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NEUROLOGIC MANIFESTATIONS OF LEGIONNAIRE'S DISEASE IN THE ABSENCE OF PULMONARY SYMPTOMS.

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ABSTRACT

Legionnaires' disease, also known as legionellosis is caused by bacteria legionella. It commonly presents with respiratory symptoms and extrapulmonary legionella disease is rare. Here we report a rare case of Legionnaire's disease with meningoencephalitis in a patient without pulmonary involvement. Imaging studies and cerebrospinal fluid analysis suggested meningoencephalitis. He was subsequently diagnosed with Legionella infection and was discharged well without any neurological deficit after antibiotic therapy. This condition should be considered in the differential diagnosis of meningoencephalitis.

KEYWORDS: Extrapulmonary, Legionnaire's disease, Legionellosis, Meningoencephalitis, Serology, Neurologic manifestations.

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ABSTRACT

Legionnaires' disease, also known as legionellosis is caused by bacteria legionella. It commonly presents with respiratory symptoms and extrapulmonary legionella disease is rare. Here we report a rare case of Legionnaire's disease with meningoencephalitis in a patient without pulmonary involvement. Imaging studies and cerebrospinal fluid analysis suggested meningoencephalitis. He was subsequently diagnosed with Legionella infection and was discharged well without any neurological deficit after antibiotic therapy. This condition should be considered in the differential diagnosis of meningoencephalitis.

KEYWORDS: Extrapulmonary, Legionnaire's disease, Legionellosis, Meningoencephalitis, Serology, Neurologic manifestations.

INTRODUCTION

Legionellae species is a known cause for both community and hospital acquired pneumonia worldwide.[1] Legionnaires' disease can also present with multisystem extra-pulmonary manifestations. Among these, neurological manifestations are the most common. Patients may present with mental confusion, hallucinations and reduced consciousness due to encephalopathy. [2] It is estimated that about 50% of legionnaire's disease is associated with neurological manifestations during the acute stage.[3] Here we report a case of meningoencephalitis secondary to Legionella infection with no pulmonary involvement. Even though this is a rare presentation of legionnaires' disease, clinicians need to be made aware of this manifestation as there are available therapy to treat and prevent complications.

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CASE REPORT

A 37-year-old man with no medical illness presented to the emergency department with fever associated with bifrontal headache, recurrent vomiting and poor oral intake for 5 days. The patient was an engineer, smoker and had been absent from work for a month prior to the symptoms due to a knee injury.

There was no recent travel or ill contact. He denied any diarrhea, neck pain or photophobia.

Initial general physical examination showed that he was alert, had stable vital signs and high temperature (39°C) with mild dehydration. The Kernig sign and Neck stiffness were absent. Other systemic examinations were unremarkable. Routine blood tests revealed leukocytosis with total white blood count 12.4x10 ^{9} /L (4.0 to 11.0) with predominant absolute neutrophils of 9.1x10 ^{9} /L (1.5 to 8.0). His hemoglobulin and platelet were within normal range. There was hyponatremia with sodium 120 mmol/L (135 to 145) with normal renal profile. Other blood investigations include alanine transaminase 19 U/L (7 to 52), aspartate aminotransferase 13 U/L (13 to 39) and normal creatinine kinase. Inflammatory markers were normal with c-reactive protein 2mg/L (0 to 0.50) and erythrocyte sedimentation rate of 10 mm/hr (0 to 15).

Chest radiography was normal (Figure 1) and electrocardiogram shown normal sinus rhythm. Initially he was treated as hypovolemic hyponatremia secondary to poor oral intake. His Legionella serology showed positive legionella pneumophilia serogroup 1 antibody titre IgM of 1:96, while mycoplasma serology Ig M was not detected. He was treated as Legionnaires' disease and oral azithromycin was started on Day 1 of admission.

On Day 7, patient developed incoherent speech and disorientation. His Glasgow coma scale was fluctuating and eventually dropped to 14/15 (E3V5M6). Cerebral CT with angiogram showed focal leptomeningeal enhancement at the right high parietal region, with generalized mild cerebral oedema (Figure 2). Lumbar puncture was performed. It demonstrated a mildly elevated cerebrospinal fluid (CSF) opening pressure of 20 cmH_2O

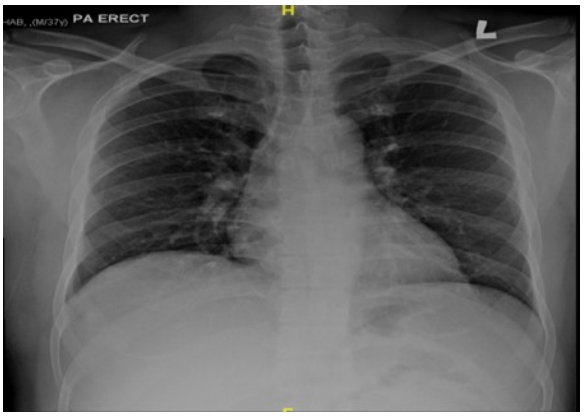

Figure 1: Normal chest x-ray. (click to enlarge image)

with CSF cell count shown 60cell/mm^3 with predominant polymorphic seen, associated with elevated protein level 1976 mg/L and low CSF / serum glucose ratio of 0.49 (CSF glucose 2.62 mmol/L with serum glucose 5.48 mmol/L). The CSF were also send for analysis for cryptococcal antigen, viral PCR, acid-fast-Bacilli and culture which were all negative. He was treated as bacterial meningitis. Intravenous ceftriaxone was started while oral azithromycin was upgraded to intravenous levofloxacin. Magnetic Resonance Imaging (MRI) of the brain performed later during his admission showed non-specific changes in the basal ganglia and thalamus area (Figure 3). His symptoms gradually improved and resolved after completed 14 days of levofloxacin and ceftriaxone. He was discharged well without any neurological deficit.

DISCUSSION

Legionnaires' disease was first recognized in 1976 after an outbreak of pneumonia at an American Legion convention in Philadelphia.[2] Clinical symptoms (fever, cough and shortness of breath) and radiological changes caused by legionella are similar to other forms of pneumonia. Of the 139 patients diagnosed legionnaires' disease during the Philadelphia epidemic, 27 had no evidence of pneumonia.[2] In our patient, he presented

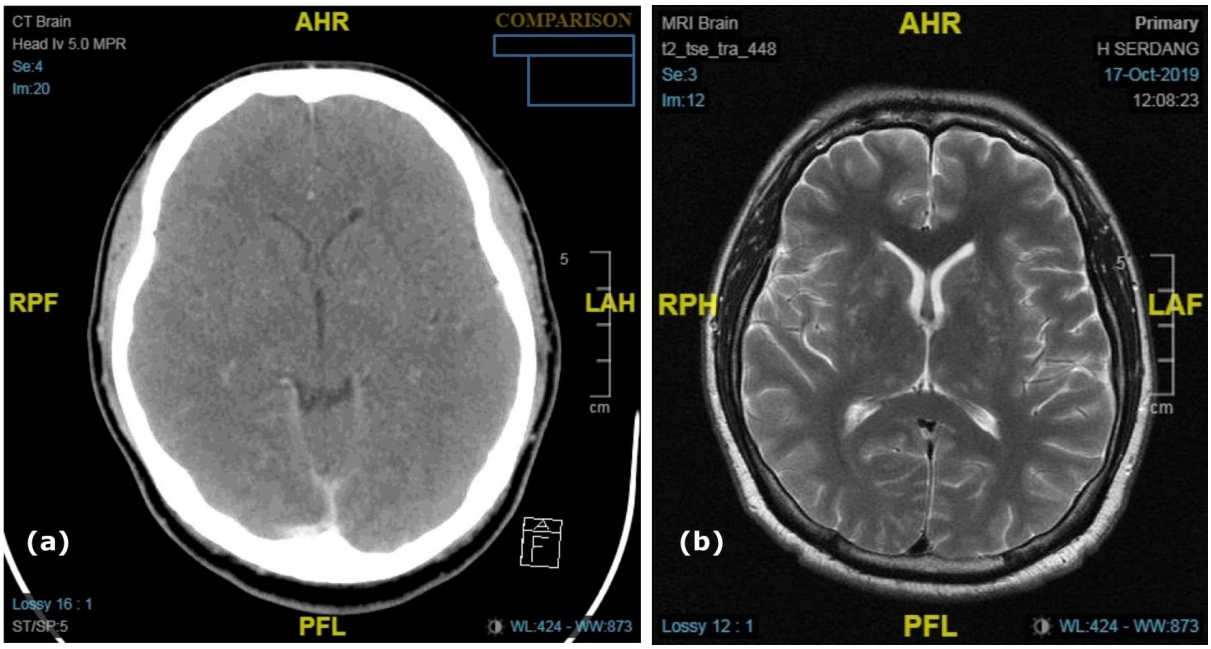

Figure 2: (a) CT angiogram of the brain showing focal leptomeningeal enhancement at the right high parietal region, with generalized mild cerebral oedema, (b) MRI Brain showing hyperintensities on bilateral basal ganglia and thalamus. (Click to enlarge image)

with non-typical symptoms such as fever associated with headache, vomiting and poor oral intake without any respiratory symptoms. The only abnormality of his blood investigation was hyponatremia which is a common finding in Legionnaires' disease.[1] Serial chest radiography were all reported as normal even when the legionella pneumophilia serogroup 1 antibody titre IgM was positive.

Most patients presented with symptoms of influenza-like illness such as fever, malaise and cough.[1-3] These presentations are subacute in onset and may later progresses into mental confusion and high temperature. Some patients also reported gastrointestinal symptoms such as vomiting, diarrhoea and abdominal pain. [4]

Legionnaires' disease is caused by the legionellae pneumophila which is a gram-negative bacteria found in natural environment such as soil, sea and lakes.[1,4] Transmission to human can occur through inhalation of water droplets and rarely via aspiration of drinking water. The incubation period for legionella infection is between 2 to 10 days.[5] Our patient had been absent from work for approximately one month before the presentation due to ankle injury, therefore it is unlikely that he contracted the disease from his work place or during his travels.

Legionnaires' disease can also present with multisystem extra-pulmonary manifestations. Among these, neurological manifestations are the most common. Patients may present with mental confusion, hallucinations and reduced consciousness due to encephalopathy.[3] In a review of patients with Legionnaires' disease in University of Louisville Affiliated Hospitals, 9 of a total 21 had abnormal mental status. Headache was the second most common neurological symptoms, occurring among 22.2% of patients diagnosed with Legionaires' disease.[2] Cases of cerebellar and brainstem involvement have also been reported before, with patients presenting with ataxia, dysarthria, dysmetria and ophthalmoplegia.[6,7] It is not clear how Legionella infection causes CNS manifestations, although direct invasion of the CNS is unlikely.[8]

Apart from these, Legionnaires' disease may also contribute to meningitis, encephalitis and peripheral neuropathies.[9] Our patient was diagnosed with meningitis based on his clinical symptoms and lumbar puncture confirmation. He had high opening pressure with elevated protein 1976 mg/L with low CSF/ serum glucose ratio 0.49. Other CSF investigations such as cryptococcal antigen, viral PCR, acid-fast-Bacilli and culture were negative. Despite this his Kernig's and Brudzinski's signs were negative, as was previously described with most Legionnaires' disease.

In a study by Johnson et al, lumbar puncture was performed in 85 of 912 patients with neurological sign and symptoms. Of this, 21 patients had abnormal CSF findings. Only 4 of the 21 patients had elevated CSF protein while 18 of 21 patients had pleocytosis.[3]

Neuroimaging findings for Legionella meningitis can be non-specific. In our patient, there was focal leptomeningeal enhancement at the right high parietal region on the CT angiogram. These findings can also be found in herpes encephalitis and should be ruled out. Misdiagnosis of herpes encephalitis may lead to inappropriate use of acyclovir and delay of starting antibiotic.[10] Other interesting neuroimaging findings in Legionnaire's disease includes reversible splenial lesion (MERS) on MRI Brain. Several case reports have been published regarding the above in mild encephalitis/ encephalopathy associated with Legionella pneumonia infection.[11] In our case, the MRI Brain showed hyperintensities in bilateral basal ganglia and thalamus. These findings could be incidental and may not be related to the Legionella infection.

Common anti-microbial agents used to treat Legionella pneumonia are macrolide or quinolones such as moxifloxacin and levofloxacin. Current evidence showed that the use of levofloxacin is associated with better outcome and a faster response compared to macrolides. High dose steroid therapy may be beneficial as studies have implicated autoimmune mechanism in Legionnaires' disease with CNS involvement.[12] Intravenous immunoglobulins have been used in treating several cases of Legionnaires' disease with CNS manifestations.[5] As our patient improved after antibiotics and a short course of steroids, this choice of treatment was not considered in his case. He made a full recovery with no residual neurological deficits.

CONCLUSIONS

In a patient who presents clinically with possible meningitis, and no obvious parameningeal focus, CT being non-specific and no contraindications for lumbar puncture, Legionnaires disease should also be ruled out by cultures. Clinicians need to consider Legionnaires' disease as a differential diagnosis in patients with neurological presentations even in those with normal chest radiographs. While most encephalopathies present temporarily in this disease, patients may develop further complications secondary to the CNS manifestations.

CONFLICT OF INTEREST

None to declare.

CONSENT

Appropriate consent has been obtained from patient and hospital authority to publish this case.

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