Focal Neurological Manifestations in Legionellosis

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Abstract
Legionnaires’ disease is an atypical pneumonia with protean multisystem manifestations. Neurological involvement in legionellosis is rare and tends to be among the presenting manifestations. We report a previously healthy young lady who developed focal sensory deficits and cerebellar dysfunction after clinical recovery from \textit{Legionella} pneumonia. The care is unusual for the delayed appearance of striking focal sensory abnormalities and cerebellar dysfunction.

INTRODUCTION
Legionnaires’ disease was initially described as a pneumonic illness among delegates to the 1976 American Legion Convention in Philadelphia\(^1\) and is now more appropriately named legionellosis to emphasize its multisystem features.\(^2\) It is caused by \textit{Legionella pneumophilia}, a Gram-negative aerobic bacillus. The causative bacillus is difficult to isolate and the diagnosis rests on serology.\(^2\)

Almost every component of the nervous system can be affected in legionellosis and the spectrum of clinical manifestations ranges from subtle confusion to frank encephalopathy in the central nervous system to peripheral neuropathy and myositis in the peripheral nervous system.\(^1\) The proposed mechanisms for the neurologic affection are a direct invasion of the neurons, elucidation of a neurotoxin and immune mediated damage.\(^1,3\) The neurological changes tend to present early in the illness. Here we report a patient who developed neurological signs later in the course of the illness.

CASE REPORT
A 24-year-old staff nurse working in an urban tertiary care hospital presented with complaints of fever with chills, reddish brown coloured urine and generalized abdominal pain since two days. She was admitted in a surgical unit with a clinical diagnosis of probable renal calculus with a urinary tract infection. Her investigations revealed a total leucocyte count of 7800/cumm, haemoglobin of 11g%, a normal platelet count and an ESR of 35 mm at the end of one hour. Her urine was negative for occult blood and RBCs. Renal biochemistry and a plain abdominal radiograph was normal. Over the next one week she developed myalgias, dry cough, right-sided pleuritic pain and progressive breathlessness. At this time a medical consult was sought. On examination she was febrile and tachypneic with mild hepatomegaly with tenderness in the right hypochondrium. Respiratory, cardiovascular and neurological examination revealed no other abnormality. Further investigations showed a markedly raised creatine kinase (CK) of 1538 U/ml (normal 21-232), LDH of 244 U/ml (normal 100-190), AST of 63 U/ml (normal 15-37) and a chest x-ray showed infiltrates in the right lower lobe. An immunofluorescent antibody test for legionella was positive in a dilution of 1:10. She was started on Azithromycin and Gatifloxacin and started improving in terms of fever, myalgias, chest pain and cough.

On day 10 of hospitalization she noticed tremors in the left upper limb along with numbness and weakness in her left thumb and index finger, which manifested as an inability to grasp objects with her left hand. Examination revealed a slightly pale, afebrile young lady with a pulse rate of 96/minute, blood pressure of 126/70 mm Hg and a respiratory rate of 28/minute. Her higher mental functions and speech were normal. She had fine nystagmus with the fast component towards the left. Other cranial nerves were normal. There was motor weakness in the left upper limb with a power of 4/5 at the shoulder and the elbow, 3/5 at the wrist extensors. The left thumb extensors and opponens pollicis were week with a power of 2/5. She also had weakness of the small muscles of the hand. She could not appreciate pinprick and thermal sensations in a small area over the dorsal aspect of the left thumb. All other sensory modalities were preserved. Superficial and deep tendon reflexes were present. She had mild truncal ataxia along with finger-nose ataxia in the left upper
limb. The rest of the neurologic and systemic examination did not reveal any abnormalities.

The patient was investigated with a gadolinium-enhanced MRI of the brain and spine in view of the cerebellar signs and an EMG for the focal sensory deficits, both of which were completely normal. Reevaluation of her laboratory data at this time showed normal metabolic and haematologic parameters, except for an ESR of 30 mm at the end of one hour. A repeat immunofluorescent antibody test showed rising titres. The test was positive in 1:60 dilution. Antinuclear antibody test was negative and thyroid functions were normal. When first seen by us, the patient did not have reddish brown coloured urine any more and hence the suspicion of rhabdomyolysis with myoglobinuria could not be confirmed. The patient was observed for few days to look for further neurological deterioration. She improved with supportive therapy over the next one week and resumed her duties as a nurse. She has since remained well with no residual neurological deficit when followed up six months later.

**DISCUSSION**

The diagnosis of Legionellosis was confirmed by the rising immunofluorescent antibody titers in paired sera, as well as the therapeutic response to a combination of azithromycin and fluoroquinolone. When the patient presented with the neurological symptoms, she had already recovered from the pneumonia and hence she was investigated for other causes of cerebellar dysfunction and radiculopathy. Her MRI brain and spinal cord, electrophysiological studies and thyroid functions were normal. Antinuclear antibodies were tested to look for a vasculitic process and were negative. The patient recovered on her own in a few days without specific therapy and has had no sequelae for the last six months. Hence we presume that the cerebellar symptoms and focal sensory deficits were manifestations of Legionnaires’ disease. Features of motor and sensory deficits in segmental distribution strongly suggested radiculopathy of right C5 to C7 segments. Guillain-Barre syndrome (GBS) and polyneuropathy have been described in legionellosis. Our patient probably had a forme fruste of GBS like radiculoneuropathy. A normal MRI brain and spine excluded other central etiologies. The normal electrophysiology study was not entirely surprising, as it was done on the third day of the onset of radicular symptoms and it may have been too early to document changes of radiculopathy. As the patient improved rapidly, no follow-up study was performed.

The cerebellar ataxia was mild and affected the trunk and gait. It was asymmetric in upper limb and nystagmus was elicited only on left side. The cerebellar affection occurred along with radiculopathy. Normal MRI scan of brain excluded possibilities of a structural lesion like demyelination. Cerebellar ataxia is rare but well documented in legionellosis. Johnson et al estimated the incidence of cerebellar dysfunction at 3.7% with limb ataxia and speech disturbances being the most common manifestations. Shelburne et al found 29 cases of Legionnaires’ disease in which cerebellar dysfunction was described as the primary neurological manifestation. Dysartria and ataxia were the most frequently reported symptoms, occurring in 79% and 72% respectively. The average time reported in literature, from the onset of pulmonary symptoms to the onset of cerebellar symptoms is 4.5 days. In the present case, the delayed appearance of cerebellar syndrome and radiculopathy in the recovery phase is in contrast to that described in literature. The delay is unusual and points to an immune-mediated pathogenesis rather than direct invasion or toxin-induced nervous system injury, which are expected to occur early.

Our patient had high CK levels with reddish brown coloured urine probably representing transient muscle damage and myoglobinuria. High CK is well described in this condition but only a single case of myoglobinuria has been reported by Posner et al.

Neurological manifestations in legionellosis go beyond ataxia and radiculopathy and range from subtle confusion and frank encephalopathy to peripheral neuropathy and myositis. A depression of conscious level and personality changes may be seen at the onset of the disease. Confusion, delirium and hallucinations disproportionate to metabolic upset in terms of fever, hypoxaemia and hyponatremia have been described. Lattimer et al have reported features of meningism and papilloedema with a sixth nerve palsy. Neuroimaging findings on CT and MRI were normal in most cases. However hydrocephalus was found in one dysarthric patient by Saleh et al. Weir et al have reported persistent cerebellar dysfunction in a patient who had cerebellar atrophy on CT scan when evaluated three years after the initial presentation. EEGs revealed diffuse slow-wave activity consistent with toxic encephalopathy in 60% of patients.

In the absence of direct invasion of the central nervous system, Legionella could produce neurological symptoms by either production of a neurotoxin or by immune-mediated mechanisms. Researchers have noted that the multiple sites of neurologic involvement make cross-reactivity between neurologic tissue and Legionella antigens improbable and propose the production of an endotoxin-like agent as the likely cause. Support for immune-mediated mechanisms in the neurologic manifestations of Legionnaires’ disease comes from observations of cases of acute disseminated encephalomyelitis and Guillain-Barre type peripheral neuropathy complicating legionellosis. However, direct findings in support of immunopathology such as decreased serum complement levels or biopsy specimens with evidence of vasculitis or immune complex
deposition have thus far been lacking. Clear risk factors and mechanisms for cerebellar dysfunction in legionellosis have yet to be identified.1 Deficits in speech and gait may persist for years.1 The only known treatment at present is therapy for the underlying Legionella infection, with anecdotal evidence in support of high dose corticosteroids in life-threatening conditions like acute disseminated encephalomyelitis.1

In conclusion, we document delayed appearance of reversible focal radicular and cerebellar dysfunction in a patient with legionellosis.

REFERENCES