

Dramatic response to high dose steroids in refractory and severe Mycoplasma pneumonia

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M. pneumoniae infection usually causes self-limiting disease. Rarely, it could lead to severe life-threatening pneumonia or refractory infection. Excessive cell mediated immune response to infection is thought to be the mechanism of refractory and severe mycoplasma pneumonia. IL-8 is thought to play a part in severe and refractory mycoplasma infections. Furthermore, serum LDH has been shown to be a marker of severe and refractory disease. However, the relationship and the mechanism of raised LDH and IL-18 are not clearly explained in the literature. There were several case studies showing the benefit of steroids amongst children with severe and refractory mycoplasma pneumonia. We report a case of a young man who developed severe and refractory mycoplasma pneumonia who showed a dramatic response to steroids.

Keywords: Mycoplasma pneumonia; lactate dehydrogenase; steroids

Introduction

M. pneumoniae infection rarely can lead to severe life-threatening pneumonia or refractory infection. Steroids were used in some studies in severe mycoplasma to favourable effect. However, the exact place of steroids in severe or refractory disease is controversial. We report a case of severe and refractory mycoplasma pneumonia that showed a dramatic response to steroids.

Case presentation

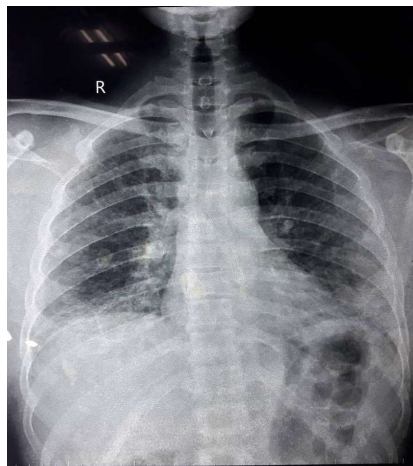
A previously healthy 35-year old mechanic presented to our facility with 7-day history of pyrexia and progressive shortness of breath. He had high grade intermittent pyrexia with chills and progressive shortness of breath limiting his exertion over the same period. He was initially treated at the local hospital, as for chest infection with oral co-amoxiclav and clarithromycin without a satisfactory response. He denied any cough, haemoptysis, wheeze or chest pain but non-specific body aches. He neither had skin rash or arthralgia. There was no history of close

contact with pulmonary tuberculosis or exposure to occupational hazards or birds.

On admission, his temperature was 38.9⁰C. His heart rate was 116 beats per minute and blood pressure was 122/88mmHg. He was in respiratory distress with respiratory rate of 36 cycles per minute. His lung fields revealed predominantly basal inspiratory crackles. He was hypoxic at oxygen saturation of 88% on 6L of oxygen via facemask. Rest of the examination was unremarkable.

Investigations revealed an inflammatory syndrome (WCC $11.2 \times 10^3/\mu\text{L}$, CRP 108mg/L) and chest x-ray showed bilateral opacifications suggestive of interstitial pneumonia (Figure 1).

Figure 1: 1st chest X-ray showing bilateral opacifications suggestive of interstitial pneumonia



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His laboratory findings are shown in Table 1. He was transferred to intensive-care unit (ICU) on the 2nd day due to progressive type 1 respiratory failure. He was started on a trial of bilevel non-invasive ventilation (NIV) to which he was tolerant with a good response. He also received nasal high flow oxygen with maximum inspired oxygen of 60% with 60L/min alternative to NIV.

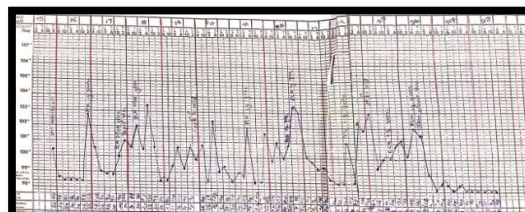
Table 1: Lab results (Haematology and Biochemistry)

Blood results	Days in ICU											
	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15
WCC 10 ³ /μL	10.9	12.9	9.2	8.5	9.3	7.1	9.4	9.4	1.8	1.5	10.0	
Hb g/dl	11.9	13.6	11.2	11.1	11.9	12.2	12.6	12.9	12.4	11.8	10.0	
Plt 10 ³ /μL	309	288	223	331	338	224	234	333	334	227	285	
CRP mg/L	14.2	8.4	1.0		1.4	1.2	1.6	1.9		1.3	12.0	65
SGOT U/L	5.9	7.1										
SGPT U/L	6.3	6.3										
Creatinine μmol/L	1.3	7.8	8.0	9.1	8.8	9.6	1.0	1.0	8.7	6.8	72	
LDH U/L									830			

His serology for Mycoplasma IgM was positive and there was a significant four-fold rising Mycoplasma antibody titre on two consecutive samples taken 10 days apart. Legionella urinary antigen, sputum for *Pneumocystis jiroveci*, *Mycobacterium tuberculosis* and blood retroviral screen was negative. He was continued on piperacillin tazobactam and clarithromycin for 10 days without much progression, as his fever continued, (Figure 2) and we were unable to wean oxygen therapy below 50%.

Due to poor response to therapy, he was started on oral doxycycline. However, despite 7 days of further therapy with doxycycline his fever continued and remained on high oxygen requirements.

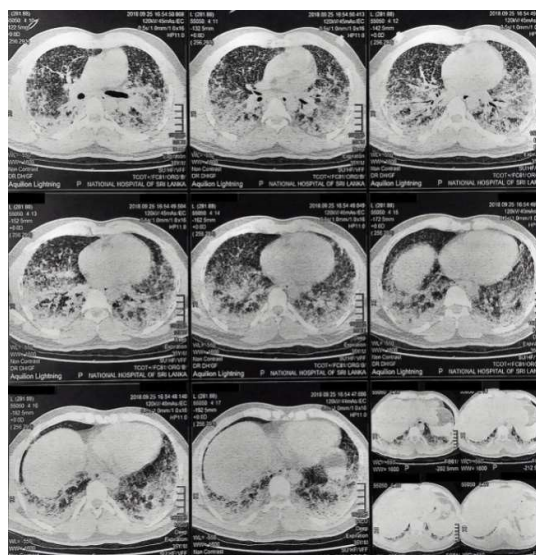
Figure 2: Temperature chart during ICU stay



Initiation of Hydrocortisone

High resolution computed tomography (HRCT) of the chest showed bilateral consolidations with a minimal right-side pleural effusion (Figure 3a, 3b).

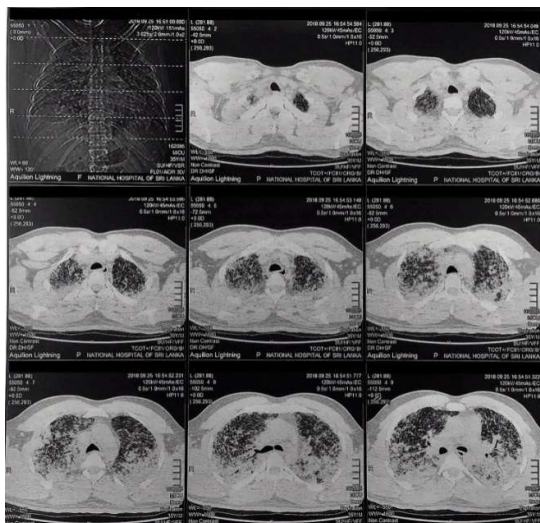
Figure 3a: High resolution Computerised tomography (HRCT) showing bilateral consolidations with a minimal right-side pleural effusion



Serum lactate dehydrogenase (LDH) level was as 830 IU/L. We decided to start him on a trial of steroid therapy as there is some evidence of beneficial effects of steroids in resistant and severe mycoplasma pneumonia. His clinical condition improved dramatically upon commencement of intravenous hydrocortisone 100mg 6 hourly. His fever subsided the next day, and oxygen therapy was weaned off successfully over 48 hours. Hydrocortisone

was changed to oral prednisolone after 4 days and the dose was tapered off over 14 days. His clinical course was complicated with right sided exudative pleural effusion. He was discharged home after further 1 week of ward stay.

Figure 3b: High resolution Computerised tomography (HRCT) showing bilateral consolidations with a minimal right-side pleural effusion



Discussion

M. pneumoniae infection usually causes self-limiting disease. Rarely it can lead to severe life-threatening pneumonia or refractory infection.¹ Continuing fever or worsening symptoms for more than 7 days or more and worsening chest x-ray infiltrates despite adequate antibiotics is considered as refractory *M. pneumoniae* pneumonia. Severe pneumonia is defined as patients who require ICU admissions due to *M. pneumoniae* pneumonia.² Excessive cell mediated immune response to infection is thought to be the mechanism of refractory and severe mycoplasma pneumonia.³ Narita and colleagues demonstrated that *M. pneumoniae* can induce IL-18 and the local production of IL-18 in the lung is associated with pulmonary disease.⁴ Furthermore, serum IL-18 level was thought to be a useful as a predictor of refractory or severe *M. pneumoniae* pneumonia.^{4,5} A study done by Inamura and colleagues showed a significant correlation between serum IL-18 and lactate dehydrogenase (LDH) levels in patients with refractory mycoplasma pneumonia.⁶

However, the relationship and the mechanism of raised LDH and IL-18 are not clearly explained in the literature.

Steroids were used in some studies in severe mycoplasma to favourable effect⁽¹⁾. There were several case studies showing benefit of steroids among children with severe and refractory mycoplasma pneumonia.^{7,8} However, in some studies rate of both inappropriate treatment and non-treatment with anti-mycoplasma antibiotics were seen up to 78.8% of cases.¹ Furthermore, the exact timing for initiation of steroid therapy has not yet been fully investigated and the doses of steroids were different in available case studies. Miyashita and colleagues suggested an LDH cut off levels to start steroids at 363 IU/L 3 days and 264 IU/L at 7 days before steroids.⁹

Our patient fell into the category of severe and refractory *mycoplasma pneumoniae* as he required ICU admission with poor response to antibiotic therapy. His LDH value was 830 IU/L 3 days prior to initiation of steroids. Furthermore, the two questions that we had to answer were, whether the poor response was due to drug resistance or a new acquired infection. Clarithromycin resistance is reported to be high in Asian countries,¹⁰ However, Sri Lankan data on clarithromycin resistance is scarce. He was treated with clarithromycin for 10 days initially and doxycycline for a further 7 days. Therefore, he should have responded to doxycycline as the resistance to doxycycline is very low. However, Miyashita and colleagues showed severe pneumonia was independent of macrolide-resistant infection,¹⁰ In addition, repeated sputum or blood cultures and serology for other respiratory pathogens were negative. This led us to start steroid therapy. Pulmonary tuberculosis was ruled out by doing sputum culture, negative gene expert studies and HRCT. Exclusion of tuberculosis is an important as it is highly prevalent in Sri Lanka and steroids might worsen the clinical condition in the presence of TB.

Conclusions

This case highlights the usefulness of serum LDH and steroids in refractory and severe mycoplasma pneumonia. However, before starting steroids therapy, antibiotic resistance, new acquired infections and exclusion of pulmonary TB are crucial as steroids are not

without any side effects and may worsen pulmonary TB. Furthermore, the exact dose and the exact duration of steroid therapy in these clinical situations are yet to be determined.

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