Unusual manifestations of infections due to *Mycoplasma pneumoniae* in children

*Manifestazioni inusuali dell’infezione da Mycoplasma pneumoniae nei bambini*

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**INTRODUCTION**

*Mycoplasma pneumoniae* (*Mp*) plays an important role in the aetiology of respiratory tract infections in all paediatric ages. In the pre-school period, *Mp* infections are asymptomatic or affect the upper airways. Pneumonia shows a higher prevalence during school age and presents a generally benign and rapid evolution. Nevertheless, *Mp* can cause different airway diseases characterised by peculiar and/or severe evolution (such as fulminant pneumonia, lung abscess, pneumatocele, extended lobar hepatisation) or by association with other lung diseases (chronic obstructive bronchopneumopathies, asthma) [1]. *Mp* also causes extra-pulmonary diseases that sometimes are the only target of infection with no associated typical respiratory tract infection [2-3]. The purpose of this study is to highlight the multiple and atypical clinical manifestations of *Mp* infection that make its diagnosis difficult. Clinical suspicion of *Mp* infection is essential, mainly in severe cases in order to start early specific therapy.

**RESULTS**

From January 2001 to December 2001, 92 children were hospitalised with diagnosis of lower airway infection. Forty-one children (50%) (median age 5 years; range 1 year and 9 months-11 years and 5 months) had clinical, serological and radiological diagnosis of pneumonia due to *Mp*. All but two patients showed a normal outcome without any complications. In two children, previously treated at home with β-lactams, *Mp* infection caused severe respiratory distress. In the first child (aged 4 years and 6 months) chest X-ray showed left pneumonia focus and some smaller postero-basal foci with pleural effusion, and chest CT revealed multiple foci and initial abscess. The second child (aged 8 years and 9 months) with thoracic neuroblastoma presented extended pneumonia, homolateral and contiguous to the large chest tumour. In the two patients the pneumonia was successfully treated with clarithromycin i.v. During the same period, nine children were observed with *Mp* infection showing exclusively extra-pulmonary manifestation (Table 1). Skin and joint manifestations, especially urticaria-like rush and arthralgia, respectively, were observed (Figure 1).

Our clinical experience reports other unusual manifestations caused by *Mp*. Three patients presented severe neurological and muscular impairment with similar clinical onset, but a very different outcome [4].
Transverse myelitis
A female, aged 13 years, with a right pneumonia presented neurological manifestations as paraesthesia. After 24 hours, the clinical picture was worsening with dyspnoea, diffuse macular exanthema, flaccid tetraparesis with hypoesthesia, and altered consciousness and then involvement of respiratory muscles. Brain and spinal cord MRI showed transverse myelitis in cervical spinal cord and medulla oblongata (Figure 2). Blood and CSF tests showed the large number of anti-Mp IgG and IgM antibodies (CF on serum 1:512, on CSF 1:16; ELISA on serum IgM 3+, IgG 2+, on CSF IgM+/-, IgG 2+). Despite i.v. clarithromycin and desamethasone and addition of ciprofloxacin, respiratory symptoms subsequently regressed, while flaccid tetraparesis with anaesthesia persisted. At one year after the acute episode, right arm paresis and paraplegia with urinary incontinence persisted. Spinal MRI showed irreversible lesions.

Neuromuscular junction involvement with myositis
A male, aged 6 years with evidence of pneumonia not responding to ceftriaxone, presented fever, asthenia, stiff neck, marked muscular pain and upper limb hyposthenia. The patient worsened within a few hours, with involvement of respiratory muscles and of upper and lower limbs, as well as intense abdominal pain with severe respiratory symptoms. Abdominal US,

Table 1 - Cases of extra-pulmonary Mycoplasma pneumoniae infection.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sex</th>
<th>Age (yrs.)</th>
<th>Symptoms</th>
<th>Anti-Mp Ab</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>5</td>
<td>Arthralgia ++++, erythema marginatum +++</td>
<td>1:160</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>8</td>
<td>Vomiting ++, vertigo +++, spinal stiffness ++, gait disorders ++</td>
<td>1:320</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>10</td>
<td>Urticaria ++</td>
<td>1:160</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>5</td>
<td>Arthralgia ++, migrating arthritis ++, urticaria +</td>
<td>1:1280</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>5</td>
<td>Arthralgia +++, urticaria ++</td>
<td>1:1280</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>1</td>
<td>Urticaria ++</td>
<td>1:160</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>9</td>
<td>Arthralgia ++++, myalgia</td>
<td>1:160</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>2</td>
<td>Urticaria ++, cough++</td>
<td>1:1280</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>9</td>
<td>Urticaria ++++, arthralgia</td>
<td>1:1280</td>
</tr>
</tbody>
</table>

Figure 1 - Skin urticaria like a rash due to Mp.

Figure 2 - MRI shows diffuse swelling of the cervical spinal cord with reduction of the perimedullary liquorhead spaces.
brain and spinal MRI, CSF analysis and nerve conduction velocity were negative; electromyography suggested minimal muscular damage without clear signs of myolysis. Anti-Mp antibodies (IgM and IgG) were detected in serum but not in CSF. Therapy with i.v. clarithromycin, ciprofloxacin, and desamethasone was started, with subsequent complete respiratory and neurological recovery without any sequelae.

Meningitis

A male, aged 12 years presented a right pneumonia with high fever, chills and drowsiness not responding to cephalosporins. After admission to hospital the boy presented muscular pain, especially to the legs with hyperaesthesia and signs of meningitis (aseptic meningitis), the title of serum anti-Mp antibodies was high (1:1280) and Mp antigen was detectable by ELISA assay in the nasal swab. The initial therapy with clarithromycin and β-lactams was modified with administration of ciprofloxacin. Cerebral TC and RMN were normal. Clinical condition improved and the child showed a complete recovery.

Other extrapulmonary manifestations due to Mp observed in children are:

*Hepatitis.* A male, aged 2 years, affected by pneumonia presented an anicteric hepatitis, documented by increased transaminase levels (TGO/TGP 108/166 IU/l); the child recovered in one week.

*Haemolytic anemia.* A female, aged 6 years, was admitted to hospital for fever, bibasal pneumonia and severe haemolytic anaemia (Hb 5.2 g/dl). Cold agglutinins, serum IgM and IgG anti-Mp were positive at the onset of disease. The patient underwent transfusion of RBC concentrate and early antibiotic therapy with macrolides and steroid was started. Haemoglobin and bilirubin levels slowly normalised after the first month of disease.

*Schönlein-Henoch purpura.* A female, aged 5 years was admitted to hospital for pneumonia, migrating arthritis and Schönlein-Henoch purpura and exanthema of the legs (Figure 3). The serological test showed anti-Mp antibodies (>1:1280), cold agglutinins and haematuria was also present. The purpura showed a fluctuating trend, with a second thrust after 10 days, despite the rapid improvement in pneumonia.

**DISCUSSION**

Our series shows that Mp infection is a frequent agent of pneumonia in paediatric age, also in younger children. However, Mp infection often presents atypical manifestations, not always correlated with pulmonary symptoms, but involving other organs or systems. Neurological complications are the most frequently reported in the literature, with estimates ranging from 2-5% to 13% or more 20-30%, muscular-articular manifestations account for 30-40% of cases [5-8]. Our case review reveals that Mp infection may give rise to complex clinical pictures. Mp infection should be suspected (especially during epidemic periods) regardless of the coexistence of pneumonia in different clinical conditions [4-10]; the Mp infection may involve different systems and organs and cause unusual clinical manifestations. In detail:

*Nervous system:* aseptic meningitis, meningoencephalitis, brain infarct, cerebellar ataxia, psychosis, polyradiculoneuropathy, Guillain-Barré syndrome, ascending paralysis, transverse myelitis, myositis and/or myalgia.

*Joints:* polyartralgia, monoarticular arthritis or rheumatic-like form (migrating).
**Mycoplasma pneumoniae (Mp)** is an important cause of pneumonia in paediatric age, but also other organs or systems can be affected even without pulmonary involvement. The purpose of this study is to stress the unusual clinical features of Mp infection in children. A review of children affected with Mp infection with peculiar pulmonary and/or extrapulmonary forms is reported. Diagnosis of Mp infection was always confirmed by serum anti-Mp antibody assay. Two patients with infection of the lower airways showed severe respiratory distress; nine cases with only extrapulmonary manifestations presented urticaria and arthralgia; three patients had severe neuromuscular impair-ment, one of these resulting in flaccid tetraparesis; one 2-year-old child had anicteric hepatitis, without any sequelae; one case of a 6-year-old child presented severe haemolytic anaemia, and a 5-year-old child with Schönlein-Henoch purpura. In conclusion, Mp infection, a frequent cause of pneumonia at all paediatric ages, may also give rise to extrapulmonary manifestations. Frequently, muscular-articular or neurological systems, skin or other organs are involved.

Clinical suspicion of Mp infection is essential in severe cases and the outcome of all pulmonary and/or extra-pulmonary manifestations depends on early diagnosis and specific therapy.

**Key Words:** Mycoplasma pneumoniae, Extrapulmonary manifestations, Childhood

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Il Mycoplasma pneumoniae (Mp) è l’agente eziologico di molti casi di polmoniti comunitarie in età pediatrica, ma possono essere coinvolti anche altri organi o apparati sia pure in assenza di patologia polmonare. Scopo del presente studio è quello di focalizzare alcuni aspetti inusuali dell’infezione da Mp nel paziente pediatrico. La casistica descritta si riferisce a pazienti pediatrici giunti alla nostra osservazione per infezione da Mp con particolari espressioni cliniche polmonari e/o extrapulmonari. La diagnosi di infezione da Mp è stata sempre confermata dalla presenza di anticorpi anti-Mp nel siero. Due pazienti con infezione della basse vie aeree presentavano una grave insufficienza respiratoria; nove casi presentavano esclusivamente sintomatologia extrapol-monare come orticaria e artralgia; tre casi affetti da sintomatologia di tipo neuromuscolare, con evoluzione in uno di essi in tetraparesi flaccida; un bambino di 2 anni con epatite anicterica, senza alcuna sequela; un bambino di 6 anni presentava una grave anemia emolitica e un bambino di 5 anni una porpora di Schönlein-Henoch.

In conclusione, il Mp è responsabile frequentemente di broncopolmoniti in tutte le età pediatriche ma anche di manifestazioni extrapulmonari a carico soprattutto dei sistemi muscolo-articolare o neurologico, della cute e di altri organi. Il sospetto clinico di infezione da Mp è fondamentale nei casi più gravi; la risoluzione favorevole di tutti i quadri clinici polmonari e/o extrapulmonari dipende dalla precocità della diagnosi e della terapia.
REFERENCES


