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What is This?
Transient Parkinsonism Following Mycoplasma pneumoniae Infection With Normal Brain Magnetic Resonance Imaging (MRI)

Chee Geap Tay, MMed (Paed)1,2, Choong Yi Fong, FRCPCH1,2, and Lai Choo Ong, MRCP1,2

Abstract
Parkinsonism caused by infection is uncommon in children. We report 2 previously healthy children with acute self-limiting parkinsonism following Mycoplasma pneumoniae infection, with normal brain magnetic resonance imaging (MRI). Our case report expands the phenotype of parkinsonism associated with M pneumoniae infection. We recommend that children with acute parkinsonism preceded by a period of febrile illness, even with a normal brain MRI, should be investigated for M pneumoniae infection.

Keywords
parkinsonism, magnetic resonance imaging (MRI), Mycoplasma pneumoniae

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Parkinsonism following Mycoplasma pneumoniae infection is rare in childhood. All the cases reported in the literature are associated with radiologic changes in the basal ganglia on brain magnetic resonance imaging (MRI). It has been postulated that direct invasion of the brain, immune mediated phenomena, toxic effects, vascular injury, and hypercoagulable state are responsible for the pathogenesis. However, the exact mechanism remains to be elucidated.

We describe 2 patients who presented with self-limiting parkinsonism following M pneumoniae infection without radiologic changes on brain MRI.

Case Report
Patient 1
A previously healthy 9-year-old boy presented with fever and flu-like symptoms that resolved after 3 days. At day 5 of illness, he developed vomiting and severe headache followed by progressive lethargy and difficulty in moving. He was unable to get out from bed and required assistance for his basic self-care activities. He had difficulty in talking, swallowing, and writing. There were no seizures or encephalopathy throughout this period. He had no recent vaccination or drug ingestion. When he was admitted at day 14 of illness, he was noted to be alert and orientated but with a slow response time to commands. There was an expressionless facies with marked bradykinesia and lead pipe rigidity. He had a shuffling gait and his speech was soft and monotonous. His reflexes were brisk, with relative preservation of muscle strength. There were no sensory, cranial nerve, or cerebellar deficits. No resting tremor, ophthalmoplegia, or Kayser-Fleischer rings were noted.

Routine laboratory investigations performed are shown in Table 1. Erythrocyte sedimentation rate was 23 mm/h. Cerebrospinal fluid study revealed pleocytosis (12 white cells per mm3) with no red blood cell. The brain MRI was normal. The particle agglutination test for M pneumoniae showed a 4-fold rise between acute and convalescent sera where the titers at day 1 of admission was 1:640, at day 10 of admission 1:1280, and at day 14 of admission 1:10 240.

He was treated with ceftriaxone and azithromycin on admission. His neurologic status started to improve from day 18 of illness and had complete recovery at 3 months. He has remained well 1 year following the infection.

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Table 1. Laboratory Investigation Performed on Both Cases.\(^a\)

<table>
<thead>
<tr>
<th>Plasma</th>
<th>Full blood count, peripheral blood film for acanthocytes</th>
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<tbody>
<tr>
<td></td>
<td>Renal profile, liver function test, calcium, creatinine kinase, thyroid function test, C-reactive protein, \textbf{erythrocyte sedimentation rate}(^b)</td>
</tr>
<tr>
<td></td>
<td>Lactate, ammonia, amino acid</td>
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<tr>
<td></td>
<td>C3 antibody, C4 antibody, antinuclear factor, anti–double-stranded DNA</td>
</tr>
<tr>
<td></td>
<td>Ceruloplasmin, copper</td>
</tr>
<tr>
<td></td>
<td>Herpes IgM, Japanese encephalitis Ig</td>
</tr>
<tr>
<td></td>
<td>Particle agglutination test for \textit{Mycoplasma pneumoniae}</td>
</tr>
<tr>
<td></td>
<td>Limbic encephalitis antibodies(^c) (NMDAR, Caspr2, IgI, AMPAR 1 and 2, GABAR)</td>
</tr>
</tbody>
</table>

| CSF | RBC, WBC\(^d\) |
|     | Protein, glucose, lactate |
|     | Herpes IgM, Japanese encephalitis IgM |
|     | Bacterial culture, viral culture |
|     | Oligoclonal band\(^e\) |

| Urine | Organic acid chromatography, 24-hour copper excretion |
|       | Brain MRI |

<table>
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<tr>
<th>Imaging</th>
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Abbreviations: AMPAR 1 and 2, \(\gamma\)-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor 1 (and 2); Caspr2, contactin-associated protein-like 2; CSF, cerebrospinal fluid; DNA, deoxyribonucleic acid; GABAR, \(\gamma\)-aminobutyric acid receptor; IgI, leucine-rich glioma inactivated 1; IgM, immunoglobulin M; MRI, magnetic resonance imaging; NMDAR, N-methyl-D-aspartate receptor; RBC, red blood cell; WBC, white blood cell.

\(^a\)All unremarkable except the test highlighted bold.

\(^b\)Done in patient 1.

\(^c\)Done in patient 2.

\(^d\)Abnormal in patient 1.

\(^e\)Abnormal in patient 2.

Patient 2

A 12-year-old boy was admitted for a 2-week history of vomiting and generalized lethargy preceded by febrile illness. He had confined himself to the bed because of postural instability and slowness in initiating movements. On examination, he was alert but had bradykinesia; mask-like facies; and hypophonic, monotonous speech. There was a positive glabellar reflex without rigidity. His reflexes were brisk but with preservation of muscle power and sensation. No resting tremor, ophthalmoplegia, or Kayser-Fleischer rings were noted. Examinations of the cranial nerves and cerebellum were unremarkable.

Routine laboratory tests performed are shown in Table 1. The cerebrospinal fluid analysis showed pleocytosis (14 white cells per \(\mu\)l) with 4 red blood cells and normal protein and glucose. The brain MRI was normal. The particle agglutination test for \textit{M pneumoniae} demonstrated a 4-fold increase in the titers between the 1st and 9th days of admission with titers of 1:80 and 1:320 respectively (Table 1).

He received ceftriaxone and acyclovir as empirical treatment. His neurologic status improved spontaneously after day 23 of illness. He had completely recovered at week 6 from the onset of the symptoms and returned to his normal daily activities. He has remained well 3 months following the infection.

Discussion

The central nervous system is the most common site of extrapulmonary manifestation of \textit{M pneumoniae} infection. Approximately 1% to 10% of serologically confirmed \textit{Mycoplasma pneumoniae} infection that required hospitalization were associated with neurologic manifestations, with children younger than age 10 years more frequently affected than adults.\(^{1,3}\) The neurologic complications are usually reversible, but one-third of patients have long-term neurologic sequelae.\(^{2,3}\) The exact pathogenesis of central nervous system manifestation of \textit{M pneumoniae} infection remained uncertain, with the current evidence favoring a postinfectious immune-mediated mechanism rather than direct invasion of the organism or neurotoxin production.\(^3\)

Encephalitis and meningoencephalitis were the most common central nervous system manifestations, followed by polyradiculitis and aseptic meningitis.\(^2\) Parkinsonism on the other hand, is an uncommon central nervous system manifestation of \textit{M pneumoniae} infection. The mean interval between the respiratory symptoms and central nervous system manifestations is 9.6 days (range 2-14 days).\(^{1,3}\) Our patients developed parkinsonism 5 to 14 days following a febrile illness and demonstrated a 4-fold increase in mycoplasma titers, consistent with a recent infection. The clinical course and laboratory investigations excluded the possibility of parkinsonism secondary to Wilson disease, mitochondrial cytopathy, or other progressive neurometabolic disorders.

To our knowledge, this is the first report of parkinsonism associated with \textit{M pneumoniae} infection without any brain MRI changes. Parkinsonism with basal ganglia MRI changes following recent \textit{M pneumoniae} infections have only been reported in pediatric patients with 7 case reports to date.\(^{4,10}\) The vast majority of these patients (6/7 cases) subsequently have residual neurologic deficits. In comparison, all of our patients had a complete recovery within 90 days of the onset of the symptoms (Table 2). We postulate that our patients potentially had a milder spectrum of parkinsonism without brain MRI changes, resulting in more rapid recovery compared to the other reported cases.

Levodopa or anticholinergic medication have been anecdo-
tally reported to alleviate symptoms in parainfectious parkinsonism secondary to \textit{M pneumoniae}.\(^{5,7}\) However, some authors did not observe these potential beneficial effects.\(^{4,8}\) Sakoulas\(^9\)
demonstrated the encouraging result of immunotherapy in hastening the short-term recovery but it did not alter the eventual outcome in his patient. Our patients did not require any medication or immunotherapy as they were making steady recovery in hospital. Adequate and appropriate antibiotic therapy did not seem to hasten the recovery period as one of our patients had rapid spontaneous recovery without macrolide therapy. This supports the possible immune-mediated phenomenon theory rather than direct invasion of the organism.

Conclusion

Our case report expands the phenotype of parkinsonism associated with *M pneumoniae* infection. We recommend that a child with newly-onset parkinsonism and a preceding history of febrile illness, even with a completely normal MRI brain, should be investigated for *M pneumoniae* infection.

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Author Contributions

CGT contributed substantially to the data collection and writing of manuscript. CYF and LCO contributed equally to the data analysis and critical revision of the manuscript for important intellectual content and gave final approval for the version to be published.

Declarations of Conflicting Interests

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