LEGIONELLOSIS COMPLICATED WITH TRANSVERSE MYELETIS: A CASE REPORT AND REVIEW OF LITERATURES

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Abstract

Acute transverse myelitis is a rare neurologic complication of legionnaire’s disease. To the best of our knowledge, this is the first case report of acute transverse myelitis associated with legionnaire’s disease in English literature. Herein, we describe a case of rapidly progressing legionella pneumonia complicated with acute respiratory and renal failure. Ventilator assistance and hemodialysis were initiated. The patient developed neurologic deficits while in respirator and manifestations were masked by sedation. After steroid and intensive physical therapy, sensori-motor impairments of both lower extremities improved but sequelae of neurogenic bladder continue to persist during one year of follow-up care after discharge. This article aims to alert health personnel to be aware of the neurologic deficit arising in intubated patient under sedation in the intensive care unit. We believe waking patient in time interval is not sufficient but frequent neurologic assessment of patient is necessary to avoid overlooking any neurologic manifestations.

Key Words: Acute transverse myelitis, Legionella pneumophila, Legionnaire’s disease

Introduction

Legionnaire’s disease is a serious respiratory system disorder caused by infection with legionella pneumophila, and is frequently associated with findings of extra-pulmonary organ system involvement including renal or liver impairment, shock, coagulopathy and neurologic disorders.¹²,³ A search of articles in Pubmed from the year 1970 to 2010 utilizing the key words legionellosis, legio- nella pneumophila, legionnaire’s disease, and transverse myelitis disclosed several cases of transverse myelitis caused by infections such as mycoplasma, scrub typhus, salmonella, hepatitis C virus, bartonella henselae, coxackie virus, and campylobacter jejuni.⁴⁻⁶ Other etiologies include immune disorders and vaccinations.¹¹,¹² The neurologic involvement in legionellosis reported by Lees and Tyrrell in 1978, and Pearson and Dadds in 1981¹³,¹⁴ included mental changes, encephalopathies, encephalomyelitis, cerebellar syndrome, and Landry Guillain-barre neuropathy.¹⁵⁻¹⁷ However, there has been no diagnosed case of transverse myelitis related to Legionella pneumophila published in English article to
We report a 72 year-old man who developed neurologic manifestations of acute transverse myelitis with subsequent neurogenic bladder after a community acquired pneumonia caused by *Legionella pneumophila*. We described the difficulties in the early diagnosis of transverse myelitis in a patient with mechanical ventilatory assistance and under sedation in the intensive care unit.

**Case Report**

A 72-year-old man was admitted due to severe non-productive cough and intermittent fever and chills for three days followed by progressive breathlessness a day before admission. He had a history of diabetes mellitus for five years and had coronary artery bypass surgery two years previously. When he was examined in the emergency room, he was febrile with respiratory distress requiring intubation and mechanical ventilatory support. Chest x-ray revealed a patchy infiltration over the right middle lobe (Fig. 1). On admission to the intensive care unit (ICU), his body temperature was 38.2°C, pulse 120 beats per minute, respiratory rate 20 cycles per minute, and blood pressure was 160/60 mmHg. Aside from crackles over right lower lung fields, cardiovascular, abdominal and neurological examination revealed no other abnormality. White blood cell count was 27,600/mm³ (76% polymorphonuclear leukocytes, and 23% band forms). Hematocrit and platelet count were normal.

Arterial blood gas measurements while in respirator with FiO₂ of 80% showed a pH of 7.29, PaCO₂ of 33.4 mmHg, PaO₂ of 67.5mmHg, HCO₃ of 20.8 mmol/L and oxygen saturation of 90%. There was a mild renal impairment with BUN 40 mg/dl and creatinine 2.69 mg/dl, but electrolytes level were normal. The lactic dehydrogenase was 230 units, total protein was 4.5 g/dl, and albumin 1.7 g/dl.

Bilirubin and serum transaminase values were normal. The following 7 days after admission, antibiotic was administered using combination therapy of piperacillin + tazobactam and levofloxacin. Central venous catheter and indwelling foley catheter were inserted for close monitoring. Methylprednisolone 40 mg intravenously every 8 hours was added to the regimen on day 3 due to consideration of acute respiratory distress syndrome. Serologic studies of blood showed no evidence for infection with influenza A & B, herpes simplex virus and Treponema pallidum. Cold hemagglutination test, mycoplasma antibody, anti-HTLV I and II , widal test and weil-felix test were also negative. Chlamydia IgG was positive but IgM was negative. Procalcitonin was >10ng/ml. Series of chest radiographs follow-up showed rapid progression of patchy infiltration from right upper lobe to right middle and lower lobes. Computed tomography of chest without contrast revealed patchy opacities with air bronchograms and consolidations in RUL and RML, with right pleural effusion and subsegmental atelectasis seen in RLL (Fig. 2). Respiratory condition continued to deteriorate requiring 80-100% of forced inspired oxygen with positive end expiratory pressure at 10-12 cm H₂O to maintain adequate oxygen saturation so patient was placed under Diprivan.
sedation. On day 6, oliguria was noted and diuretic was prescribed. On day 8, BUN was 128, creatinine 8.07 mg/dl, and potassium level was 6.3 mmol/L. Hemodialysis was begun and there was hypotensive episodes during dialysis. Fluid challenge with crystalloids and colloids were given. Blood transfusions and vasopressors were occasionally added to keep adequate hemodynamics. Several sets of blood and sputum cultures were negative, as well as acid fast stain and gram stain. Fiberoptic bronchoscopy was performed at bedside and showed inflammatory process. Pathology of bronchoscopic biopsy specimen disclosed a picture compatible with organizing pneumonia. There was exudates filling the alveolar spaces and alveolar septa are thickened and infiltrated with chronic inflammatory cells but there was no organism found on smears and cultures obtained from bronchial lavage, bronchoscopic biopsy and brushing. Five days after antibiotic therapy, fever resolved and leukocytosis declined. On day 7, a report from CDC (Center for Disease Control) showed a positive indirect immuno-fluorescent assay (IFA) antibody response to *Legionella pneumophila* (serogroups 1-4) in a dilution titer of ≥ 1:128 in the serum drawn on day 3 and a rise in titer of 1:256 in the serum of day 8, piperacillin + tazobactam was hence discontinued.

Pneumonia and respiratory condition remarkably improved so on day 10, weaning from respirator was started, sedative agent was discontinued, and patient was encouraged to sit on bed. At this time patient complained of numbness and weakness of lower extremities which he claimed to have developed several days previously but of which he considered as an effect of sedation. Neurologist was consulted and sensory testing demonstrated he was insensitive to light touch and there was subjective diminution of response to pain, heat and proprioception sense below the T10 dermatome level. Muscle power was grade 2/5 with hyperreflexia of both lower extremities and positive babinski sign bilaterally. There was no evidence of cranial nerve palsy and cerebellar signs. No nuchal rigidity and brudzinski sign elicited.

Residual urine was 360 ml. and there was a need for laxative suppositories and enemas to aid his bowel movement most of the time. Cerebrospinal fluid (CSF) obtained from lumbar puncture on day 12 contained 132 mg/dl of glucose and 182 mg/dl of protein with red cell count of 121/mm³ and zero WBC. Gram stain, acid fast stain and India ink stain of CSF showed no organism seen on smears. The total IgG in CSF was 36.6 mg/dl (normal range 0.48-5.86) and 2030 mg/dl in the serum (normal range: 751-1560). Microalbumin was 101 mg/dl and anti-nuclear antibody (ANA) was negative. On day 14, patient was extubated and magnetic resonance (MRI) study of thoracolumbar spine was performed. A long segment hyperintensity in T2W1 at T9-T12 segment of spinal cord and a ring-like contrast enhancement at T12-L1 segment (Fig. 3). There was diffuse contrast enhancement over soft tissue below L1 level. Motor nerve conduction velocity (MNCV) disclosed a sensori-motor polyneuropathy. Due to incomplete resolution of pneumonia, after 14 days of intravenous levofloxacin, treatment was contin-

Fig. 2. Computed tomography of chest without contrast revealed patchy opacities with air bronchograms and consolidations in RUL and RML, with right pleural effusion and subsegmental atelectasis seen in RLL.
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Fig. 3. MRI study of thoracolumbar spine revealed a long segment hyperintensity in T2W1 at T9-T12 segment of spinal cord.

Fig. 4. MRI revealed a ring-like (owl-eye figure) contrast enhancement at T12-L1 segment.

ued for another 7 days with oral form of levofloxacin 500 mg once daily and there was clearing of pneumonia in chest x-ray before discharge. After using solumedrol 40 mg IV q 8 hrs for one week, the dose was reduced to 20 mg IV q 8 hrs for another week followed by 20 mg IV every 12 hrs on the third week but was later discontinued due to gastric and duodenal ulcers bleeding confirmed by gastroenterologist in UGI panendoscopy. Local epinephrine injection on bleeding ulcers was done for hemostasis. Biopsy of gastric mucosa showed acute and chronic inflammatory cells with no evidence of malignancy and no helicobacter pylori was demonstrated. After ten episodes of hemodialysis, urine output increased to >1500 ml/day and renal function improved with BUN = 39 mg/dl and creat = 2.52 mg/dl. Hemodialysis was discontinued. His blood sugar initially required 38 U to 46 U/day of insulin due to sepsis and steroid, however, after infection was controlled and steroid was stopped, his fasting blood glucose level was stable at insulin dose of 8-12 U/day, so it was changed to oral hypoglycemic agent and by discharge, he was using glucobay at 1 tablet and novonorm 2 tablets thrice a day.

After the diagnosis of transverse myelitis was made, patient received intensive physical rehabilitation therapy throughout the course and was able to ambulate with occasional assistance of walker on discharge. However, neurogenic bladder continues to persist one year after discharge and necessitates intermittent urinary catheterization and regular follow-up in neurology and urology outpatient department until this time of writing.

Discussion

This 72 year-old patient acquired a rapidly progressing pneumonia of which all specimens obtained demonstrated not a single pathogenic organism. It is known that this gram negative aerobic bacillus is difficult to isolate in culture and most often diagnosis depends on serology test.\(^\text{18}\) So we resorted to serologic tests on the second hospital day and sent specimens to CDC on the third day. The pulmonary infection of Legionnaires’ disease is caused directly by *Legionella pneumophila*, but the other organ-involvements have not been asso-
associated with direct invasion by this organism.\textsuperscript{19}

Following pneumonia and acute respiratory failure, our patient went into acute respiratory and renal failure. The presence of circulating toxin has been postulated for the apparent multi-organ involvement in Legionnaires’ disease, and recently an endotoxin-like substances has been isolated from the legionnaire’s disease bacterium.\textsuperscript{3,20,21} Hepatic impairment, renal failure, encephalopathy, and coagulopathy are well-recognized features of endotoxemia,\textsuperscript{22,23} but sepsis, metabolic events and hypoxia cannot be excluded.\textsuperscript{15}

Acute transverse myelitis (ATM) is an intramedullary heterogenous inflammatory disorder of the spinal cord, characterized by symptoms and signs of a motor, sensory and autonomic dysfunction in acute or subacute onset.\textsuperscript{24} ATM may exist as part of a multisystem or multifocal CNS disease, or as an isolated disease or idiopathic entity.\textsuperscript{25} The etiologies of ATM include vascular, infectious, neoplastic, immunologic, andiatrogenic causes.\textsuperscript{26,27} Viral, bacterial, fungal, and parasitic agents are among the infectious agents that can cause acute transverse myelitis. Prompt investigation for a causative agent, especially a treatable etiology, is indicated for institution of effective treatment and better outcome, and other differential diagnoses need to be excluded.

The factors involved may include a neurotoxin-mediated nerve injury, an immune mechanism, a metabolic disturbance or a combination of these.\textsuperscript{15} Since 1979, there has been several case reports on neurological involvement of legionnaire’s disease which included both central and peripheral nervous system.\textsuperscript{28} In 1984, Bernardini et al. reported a case of serologically proved legionnaires’ disease with evidence of severe persistent cerebral, cerebellar, and brainstem involvement.\textsuperscript{29} In addition, there was a report of neurogenic bladder presumably due to injury to sacral cord (S2 to S4), the cauda equine, and / or the nerve roots of the sacral plexus. There was no evidence of direct bacterial invasion as stated. The possibility of circulating immune complexes was considered. In 1983, Pendleburg et al.\textsuperscript{30} made a neuropathologic examination of 40 autopsied cases of confirmed Legionella pneumonia and found sixteen patients (40\%) had clinical evidence of cerebral disorder but their neuropathologic features were not explained by preexisting disease. Aside from normal findings, others include cortical atrophy, arteriosclerotic cerebral vascular disease with and without infarction, metastatic carcinoma, subependymal glomerate astrocytoma, subependymal ectopic gray matter, Wernick’s disease and Alzheimer’s type II astrocytosis. The neuropathologic examination in all 40 cases failed to demonstrate the bacillus L. pneumophila. This suggest that direct invasion of the brain by L. pneumophila is exceedingly uncommon.

Our patient developed neurologic deficits while in mechanical ventilator and sedation. There was muscle weakness of the lower extremities but the muscle power was not totally absent and the upper limbs were normal. During periods of wakefulness, there was no mental change and no cranial nerve abnormality noted.

The patient was able to communicate with family and ICU personals in writing form. Initially, he thought the weakness of lower limbs were due to effect of sedative agent, so he did not made any complain about it. Indwelling foley catheter was inserted earlier due to oliguria so urinary retention was not noted and residual urine was not elicited at the start. Due to unstable hemodynamics and use of ventilator assistance, the magnetic resonance (MRI) of thoracolumbar spine was delayed until the patient’s condition was stable and extubated. Although late but the MRI studies confirmed the diagnosis of ATM. Fortunately steroid therapy was instituted in the early course of illness due to consideration of ARDS. After appropriate antibiotic therapy, there was rapid improvement of respiratory condition and subsequently there was recovery of the muscle power except for neurogenic bladder which persisted as sequelae.

We believe there is possibility of overlooking neurologic signs in patient with ventilator and sedation because these hinders their communication ability especially in those with writing illiteracy. In patient without any conscious disturbance and significant cranial nerve deficits, mere assessment
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using Ramsay score is insufficient and could easily neglect any abnormal neurologic manifestations involved. Therefore we suggest that Glasgow coma scale and muscle power should not only be routinely used in neurology or neurosurgical patients but also in other patient being sedated.

Neurologic assessment should at least be performed twice a day when patient are awake during morning care and visiting hours. Patient should be encourage to communicate with health care personnel and family members too.

References

退伍軍人症引發橫貫性脊髓炎：—病例報告及文獻回顧

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摘要
急性橫貫性脊髓炎是退伍軍人症引發神經病變中最罕見的併發症而且在英文文獻中未曾發表過。本病例報告描寫一位病患因嚴重退伍軍人性肺炎迅速進展為急性呼吸衰竭及腎臟衰竭使用呼吸器和洗腎治療。在加護病房無法配合呼吸器故予鎮靜劑使用，於過程中無法有效評估神經學反應，導致病人出現神經障礙卻被掩蓋。幸好抗生素治療有效而且早期使用類固醇加上積極復健，出院時雙下肢的感覺和運動神經機能獲得改善。但出院一年後門診追蹤病人仍然無法正常排尿並需要定時導尿。在這裡藉此提醒大家在照顧使用鎮靜劑的病人時，務必暫時關閉藥物並且定期評估神經學反應，予避免忽略症狀而延誤診斷及其治療。

關鍵詞：急性橫貫性脊髓炎，退伍軍人症，退伍軍人性肺炎菌

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