

CASE REPORT

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Cavitary necrotising pneumonia with extrapulmonary multi-systemic involvement — a rare presentation of macrolide-resistant *Mycoplasma pneumoniae*

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Abstract

Background *Mycoplasma pneumoniae* is one of the leading causes of community-acquired pneumonia. Due to its microbiological variation, clinical presentations of mycoplasma infections are atypical and diverse. Multiple pulmonary and extrapulmonary manifestations of *Mycoplasma pneumoniae* have been documented. Among pulmonary, common manifestations are fever, malaise, lymphadenopathy, pneumonia, upper respiratory tract infections, sinusitis, etc. Necrotising pneumonia leading to cavitation as a manifestation is rather an uncommon presentation.

Case presentation We are reporting a rare case of a 5-year-old female child who presented with bilateral haemorrhagic pleural effusion and necrotising pneumonia with cavitation along with extrapulmonary manifestation in the form of maculo-papular rash, Coombs-positive haemolytic anaemia and serositis. The child was started on azithromycin and symptomatic management, but she did not respond to it; she had clinical worsening and evidence of radiological necrotising pneumonia. The child was treated as macrolide-resistant mycoplasma pneumonia with levofloxacin, steroids and rigorous physiotherapy.

Conclusions Accurate clinical acumen along with timely radiological imaging is the need of the hour for early diagnosis of macrolide-resistant mycoplasma pneumonia (MRMP). This case also emphasises role of fluoroquinolones and steroids in treatment of macrolide-resistant mycoplasma pneumonia.

Keywords Macrolide-resistant mycoplasma pneumonia (MRMP), Cavitary necrotising pneumonia, *Mycoplasma pneumoniae*

Background

Mycoplasma pneumoniae (MP) is one of the leading etiological agent causing respiratory tract infections in children. In India, MP contributes to up to 30% of community-acquired pneumonia [1]. MP is a pathogen of *Mycoplasmataceae* family, characterised by its small

size and the absence of cell wall which contributes to its inherent resistance to beta-lactam antibiotics. MP usually causes mild or moderate pneumonia which improves without sequelae, and rarely, it takes a fulminant course causing necrotising pneumonia, bronchiolitis obliterans, acute respiratory distress syndrome, lung abscesses, etc. Extrapulmonary manifestations like arthritis, maculo-papular rash, Steven-Johnsons syndrome, hepatitis, encephalitis and glomerulonephritis are seen in up to 25% MP infections [2].

The diagnosis of MP is usually based on immunological titres, as blood cultures are seldom positive.

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Enzyme-linked immunoassays IgM and IgG have 99% specificity and 98% sensitivity [3].

Case presentation

A previously healthy 5-year-old female child admitted to our tertiary care hospital, with complaints of fever and dry cough for 1 week. Prior to admission, she was treated with oral antibiotics for 5 days. On admission, the patient was febrile (38.5 °C), lethargic, tachycardic and tachypneic, and oxygen saturation was 88% on room air. She also had pallor but no cyanosis, clubbing or oedema. On respiratory system examination, the patient had reduced breath sounds bilaterally with fine crepitations. Chest X-ray revealed right lower zone pneumonia as shown in Fig. 1. She was started on oxygen by nasal prongs with flow of 4 L/min. On laboratory investigations, complete blood count (CBC) revealed anaemia with Hb of 7.1 g/dL (11–14 g/dL) and leucopenia-3300 cells/mm³ (4000–11,000 cells/mm³) with neutrophilic predominance (84%), CRP-74 mg/dL (N < 1 mg/dL) and ESR-100 mm/h (N < 5 mm/h), and blood culture had no growth. The patient developed erythematous nonpruritic maculo-papular rash, which started on the chest and later progressed to trunk and limbs (Fig. 2). She received packed cell transfusion by 10 ml/kg body weight in the setting of anaemia, clinical worsening and increased oxygen requirement. Posttransfusion CBC had evidence of haemolysis with fall in Hb to 6.8 g/dL with corrected reticulocyte count of 4%. Sputum culture showed no growth, and sputum CBNAAT was negative. On further evaluation, direct Coomb's test was strongly positive (4+). MP was suspected as there was evidence of

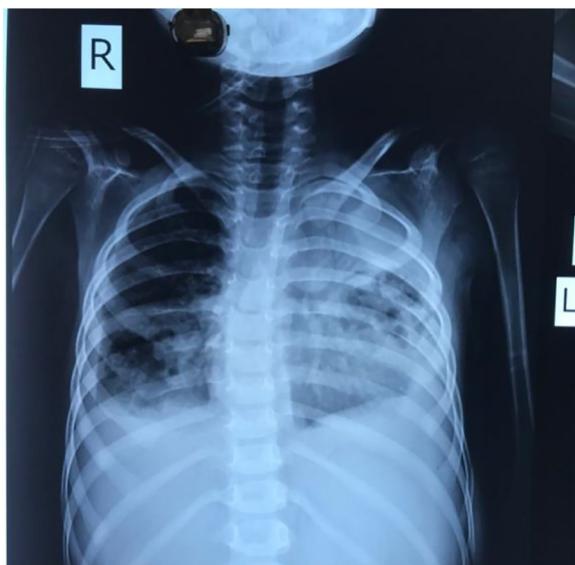


Fig. 1 Chest X-ray



Fig. 2 Erythematous nonpruritic maculo-papular rash on the chest and progressed to trunk and limbs

pneumonia with autoimmune haemolytic anaemia, rash and serositis. Mycoplasma IgM levels were high 33 ng/dL (> 11 ng/dL considered significant), and cold agglutinins were positive. The patient was given symptomatic management and was started on intravenous azithromycin at 10 mg/kg/dose; detailed evaluation with computed tomography (CT) thorax was done which revealed pneumonia with air bronchogram on left upper lobe, lingula and entire right lobe, with ground-glass opacification in left lower lobe and infrahilar region of right lower lobe with mild bilateral pleural effusion and mildly enlarged mediastinal lymph node. Diagnostic pleural tapping had haemorrhagic aspirate (Fig. 3). Pleural fluid examination showed transudative fluid with 20,000 RBCs and 5000 WBCs (75% neutrophils and 25% lymphocytes). Pleural fluid protein was 1.3 g/dL, and sugars were 93 mg/dL. Pleural fluid smear and CBNAAT (cartridge-based nucleic acid amplification test) were negative for mycobacterium tuberculosis. Patient also developed ascites in the meantime. As the patient had multisystem involvement with serositis, muco-cutaneous ulcers, high erythrocyte sedimentation rate and bicytopenia (thrombocytopenia and anaemia), she was investigated for autoimmune disorders such as systemic lupus erythematosus (SLE — antinuclear acid antibody (ANA) came weakly

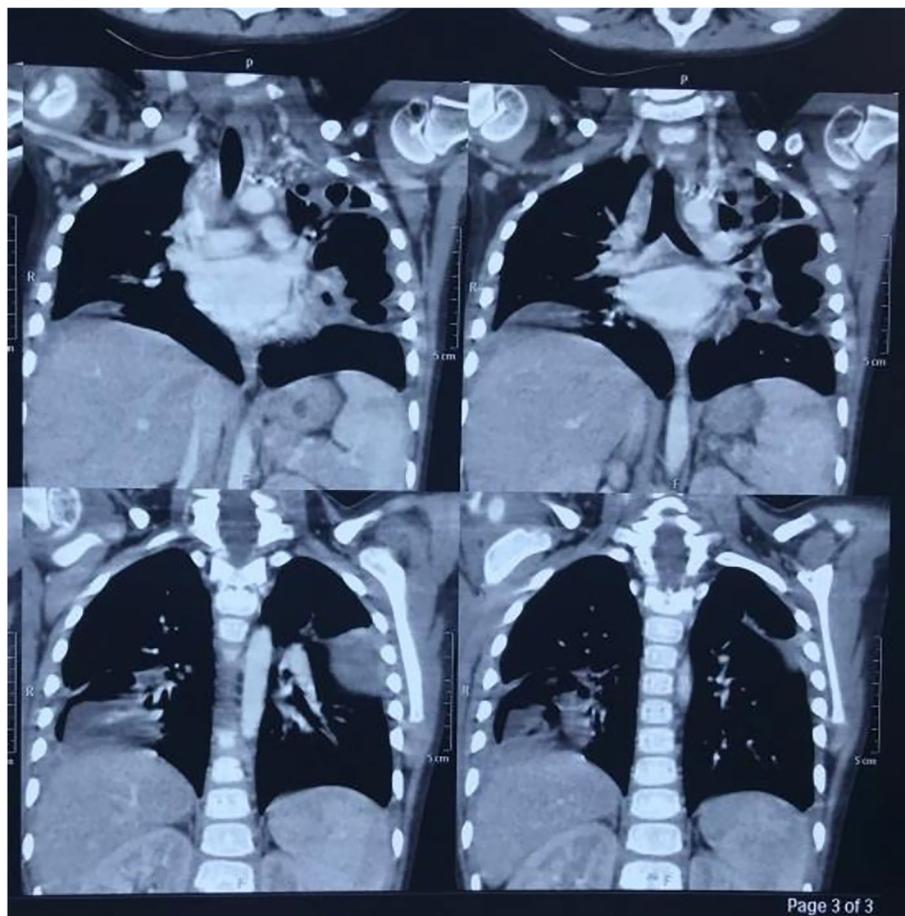


Fig. 3 Pleural fluid

positive (1:80, fine speckled pattern), and anti double-stranded DNA (anti dsDNA) was negative. The child continued to have fever spikes, respiratory distress and extrapulmonary manifestations which pointed towards macrolide-resistant mycoplasma pneumonia (MRMP) infection. Repeat HRCT thorax was done, which revealed (Fig. 3) areas of consolidation with secondary large thick-walled cavitary changes seen involving apico-posterior and anterior segment of left upper lobe (4.6*3.6 cm) and superior and basal segment of right lower lobe (4.4 × 4.1 cm). These findings of necrotising pneumonia with cavitations were suggestive of progression of disease despite adequate treatment with macrolide group of antibiotics as the other common causes of necrotising pneumonia are *Staphylococcus aureus* and streptococcus pneumonia. The sputum culture showed no growth, and blood culture also did not show any growth. Tuberculosis was also ruled out with sputum cartridge-based nucleic acid amplification test (CBNAAT).

The antibiotics were changed to intravenous levofloxacin at 10 mg/kg/dose, and oral steroids were started at

a dose of 2 mg/kg/day, which was tapered over a period of 2 weeks. Intensive physiotherapy was started which included manoeuvres of percussion, vibration and incentive spirometry.

Clinically, improvement (fever decreased) was seen after 3 days of injection of levofloxacin and steroids, respiratory symptoms required 3 weeks to settle, Hb improved to 9 g/dL and platelets improved to 185,000 cells/mm³ by the end of 2 weeks. Patient was discharged after 28 days of admission. After 2 weeks of discharge, DCT was negative. HRCT thorax was done after 6 months of discharge which showed complete resolution of cavitation and fibroatelectatic changes Table 1.

Discussion

MP infection usually presents with minor respiratory illnesses, which are self-limiting and characterised by constitutional symptoms; however, 3–15% patients will develop pneumonia, and on rarer occasions, MP can present as tracheobronchitis with asthma-like clinical picture. Schoolgoing children and adolescents in the age

Table 1 Investigations

	Reference value	Day of illness — 7	Day of illness — 12	Day of illness — 15	Day of illness — 25
Haemoglobin	11.3–14.2 g/dL	7.1	6.8	8	9.2
WBC	5500–15,500	3300	28,000	21,000	10,200
Platelet	150,000–450,000	216,000	18,000	32,000	185,000
ESR	0–30 mm/h	35		100	20
CRP	1–3 mg/L	29.5	70	74	3
SGOT/PT	13–35/5–45 U/L	95.5/62.7	40/24	36/23	42/24
Dengue NS1/IgM		Negative			
Leptospira IgM		Negative			
Widal		Negative			
Blood culture		No growth		No growth	
PT/INR	11–13.5 s/0.8–1.2			12.6/1.03	
Direct Coomb's test				4+	3+
Sputum culture			No growth		
Sputum CBNAAT			Negative		
Mycoplasma IgM				33 ng/dL	

group of 5–20 years of age are most susceptible for MP infection. MP has an incubation period of 2–4 weeks, and mode of transmission is via droplets and fomites. Macrolide resistance is observed in 90–100% mycoplasma pneumonia infections in Asia [4]. Conventionally, MP was treated with macrolides — oral azithromycin or clarithromycin in adequate dosage. Macrolide-resistant strains of MP are treated with either fluoroquinolones or tetracyclines. Clinically, symptoms of macrolide-resistant MP are similar to macrolide-sensitive MP, but worsening or persistence of clinical signs and symptoms and early radiological evaluation can guide to a diagnosis of macrolide-resistant MP [4].

In our case, the patient had persistent fever and respiratory distress with CT thorax showing cavitary necrotising pneumonia (NP) giving evidence of inadequate response to macrolide group of antibiotics. NP is characterized by cavitary lesions which are caused by necrosis and liquefaction of lung tissues. Most common causes of necrotizing pneumonia are *Staphylococcus aureus* and streptococcus pneumonia. These organisms could be ruled out as there was no growth in neither blood culture nor in sputum culture. Tuberculosis was also ruled out as there was no significant contact history and sputum CBNAAT was negative. This helped us narrow down our diagnosis to an organism which is not usually grown in cultures and also present with multiple extrapulmonary manifestations. Thus, provisional diagnosis was mycoplasma pneumonia with extrapulmonary manifestations. It was late confirmed with mycoplasma antibody titers.

Children with necrotizing pneumonia are very sick, febrile and usually will not respond to even adequate

dose of appropriate antibiotic. In some cases, there may be associated empyema which might require surgical drainage. Bronchopleural fistula is a rare complication of MP, which may be diagnosed with spontaneous pneumothorax. Lung necrosis can be detected at an early stage with contrast-enhanced chest CT. A study of 37 patients with MP by Baoying Zheng et al. describes the average time from onset of symptoms to development of necrotic lesion was 24 + / - 10 days [5]. Similarly, our patient had developed necrotising pneumonia by the 3rd week of illness which was identified with CT thorax. Another study of 25 children with MP caused by MRMP by Xia Wang et al. describes the usual antibiotic duration for treatment was 32 days, 80% had pleural effusion, 55% required thoracocentesis and 10% requires chest drainage [6, 7]. Our patient did not require any surgical intervention and was treated with fluoroquinolones and steroids for 7 days with complete recovery.

Extrapulmonary manifestations are in the form of rash, arthritis, serositis and autoimmune haemolytic anaemia. These are early signs which point towards diagnosis of MP infection. Extrapulmonary manifestations of MP are attributed to immunological cross-reactivity; steroids are therefore indicated in counteracting these immune responses [6, 8–10].

Our patient, even though it had developed necrotising pneumonia, pleural effusion and cavitation, did not require any invasive treatment. This emphasises that timely interventions along with appropriate antibiotics, good supportive care and intensive physiotherapy can result in complete recovery without compromising quality of life.

Conclusion

MRMP is on the rise in community. Accurate clinical acumen along with timely radiological imaging is the need of the hour for early diagnosis of MRMP. Mycoplasma pneumonia infection can have varied extrapulmonary manifestations which may sometimes present with multisystem involvement, and well-timed treatment of these manifestations might call for use of immunosuppressive treatment with steroids in addition to the usual antibiotic regimen. It should also be noted that macrolide resistance should be evaluated at a community level and appropriate antibiotic should be given. As macrolide-resistant mycoplasma pneumonia is becoming more prevalent in Asia, clinicians should rethink macrolides as first-line treatment to mycoplasma pneumonia.

Abbreviations

MRMP	Macrolide-resistant mycoplasma pneumonia
MP	Mycoplasma pneumonia
SLE	Systemic lupus erythematosus
ANA	Anti-nucleic acid antibody
NP	Cavitary necrotizing pneumonia

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Not applicable.

Authors' contributions

VS data collection; NM data collection and idea of research; AK idea of research, writing and proofreading; VS analysed and interpreted data; and the authors read and approved the final manuscript.

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Availability of data and materials

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Consent for publication

Consent for publication from parent was taken.

Competing interests

The authors declare that they have no competing interests.

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