to standard doses of intravenous methyl prednisolone.

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#### Announcement

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