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CASE REPORT

Mycoplasma pneumoniae infection presenting as stroke and meningoencephalitis with aortic and subclavian aneurysms without pulmonary involvement

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SUMMARY

A 39-year-old Philipino man presented with acute onset fever and headache. Neurological examination was normal except for neck stiffness. There was no history of chest pain, cough or breathlessness. Cerebrospinal fluid (CSF) showed a mild increase in protein with normal sugar and lymphocytic pleocytosis. CSF PCR for herpes simplex and varicella zoster virus was negative. He developed acute right haemiplegia a week after hospitalisation. MRI showed acute infarct in the left centrum semiovale. His angiogram showed aneurysm in the left subclavian artery and aortic arch. The mycoplasma antibody test came positive with very high titres, while rest of the workup was negative. He was treated with azithromycin and his symptoms improved completely.

He was asymptomatic on follow-up after a month. His repeat immunoglobulin G mycoplasma antibody titre showed elevation. Mycoplasma infection is a treatable cause of meningoencephalitis and stroke secondary to vasculitis. Arterial aneurysms are known to occur with mycoplasma infection although rare.

BACKGROUND

Neurological complications due to *Mycoplasma pneumoniae* infection are very rare being 1%–3% and can include meningoencephalitis, stroke, transverse myelitis, peripheral neuropathy and Guillain-Barre syndrome.^{1–3} They are relatively more common in children.^{3–18} However, isolated neurological presentation without pulmonary manifestations has not been reported.

Central nervous system (CNS) damage occurs through an autoimmune mechanism in which anti-*M. pneumoniae* antibodies cross-react with CNS tissue. Most cases of *M. pneumoniae*-associated CNS disease occur after a respiratory illness has been present for ≥ 2 weeks, allowing for the production of IgM autoantibodies, which may cross-react.^{4–6}

We report this case of mycoplasma infection presenting with CNS manifestations in the form of stroke and meningoencephalitis, with asymptomatic arterial aneurysms. We suggest that mycoplasma infection should be considered in patients presenting with fever, aseptic meningitis and stroke even in the absence of respiratory symptoms

because early detection and treatment with appropriate antibiotics offers excellent outcome.

Mycoplasma infection can be an aetiology for large vessel aneurysms as well. The presence of arterial aneurysms in a patient with fever should heighten the suspicion of mycoplasma infection.

CASE PRESENTATION

A 39-year-old Philipino man, with no previous comorbidities, drug or substance abuse or history of promiscuity presented with acute-onset, moderate-grade, intermittent fever, which was not associated with chills or rigour. There was no history of chest pain, cough or breathlessness. There were no urinary symptoms as well. He also complained of bifrontal dull aching type of headache associated with neck pain. The pain was more in the early morning hours. There was no blurring of vision or diplopia. He also complained of few episodes of vomiting. He was continuing to work in the initial few days of fever, but over 3–4 days, he became more lethargic and was unable to concentrate on the work while the headache and fever persisted. He consulted a local physician and was advised paracetamol and amoxicillin–clavulanic acid tablets. However, there was no relief for his symptoms. His friends who were staying with him noticed that he remained sleepy during most of the day hours and his food intake was reduced. He was able to speak coherently to them and was able to walk, although tired. They brought him to our hospital for further treatment.

At presentation he was febrile, with temperature of 100.6°F. The pulse rate was 100/min, blood pressure was 110/70 mm Hg and respiratory rate was 18/min. There was no skin rash. Chest and cardiovascular examinations were normal. Abdominal examination did not reveal any organomegaly. On neurological examination, he appeared lethargic although responding coherently to queries. Speech was normal. Cranial nerve examination including the optic fundi was normal. Motor sensory and cerebellar examination was normal. Neck stiffness and Kernig's sign were positive.

A week after hospitalisation, he developed acute onset right-sided weakness with mild Upper Motor Neuron (UMN) type facial weakness and mild dysarthria, but there was no aphasia.



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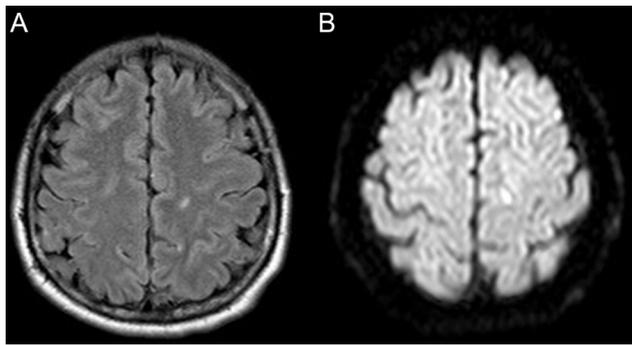


Figure 1 MRI FLAIR axial and DWI image showing acute infarct in the left centrum semi-ovale. DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery.

INVESTIGATIONS

Complete blood cell count testing revealed a haemoglobin level of 13.9 mg/dL; platelet count of 450 000/ μ L; white cell count (WBC) of 10 700/ μ L, with a differential of 86% neutrophils, 12% lymphocytes and 2% monocytes. ESR was 35 mm/hour.

Cerebrospinal fluid (CSF) analysis showed mild increase in protein (52 mg/dL) with normal sugar (80 mg/dL) with 58 WBCs (neutrophils 8, lymphocytes 92) and no red blood cells. CSF gram stain and culture were negative. CSF PCR for herpes simplex and varicella zoster virus was negative. Chest X-ray was normal. MRI showed acute infarct (hyperintense signal on fluid-attenuated inversion recovery and diffusion-weighted imaging images) in the left centrum semi-ovale (figure 1A, B). Electroencephalogram showed generalised slowing. His conventional angiogram showed aneurysm in the left subclavian artery and aortic arch (figure 2). Mycoplasma immunoglobulin (Ig)M antibody came positive, with a titre of 1:100 (positive 1:80 or more), while IgG



Figure 2 Aortic angiogram showing small aneurysm involving the aorta and left subclavian artery (red arrow head).

titre was 1:120. The rest of the work up was negative. The IgG titre tested 2 weeks later showed an increase to 1:320 and was 1:80 after 3 months.

DIFFERENTIAL DIAGNOSIS

Viral meningoencephalitis, vasculitis, infective endocarditis with septic emboli and reversible cerebral vasoconstriction syndrome.

TREATMENT

He was initially treated with ceftriaxone and acyclovir with a provisional diagnosis of partially treated pyogenic/viral meningoencephalitis, which was stopped once the CSF culture PCR for herpes simplex and varicella zoster virus came negative. He received paracetamol for fever and headache and pantoprazole for gastric prophylaxis. He received aspirin when he developed stroke. He was started on azithromycin once the mycoplasma antibody came positive, which was continued for 5 days.

OUTCOME AND FOLLOW-UP

He became afebrile, headache subsided and sensorium improved after being initiated on azithromycin. His neurological deficits completely improved with physiotherapy. He was asymptomatic at a 1-month and 3-month follow-up.

DISCUSSION

M. pneumoniae has extrapulmonary manifestations in 25% of cases. Neurological complications of *M. pneumoniae* infection are well known and include both peripheral and CNS manifestations.¹ In one study with CSF culture or PCR-proved mycoplasma, the CNS symptoms were diverse and included headache, somnolence, seizures, agitation and coma.²

Although it is rare, stroke is recognised as one of the complications, and haemiparesis had been described in the literature since 1945. However, all these manifestations were reported to be more in the paediatric population.^{3–18} One prospective study mentioned that the risk of ischaemic stroke was higher among people who had *M. pneumoniae* infection compared with controls.¹⁹ There is no clear predilection to either anterior or posterior circulations as both were described.^{9 11 14} The mechanism by which stroke happen is largely not understood although many has been proposed. Garcia *et al* proposed that *M. pneumoniae* infection induces a hypercoagulable state.¹⁸ This was supported by another study which showed a decrease in the circulating antithrombotic enzyme-activated protein C (APC), elevated plasma C4b-binding protein and lower ratio of active tissue plasminogen activator to plasminogen activator inhibitor in the stroke group with antecedent infection/inflammation within 1 week preceding brain infarction compared with the control group.²⁰ However, thrombotic profile including APC was negative for our patient. Another mechanism suggested was the inflammatory process and vasculitis. This mechanism was supported by evidence of mycoplasma-like structure in the granulomatous angiitis of the CNS.²¹ In addition, both antibodies to the brain and immune complexes were described after *M. pneumoniae* infections.^{22 23} This is supported by the delay of the neurological presentation in most of the patients. On the other hand, the possibility of direct invasion to the CNS was proposed based on some cases where the CSF was positive either by PCR or culture for *M. pneumoniae*.^{2 10} Although the CSF of our patient was negative for *M. pneumoniae*, the patient improved with antibiotic treatment, which support the mechanism of direct invasion. However, the delay in the neurological presentation for days

may possibly suggest autoimmunity, direct invasion or possibly both mechanisms together.

The presence of arterial aneurysms like in our patient had been previously described as a possible complication of *M. pneumoniae* infection.²⁴ As with CNS manifestations, aneurysms can also be a result of direct invasion by the organism with the resultant inflammation, or because of inflammatory process caused by autoimmunity.²⁵

Learning points

- ▶ Mycoplasma infection should be considered in patients presenting with fever, aseptic meningitis and stroke even in the absence of respiratory symptoms because early detection and treatment with appropriate antibiotics offers excellent outcome.
- ▶ Mycoplasma infection can be an aetiology for large vessel aneurysms as well.
- ▶ Presence of arterial aneurysms in a patient with fever should heighten the suspicion of mycoplasma infection.

Contributors PS: primarily responsible for the design of the work; acquisition of data, analysis and drafting the work. AMA, AARAM and JI: assisted in the design of the work; acquisition of data, analysis, drafting the work and review of final version.

Competing interests None declared.

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