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Clinicoradiologic features of *Mycoplasma pneumoniae* bronchiolitis in children

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ABSTRACT

Importance: Acute *Mycoplasma pneumoniae* bronchiolitis can progress into bronchiolitis obliterans (BO) in children, which has a major influence on a child's quality of life and is associated with *M. pneumoniae* bronchiolitis. Early identification and treatment of *M. pneumoniae* bronchiolitis is important to prevent the development of BO.

Objective: To enhance the understanding of the diagnosis and treatment of *M. pneumoniae* bronchiolitis in children.

Methods: Eight patients with *M. pneumoniae* bronchiolitis were retrospectively analyzed.

Results: Five of the patients with *M. pneumoniae* bronchiolitis were male and three of them were female. All patients suffered from fever and cough. Moist rales and wheezing were noted in both lungs in six patients. High-resolution computed tomography of the chest showed bronchiolitis in all patients, with large airway injury in two and focal bronchopneumonia in six. Two patients were confirmed to have asthma. Seven patients had personal and/or family histories of atopic diseases. Allergen testing was performed in six patients, which produced positive results in four; the remaining two patients had negative results, but their total IgE levels were > 200 IU/ml. Azithromycin therapy and glucocorticoid therapy was administered to all eight patients. One patient required noninvasive ventilation. Treatment of all patients was successful, with no development of bronchiolitis obliterans during the 4- to 8-month follow-up.

Interpretation: *Mycoplasma pneumoniae* bronchiolitis can occur in children, especially in atopic individuals. The use, time of initiation, and effects of glucocorticoids administration in these patients for the prevention of BO require further investigation.

KEYWORDS

Mycoplasma pneumoniae, Bronchiolitis, Glucocorticoid, Bronchiolitis obliterans

INTRODUCTION

Mycoplasma pneumoniae can cause upper respiratory infection, bronchitis, bronchiolitis, and pneumonia. To our knowledge, only one pediatric case report of *M. pneumoniae* bronchiolitis in a 17-year-old girl has been published.[1] Although *M. pneumoniae* bronchiolitis is uncommon, acute *M. pneumoniae* bronchiolitis may

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progress into bronchiolitis obliterans (BO) in children.[2] There are also reports of *M. pneumoniae* bronchiolitis-associated restrictive BO in adults.[3-5] Because BO has a major influence on a child's quality of life and is associated with *M. pneumoniae* bronchiolitis, early identification and treatment of *M. pneumoniae* bronchiolitis is important to prevent the development of BO. To this end, we herein report eight cases of *M. pneumoniae* bronchiolitis in children to enhance the understanding of this disorder.

METHODS

Patients

Eight patients diagnosed with *M. pneumoniae* bronchiolitis from February 2016 to July 2017 were included in this study. The diagnosis of *M. pneumoniae* bronchiolitis was based on high-resolution computed tomography (HRCT) findings, including centrilobular nodules, branching linear opacities (tree-in-bud pattern), and bronchiolar wall thickening;[6] a serum IgM-specific anti-Mycoplasma antibody titer of ≥ 1:160 in the acute phase or a four-fold rise during convalescence; and negative bacterial cultures of the blood, sputum, and/or bronchoalveolar lavage fluid were also suggestive of bronchiolitis.

Data collection

This was an observational and descriptive study. The medical records of all patients were retrospectively reviewed. We collected data on demographic characteristics, clinical presentations, physical examination findings, chest HRCT findings, atopic data, and treatment. We also gathered follow-up information on all patients. The data of all eight patients are shown in Table 1.

Clinical definition

An atopic background was defined as one of three findings: positive personal and/or family history of atopic disease, allergy to airborne allergens, or a history of atopic disease.

RESULTS

Demographic characteristics

The eight patients in this study ranged in age from 3 years 10 months to 8 years 9 months (mean age: 6 years 1 month). Five patients were male and three were female.

Clinical features

All patients had a fever and cough for 3 to 14 days. Three patients had wheezing for 2 to 14 days. Moist rales and wheezing were noted in six patients.

Radiologic findings

Chest HRCT findings included centrilobular nodules, branching linear opacities (tree-in-bud pattern), and bronchiolar wall thickening (unilateral distribution in two patients [Figure 1] and bilateral distribution in six patients [Figure 2]). Focal bronchopneumonia was observed in six patients, and bronchial wall thickening and mucus plugs in two.

Co-existing asthma and atopic background

Two patients had asthma and two had allergic rhinitis before the onset of bronchiolitis. Seven patients had a personal and/or family history of atopic disease. Allergen testing was conducted in six patients, whereby four had positive results and two had negative results, although their total IgE levels were > 200 IU/ml.

Treatment

All patients received azithromycin at a dose of 10 mg/kg/day for 5 days; this dose was repeated once more after an interval of 3 days. Six patients began treatment with 1 to 2 mg/kg/day of methylprednisolone on days 4, 9, 10, and 11 after the onset of illness, respectively. The total course ranged from 8 to 15 days in these patients. The remaining two patients (Patients 5 and 8) received a glucocorticoid via inhalation. One patient (Patient 1) developed respiratory failure and was given nasal continuous positive airway pressure ventilation. The remaining seven patients did not require supplemental oxygen therapy.

Follow-up

All patients were followed up for 4 to 8 months. All were asymptomatic and had normal lung function and chest X-rays at follow-up.

DISCUSSION

We have herein reported the clinical features of childhood *M. pneumoniae* bronchiolitis. Although six patients had bronchopneumonia and two had large airway injury, the prominent findings on chest HRCT in all patients were in accordance with bronchiolitis (Figures 1 and 2). Furthermore, all patients had evidence of *M. pneumoniae* infection. Therefore, the diagnosis of *M. pneumoniae* bronchiolitis was confirmed.

To the best of our knowledge, seven case reports and one case series of *M. pneumoniae* bronchiolitis have been published to date in the English-language literature,[1, 3-5, 7-10] comprising nine adult cases and one pediatric case. In addition, Cha et al[11] described 29 adult patients with *M. pneumoniae* infection, of whom eight had bronchiolitis (28%) and 21 had pneumonia. We conclude from these reports and our study that *M. pneumoniae* can cause bronchiolitis.

Why did *M. pneumoniae* infection cause bronchiolitis rather than airspace consolidation in these individuals?

TABLE 1 Clinical data of eight patients diagnosed with *Mycoplasma pneumoniae* bronchiolitis

No.	Gender	Age	Complaint	PE of lung	MP-IgM	Chest HRCT of MP-bronchiolitis	Personal history of atopic disease	Family history of atopic disease	Allergen test & total IgE	Systemic glucocorticoid (methylprednisolone)
1	M	3y10m	fever for 3 days, cough and wheeze for 2 days	moist rales and wheezing	1:160	bilateral and diffuse centrilobular nodules, ground glass	asthma	father AR	house dust mite grade-1, total IgE > 200 IU/ml	D4, 2mg/kg/day
2	F	4y9m	fever for 5 days, cough and wheeze for 3 days	moist rales and wheezing	1:320	bilateral and diffuse centrilobular nodules, ground glass	(–)	brother AR	not done	D10, 1 mg/kg/day (transfer from other hospital to our hospital on D10)
3	M	5y2m	fever and cough for 9 days	(–)	1:320	bilateral and diffuse centrilobular nodules, patchy shadow	AR	mother AD	negative，total IgE > 200 IU/ml	D9, 2 mg/kg/day
4	M	5y11m	fever and cough for 7 days	moist rales and wheezing	1:320	bilateral tree-in-bud, ground glass and patchy shadow	urticaria	(–)	not done	D9, 2 mg/kg/day
5	F	8y7m	fever, cough and wheeze for 14 days	moist rales and wheezing	1:320	bilateral centrilobular nodules, bronchial wall thickening	eczema, asthma	(–)	mould grade-4, house dust mite grade-3, total IgE > 200 IU/ml	no use
6	M	5y10m	fever for 9 days,cough for 7 days	moist rales and wheezing	1:320	diffuse centrilobular nodules, small patchy within right lung	(–)	mother asthma	negative，total IgE > 200 IU/ml	D9, 2 mg/kg/day
7	M	6y	cough for 11 days, fever for 9 days	wheezing	1:320	bilateral and diffuse centrilobular nodules, tree-in-bud and patchy shadow	(–)	(–)	house dust mite grade-3，cat hair grade-2，total IgE > 200 IU/ml	D11, 2 mg/kg/day
8	F	8y9m	cough for 10 days, fever for 9 days	(–)	1:320	unilateral centrilobular nodules, tree-in-bud and patchy shadow within the right lung	AR	mother AD	mould grade-2, total IgE < 100 IU/ml	no use

PE, physical examination; MP, *Mycoplasma pneumoniae*; HRCT, high resolution computer tomography; F, female; M, male; AD, allergic dermatitis; AR, allergic rhinitis; D, day.

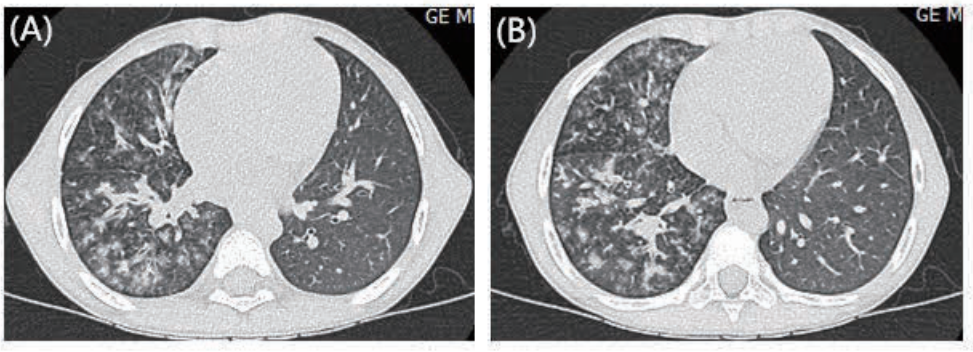

FIGURE 1 Chest high resolution computer tomography scans of patient 8. (A, B) Unilateral centrilobular nodules, a tree-in-bud pattern, and a patchy shadow within the right lung were observed.

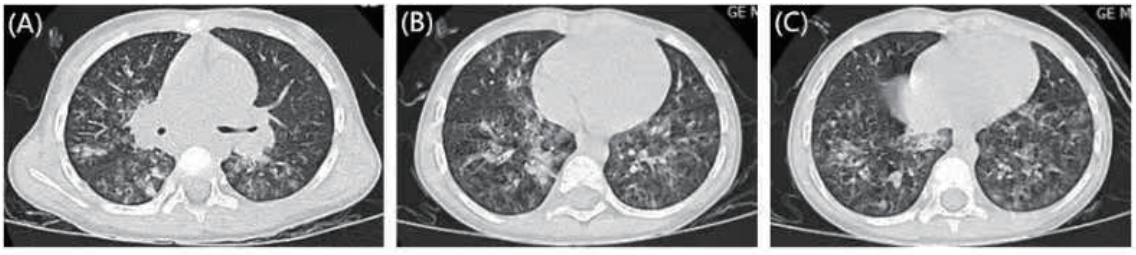

FIGURE 2 Chest high resolution computer tomography scans of patient 7. (A-C) Bilateral and diffuse centrilobular nodules, a tree-in-bud pattern, and patchy shadows were observed.

Tanaka[12] found that the type of *M. pneumoniae* infection might be associated with host factors: in their study, upregulation of host cell-mediated immunity predominantly caused centrilobular nodules, whereas downregulation of host cell-mediated immunity changed the radiological pattern to consolidation. We propose that *M. pneumoniae* bronchiolitis might be associated with an atopic constitution because all patients in this study had atopic backgrounds. Vasudevan et al[7] reported that an adult with severe *M. pneumoniae* bronchiolitis had a history of asthma; moreover, Kawamoto et al[8] found elevated levels of eosinophil cationic protein and IgE in two patients with *M. pneumoniae* bronchiolitis, further supporting the hypothesis that atopy may be associated with the occurrence of *M. pneumoniae* bronchiolitis.

Our previous study[2] and other reports[3-5] have shown that BO can develop following acute *M. pneumoniae* bronchiolitis. Because BO is a chronic airway obstruction disease and is irreversible, it is important to prevent the development of BO after acute *M. pneumoniae* bronchiolitis.

BO is caused by granulation tissue obstruction, and glucocorticoids can inhibit the formation of granulation tissue. In our previous study, 17 patients with acute *M. pneumoniae* bronchiolitis developed BO soon after acute *M. pneumoniae* bronchiolitis, and only 10 (59%) of them received systemic glucocorticoid therapy.[2] Therefore, we speculate that glucocorticoids might have a beneficial effect on preventing the development of BO after acute *M. pneumoniae* bronchiolitis. Additionally, because the features of BO on HRCT, such as pronounced air-trapping and a mosaic pattern, were noted within 2 to 3 weeks following the onset of bronchiolitis,[2] we surmise that initiation of glucocorticoids within 2 weeks might play a preventive role. However, the appropriate time window for starting glucocorticoids and for how long they may be used require further study.

To explore the effect of glucocorticoid therapy on preventing the development of BO after acute *M. pneumoniae* bronchiolitis, we treated six patients (75%) in this study with 1 to 2 mg/kg/day of methylprednisolone after admission at 9.2 ± 2.3 days after onset of acute *M. pneumoniae* bronchiolitis, as shown in Table 1. Compared with the 10 patients who developed BO and received 1 to 2 mg/kg/day of methylprednisolone at 12.2 ± 3.5 days as reported in our previous study,[2] the time of glucocorticoid initiation in these six patients was 3 days earlier (9.2 ± 2.3 versus 12.2 ± 3.5 days). The remaining two mildly affected patients received a glucocorticoid via inhalation. The fact that none of our eight patients developed BO supports the notion that earlier initiation of glucocorticoid therapy might favor the prognosis of acute *M. pneumoniae* bronchiolitis.

This study has some limitations. Because acute bronchiolitis caused by *M. pneumoniae* is rare, the patient sample was too small to support a definitive conclusion. However, given that BO has such a harmful influence on children's quality of life and acute *M. pneumoniae* bronchiolitis is not widely encountered, this study carries some significance. The utilization, time of initiation, and effects of glucocorticoids administration in the prevention of BO development warrant further investigation.

M. pneumoniae bronchiolitis can occur in children, especially in atopic individuals. The use, time of initiation, and effects of glucocorticoids administration in these patients for the prevention of BO require further investigation.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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