

## Short Communication

# Guillain-Barré Syndrome in a Pediatric Patient Following Infection Due to *Leptospira*

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**SUMMARY:** Leptospirosis is a disease with protean manifestations. We report a case of Guillain-Barré syndrome (GBS) in a pediatric patient following infection with *Leptospira*. Infecting *Leptospira* presumably belonged to serovar Copenhageni. The patient recovered completely. The possibility of GBS developing as a result of antecedent leptospiral infection should be kept in mind.

Leptospirosis is usually a biphasic febrile illness composed of a septicemic phase and an immune phase (1). The commonest neurological manifestation in leptospirosis is aseptic meningitis which usually lasts for only a few days and is possibly immune mediated (2). Peripheral nerve involvement following leptospiral infection is rare. We report a case of Guillain-Barré syndrome (GBS) which occurred following infection with *Leptospira interrogans* serovar Copenhageni.

A 12-year-old girl presented with weakness of both lower limbs for 6 days. The patient was residing in a small village near Pune, a city in western India. She gave a history of fever, headache, myalgia, and cough for the previous 3 weeks for which she was treated by a local practitioner. Details of the treatment could not be obtained. There was no history of diarrhea, vomiting, urinary incontinence, urinary retention, trauma, or antecedent vaccination. There was no history of any febrile illness in the past 1 year. General examination revealed a normal pulse rate (80/min) and blood pressure (104/76 mm of Hg). On neurological examination, the patient had diminished (grade 2) muscle power in the lower extremities. Muscles in the lower extremities were hypotonic accompanied by diminished tendon reflexes demonstrated by loss of knee jerk and ankle jerk. Plantars were flexors. No sensory abnormalities were noted. Neurological examination of upper extremities was normal. No involuntary movements were seen and there were no signs of cerebellar involvement. No auditory and visual abnormalities were found on examination and cranial nerve palsies were not detected. The patient was well oriented in time and space. Cardiovascular, respiratory and per abdomen examinations were normal. Roentgenogram of the spine did not show any abnormality. The patient was hospitalized. During the first week of hospital admission, the patient developed urinary incontinence requiring a continuous indwelling catheter. Subsequently, she developed weakness of upper extremities as well with reduced tone and power as judged clinically, accompanied by loss of biceps and triceps jerk. Weakness was bilaterally symmetrical. However, she did not suffer from respiratory paralysis and no ventilatory

support was required. The patient was diagnosed as a case of GBS and was kept under observation for 6 weeks.

On investigation at the time of presentation, her hemoglobin was 10 gm%, total leucocyte count was  $12 \times 10^9/L$ , and platelet count was  $300 \times 10^9/L$ . Erythrocyte sedimentation rate was 5 mm at the end of 1 h. Her blood urea (22 mg%), serum creatinine (0.9 mg%), serum bilirubin (0.9 mg%), alkaline phosphatase (110 units/L), and electrolyte values (sodium 140 mmol/L; potassium 3.9 mmol/L) were within normal limits but levels of aspartate amino-transferase (110 units/L), alanine amino-transferase (96 units/L) and creatine phosphokinase (CPK) (270 units/L) were elevated. Cerebrospinal fluid (CSF) examination revealed a raised protein level (287 mg%), a normal glucose level (52 mg%) and no cellularity. CSF culture did not yield any bacterial growth. She had negative serologies for HIV and Hepatitis B surface antigen. Widal test was negative. On the basis of her history of antecedent fever with myalgia, moderately elevated hepatic enzyme levels, and elevated serum CPK at presentation, serum obtained on the second day of admission was tested for antibodies to *Leptospira* by immunoglobulin (Ig) M specific indirect immunofluorescence assay (IFA) and by microscopic agglutination test (MAT). MAT was carried out using a battery of representative serovars, namely, Australis, Autumnalis, Bataviae, Canicola, Copenhageni, Grippotyphosa, Hebdomadis, and Pomona. Patoc-I strain of *L. biflexa* serogroup Semaranga serovar Patoc was also included in the test. This saprophytic strain behaves as a genus-specific antigen and detects antibodies against most pathogenic serovars (3). Leptospiral strains were obtained from the WHO-FAO Collaborating Centre for Reference and Research on Leptospirosis, Brisbane, Australia. All strains were maintained in Ellinghausen-McCullough-Johnson-Harris medium. MAT was put as per standard methods and the serovar that reacted most strongly was considered as the infecting serovar (4). CSF sample was also tested for antibodies to *Leptospira* by MAT following a leptospiral serology report. MAT was carried out on CSF sample using dilutions from neat to 1:400. Serovar Patoc was used as an antigen for IFA, and IgM antibodies in the patient's sample were detected with the help of fluorescein isothiocyanate conjugated anti-human IgM (Rashmi Diagnostics, Bangalore, India). The test was performed as per standard protocol (5). A convalescent serum sample obtained

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3 weeks from the date of collection of the first sample and a third serum sample obtained 6 months after illness were also subjected to MAT and IFA. Dark field microscopic observation was also carried out on urine and CSF samples. Using enzyme-linked immunosorbent assay (ELISA), acute and convalescent sera were tested for IgM antibodies to cytomegalovirus (Bremancos Diagnostic Inc., Brampton, Ontario, Canada) and *Mycoplasma pneumoniae* (Cal Biotech Inc., Spring Valley, Calif., USA). Sera were also tested for IgM antibodies to Japanese encephalitis virus, dengue fever virus and West Nile fever virus at the National Institute of Virology, Pune, India by ELISA indigenously developed at the institute.

The acute phase serum sample was shown positive by MAT with a titer of 6400 reactive against serovar Copenhageni. The convalescent sample showed a fall in titer to 800 also reactive against serovar Copenhageni. Titers greater than 400 possibly reflect recent infection even in endemic areas (6). No cross reactivity with other pathogenic serovars was observed in either serum sample. However, both sera were reactive to serovar Patoc at a titer of 400. The acute phase serum was positive by IFA but the convalescent sample was negative. Based on these observations, neuropathy was thought to be triggered following leptospirosis. The third sample was positive by MAT at a titer of 200 but negative by IFA. MAT carried out on CSF was negative. Dark field microscopy was also negative. Sera were negative for IgM antibodies to cytomegalovirus, *M. pneumoniae*, and Flaviviruses. The patient was administered intravenous penicillin G 1.5 million units every 6 h for 5 days. Plasmapheresis and intravenous Ig therapy could not be given due to economic constraints. During the period of observation, there was slow but steady improvement in her clinical course. Supportive physiotherapy was also provided during this period. Only a mild residual weakness was present at the time of discharge. The patient was followed up for 7 months. She made a complete recovery.

GBS is an illness characterized by areflexic motor paralysis with mild sensory involvement and acellular rise in CSF total protein. It has been reported as sequelae to several infections including *Campylobacter jejuni* gastroenteritis and infections due to Epstein-Barr virus and cytomegalovirus. Other cases occur on a background of Hodgkin's disease, systemic lupus erythematosus, and lymphoma (7). Recently, antecedent Japanese encephalitis virus infection was suspected as a cause of GBS in 60% of cases in endemic regions of southern India (8). In another report from India, 26% of cases had high antibody levels to *C. jejuni* Penner serotype O19 (9). Although its pathogenesis is not clear, GBS may be induced by molecular mimicry, toxin, or immune dysregulation (10). Molecular mimicry has been suspected to play a role in *C. jejuni*- and cytomegalovirus-induced GBS (11,12). However, immunological studies delineating the mechanism for neuropathy triggered by *Leptospira* have not been carried out perhaps because of the rare association.

In the present report, the polyneuropathy followed approximately 3 weeks after an acute febrile illness. The history and investigations were compatible with GBS notably symmetric ascending muscular weakness and albumino-cytologic dissociation in the CSF. MAT titers were suggestive of a recent leptospiral infection. As the MAT titers were highest against serovar Copenhageni, it was presumably the infecting serovar. We have earlier reported leptospirosis due to serovar Copenhageni from sporadic as well as epidemic cases from

western India (13,14). Morgan and Cawich also reported a case of GBS which was triggered following infection with *L. icterohaemorrhagiae* in a 65-year-old woman (15). Other reported cases of flaccid paraplegia following leptospirosis have been diagnosed only on the basis of IgM-ELISA serology without any information regarding the probable identity of the infecting serovar (16,17). In these earlier reports, acute neuropathy was not the sole presentation but was noted in association with renal failure (15) or jaundice (16).

A definite relationship between an infection episode and neuropathy is difficult to establish as in most cases it is not possible to isolate the causative organism by the time neuropathy appears. The diagnosis is usually ascertained on the basis of relevant serological tests. In the present report, a history of fever, headache, and severe myalgia 3 weeks before the onset of neuropathy and elevated CPK levels at presentation were compatible with leptospirosis. A relatively high titer of agglutinating antibodies to *Leptospira* and detection of anti-leptospira IgM antibodies by IFA and negative serology for other possible etiologies support the presumption that neuropathy was triggered by a recent leptospiral infection although some relevant investigations such as detection of antibodies to *C. jejuni* could not be undertaken. Antibiotic therapy shortens the duration of illness even late in leptospirosis (18) and in the absence of data regarding such clinical situations the decision to administer penicillin was made.

Although leptospirosis can often be clinically suspected in its classic presentation, anicteric manifestations and rare manifestations such as pancreatitis, uveitis, and neuropathy are difficult to diagnose without a high index of suspicion and adequate laboratory support. This case illustrates that peripheral neuropathy can be triggered by infection with *Leptospira* and relevant history should be sought in similar cases.

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