**Increasing number of clinically severe of *Mycoplasma pneumoniae* infections in children after the COVID-19 pandemic: a single centre case series**

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**Abstract**

In 2024, there have been increases in laboratory confirmed infections of Mycoplasma Pneumoniae infection worldwide. This case series highlights increasing frequency of *Mycoplasma pneumoniae* positive PCR specimens and an increased number of hospital admissions with *Mycoplasma pneumoniae* clinical syndromes. Within this case series, we observed, a change in the epidemiology and clinical burden of childhood Mycoplasma pneumonia disease in the post COVID-19 era.

## Introduction

There have been significant declines in the rates of Mycoplasma pneumoniae (*M. pneumoniae*) infection in children in a regional study in China during the COVID-19 pandemic and an uptick in laboratory confirmed positive reports once societal restrictions lifted (1). In the last 12 months, there have been increases in laboratory confirmed notifications of *M. pneumoniae* across Europe and the USA (2-7). Our understanding of any association between increased microbiological rates and correlation with disease severity in children after the COVID-19 pandemic is limited. A recent population based cohort study demonstrated that Mycoplasma PCR positivity and hospitalisations among children increased 2.9 and 2.6 fold respectively in 2023-2024, however the disease severity was unchanged (8). The aim of this study was to describe hospital admissions with positive *M. pneumoniae* PCR results in a large tertiary paediatric centre and compare disease severity before, during and after the COVID-19 pandemic.

## Methods

This retrospective case series was undertaken at Great Ormond Street Hospital for Children, United Kingdom during 1/10/18 to 31/5/24. Rapid syndromic multiplex PCR testing for respiratory pathogens (QIAstat-DX Respiratory Panel Plus, Qiagen) was introduced in October 2018 for detection of a range of bacterial and viral targets including *M. pneumoniae.* The study start date reflects the introduction of the QIAstat-DX multiplex PCR test and this test was used throughout the study. The *M. pneumoniae* detection rate and reproducibility for this platform is reported as 100% (95% CI 93.9-100%). The sensitivity is 100% (91.8-100%) and specificity 99.63% (99.3-99.8%). Positive samples from nasopharyngeal aspirates or bronchoalveolar lavage were included. Data were obtained from the electronic medical record and collected from March to May 2024. All positive *M. pneumoniae* PCR tests from children (<16 years) were identified via local laboratory databases and cross checked with hospital discharge coding data. Hospital admissions related to *M. pneumoniae* were defined as a positive PCR test during admission where the discharge diagnosis was an *M. pneumoniae* associated clinical syndrome. Severe disease was defined as those patients requiring paediatric intensive care unit (PICU) level care. This

study received approval as service evaluation (#3803) with the clinical audit/quality service at GOSH, in line with the criteria outlined by the National Health Service's Health Research Authority and adhering to the respective ethical guidelines.

**Results**

In total, 10, 390 multiplex respiratory PCR tests were performed during the study period. Extended multiplex PCR testing is performed in children who are admitted to ICU, urgent transplant or routine inpatient screen in a BMT/immunology patient. The overall positivity rate for *M. pneumoniae* DNA detection was 0.4% (n=43). There has been a marked increase in the positivity rate in the first 5 months of 2024, increasing 10-fold from 0.35% in 2023 to 3.1% to May 2024 (Figure 1A). Of the 43 positive *M. pneumoniae PCR results from October 2018 to May 2024* , 29 were among hospital inpatients (67%). Nine (31%) were asymptomatic, for example identified on peri-operative screening and excluded. Therefore, 20 cases were included. Of these, 16 (55%) required Paediatric Intensive Care Unit (PICU) admission and 4 (14%) required ward-level care. Of the 4 symptomatic, non-PICU infections, 3 were diagnosed with pneumonia and 1 patient had febrile neutropaenia. As this study is a case-series, denominators of pneumonia or other clinical syndromes were not available to determine mycoplasma disease rates overall.

Of the 16 cases requiring PICU admission, the mycoplasma clinical syndromes identified were pneumonia with respiratory failure (6), encephalitis (7), Mycoplasma-induced rash and mucositis (MIRM) (1), fluid refractory shock (1) and steroid-responsive nephrotic syndrome (1). The number of PCR confirmed and severe infections requiring PICU admission increased from October 2023 to May 2024(Figure 1B). Eleven of sixteen cases (69%) requiring PICU admission at our institution over the 4.5 year study period have occurred since October 2023 (Figure 1C). The clinical phenotype of these recent patients has been severe pneumonia (n=6, 55%), encephalitis (n=4, 36%) and toxic epidermal necrolysis (n=1, 9%). All 11 patients required invasive ventilation. Three patients were referred from PICU for Extra Corporeal Membrane Oxygenation (ECMO) assessment and one patient subsequently required VV ECMO treatment (Table 1). The number of patients with severe *M. pneumoniae*

pneumonia associated with respiratory failure appears to have also increased since November 2023 (Figure 1C).

The median age of patients in this cohort was 7.1 years and did not differ by diagnosis (pneumonia 5.6 years, encephalitis 8 years, other 6.5 years). None of the patients with encephalitis had *M. pneumoniae* DNA detected in CSF. The median duration of PICU admission for the whole cohort was 4.5 days (IQR 2-6 days). Patients with pneumonia had longer PICU stays than children with encephalitis or other presentations (5.5 vs 2 vs 2 days).

*M. pneumoniae* was the only pathogen isolated in 5 of 6 patients admitted to PICU with respiratory failure. In contrast, children with encephalitis or other diagnoses had viral co-infection in 6 of 10 cases (SARS-CoV-2 n=3, Rhino/enterovirus n=2, Influenza B n=1) (Table 1). All of our patients received macrolide therapy with duration ranging from 7-21 days. Two patients with severe pneumonia received additional doxycycline and one moxifloxacin during treatment. Resistance testing was performed in one of these patients and macrolide point mutations were not detected. Twelve (60%) patients required immunomodulatory treatment. Four of six pneumonia patients received corticosteroid therapy during PICU admission, five of 7 encephalitis patients received a combination of corticosteroids, IVIG or plasma exchange and all three patients with alternative diagnoses received immunomodulation. All patients in this cohort survived to hospital discharge.

**Discussion**

There has been a notable increase in the rate of *M. pneumoniae* detection and the number of severe disease presentations at our institution since October 2023. This is consistent with an increase in the incidence of *M. pneumoniae* laboratory confirmed notifications globally in the aftermath of the COVID-19 pandemic (3, 9). Our experience highlights that symptomatic paediatric *M. pneumoniae* infection generally affects older children and may be associated with clinical complexity (e.g. extra-pulmonary manifestations) and severe disease in the post COVID-19 era.

The reason for the observed increase in *M. pneumoniae* detection and severe infection may reflect host or pathogen factors. The reduced exposure during the COVID-19 pandemic as a result of national lock downs may have resulted in a larger susceptible population and subsequent increased prevalence of disease in the post-pandemic period, as has been observed for other respiratory pathogens (10). We observed an increase in Mycoplasma detection from Autumn 2022 which may reflect the end of mask mandates in the UK in January 2022 followed by the typical seasonal peak in *M. pneumonia* infection in the Autumn. We hypothesise that the number of children requiring hospitalisation increased during the 2023 season due to increasing overall *M. pneumoniae* circulation and colonisation in the community. This could also result from a shift in dominant circulating strain of *M. pneumoniae* with the emergence of a more pathogenic or transmissible strain. For example, an A2063G mutant strain was the predominant strain in the outbreak in northern and central China. While this mutation confers macrolide resistance, there is currently limited evidence to support increased virulence (4, 11).

Macrolide resistance is increasing in Europe and in China but remains uncommon in the USA (7). This is proposed to be due to increased circulation of EC2 clones with 100% macrolide resistance due to acquisition of a mutation (A2063G) in the 23S rRNA (12). In our cohort, first line macrolide treatment was used in all patients. Two patients with severe respiratory tract infection received additional antibiotic treatment including Doxycycline and Moxifloxacin. Macrolide resistance testing was only performed for one patient with a protracted clinical course and was negative. The majority of our cohort did receive corticosteroids during PICU admission despite lack of robust data supporting this. Severe or fulminant *M. pneumoniae* infection has been proposed to be due to a variety of factors including a host driven hyperimmune response, in particular an overzealous innate immune response resulting in macrophage activation. This hypothesis is driven by the finding of elevated levels of serum IL-18 among patients with severe disease (13). None of the patients with encephalitis attributed to Mycoplasma had Mycoplasma detected in CSF. Two distinct clinical patterns of Mycoplasma associated CNS presentations are described, early which occurs less than 7 days from onset of respiratory symptoms or fever and in which CSF PCR is frequently positive and later presentations in which CSF PCR is more frequently negative (14). In contrast to this observation, despite negative CSF PCR in all of the encephalitis

presentations included in this series, the duration of symptoms prior to admission was less than seven days.

This study has several limitations. This is a single centre study, performed in a large tertiary paediatric unit with PICU. Our cohort therefore may over-represent severe disease manifestations of *M. pneumonia* (i.e. being referred for specialist services) and under-represent the actual burden of asymptomatic/mild infection (i.e. this is not a population based screening study). Asymptomatic colonisation with Mycoplasma is increasingly recognised (15). While we report hospital in-patients with positive diagnostic tests for Mycoplasma, we cannot out-rule that in some of these cases Mycoplasma may have been a colonizer rather than the responsible pathogen as neither quantitative PCR nor serology distinguishes between asymptomatic colonisation and disease. The total number of admissions with Mycoplasma associated clinical syndromes such as pneumonia or encephalitis were not available to review and therefore we cannot confirm whether rates of Mycoplasma associated disease are increasing or if this increase reflects an increase in total admissions. We have no long term follow up data after hospital discharge and isolates were not routinely tested for macrolide resistance.

This study highlights an increase in *M. pneumoniae* detection rates and a striking cluster of severe pulmonary and extra-pulmonary disease manifestations in affected children in the post COVID-19 era. Our experience highlights the importance of prompt *M. pneumoniae* testing in severely unwell children with compatible disease syndromes in the UK setting and developing clinical studies to better understand the efficacy of immunomodulatory treatment.

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Data availability statement: all patient are data are fully anonymised. The data that support the findings of this study will be available from the corresponding author upon reasonable request.

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| **Table 1: Clinical and demographic characteristics of paediatric patients with severe *Mycoplasma pneumoniae* infections from 2019-2024 (n=16)** | | | | | |
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| **Demographic variables** | **Clinical presentation** | **Investigations** | **Supportive management** | **Treatment** | **Outcome** |
| **Respiratory** | | | | | |
| 13 years 5 months<br>Female<br>No co-morbidities<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | 7 day history of fever, cough, coryza, shortness of breath, fatigue, nausea and vomiting and abdominal pain. | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 13.4<br>Blood: Detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Complete consolidation of right lung with moderate right pleural effusion, patchy consolidation of left lower lobe. | Respiratory support:<br>VV ECMO (8 days),<br>Intubated and ventilated (HFOV) (12 days), inhaled nitric oxide,<br>Non-invasive ventilation (1 day),<br>Oxygen therapy (28 days)<br>Ionotropic support: Yes<br>LV ejection fraction on echo: 63% (M-mode)<br>Renal replacement therapy: Yes<br>Blood products: Fresh frozen plasma | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (10 days),<br>Moxifloxacin (6 days),<br>Doxycycline (28 days)<br>Adjunctive therapy:<br>Dexamethasone (0.3mg/kg 2 doses) | PICU LOS: 11 days<br>Total LOS: 33 days<br>Discharge destination<br>Home<br>Follow up duration:<br>1 month<br>Discharge outcome:<br>Mild persistent cough and reduced exercise tolerance |
| 15 years 6 months<br>Female<br>Soto's syndrome<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | 7 day history of cough, coryza, shortness of breath, fatigue, nausea and vomiting. | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 19.6<br>BAL: DNA Detected, CT Value 23.8<br>Blood: Detected<br>Macrolide point mutation test: Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Left lower lobe consolidation with bronchial wall thickening, left pleural effusion. | Respiratory support:<br>Intubated and ventilated (6 days – ongoing at transfer), inhaled nitric oxide<br>Ionotropic support Yes<br>LV ejection fraction on echo: 65% (M-mode)<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Moxifloxacin (3 days)<br>Doxycycline (6 days) – transferred to another hospital to complete course<br>Adjunctive therapies:<br>Methylprednisolone (1mg/kg x 3 doses) | PICU LOS: 6 days<br>Total LOS: 6 days<br>Discharge destination<br>Transferred to PICU in another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Unknown |
| 7 years 10 months<br>Male<br>No co-morbidities<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | 8 day history of fever, cough, coryza and shortness of breath. | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 32<br>Blood: Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging: | Respiratory support:<br>Intubated and ventilated (2 days),<br>Supplemental oxygen (4 days – ongoing at transfer)<br>Ionotropic support No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (10 days)<br>Adjunctive therapy:<br>Nil | PICU LOS: 5 days<br>Total LOS: 6 days<br>Discharge destination<br>Transfer to another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome: |

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| | | Right upper lobe and Left lower lobe consolidation on a background of ground glass opacification and bilateral pleural effusions. | | | Unknown |
| 3 years 7 months<br>Male<br>Type 1 Diabetes<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | 5 day history of fever, cough, coryza, wheeze, shortness of breath, fatigue and diarrhoea. | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 20.7<br>Blood: Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Dense consolidation of left upper lobe, patchy consolidation in lower lobes bilaterally. Bilateral peri-bronchial thickening, | Respiratory support:<br>Intubated and ventilated (2 days), Supplemental oxygen (2 days – ongoing at transfer)<br>Ionotropic support: Yes<br>LV ejection fraction on echo: 63% (biplane)<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (10 days)<br>Adjunctive therapy:<br>Dexamethasone 03mg/kg PO x 1 dose | PICU LOS: 3 days<br>Total LOS: days<br>Discharge destination<br>Transferred to another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Unknown |
| 4 months<br>Male<br>No co-morbidities<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | 22 day history of cough, coryza, shortness of breath and seizures. | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 22.2<br>Blood culture: Negative<br>Co-infection: RSV<br>Diagnostic imaging:<br>Bilateral widespread patchy consolidation, minor blunting of costophrenic angles. | Respiratory support:<br>Intubated and ventilated (3 days), Non-invasive ventilation (1 day-ongoing at transfer)<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Azithromycin (7 days)<br>Adjunctive therapy:<br>Dexamethasone (0.15mg/kg IV x 5 doses) | PICU LOS: 4 days<br>Total LOS: 4 days<br>Discharge destination<br>Transferred to another hospital<br>Discharge outcome:<br>Unknown |
| 5 days<br>Female<br>Prematurity (31 weeks)<br><br>Diagnosis:<br>Pneumonia with hypoxic respiratory failure | Birth asphyxia and respiratory distress | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 30.4<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Right upper lobe consolidation and sub-segmental left lower lobe atelectasis | Respiratory support:<br>Intubated and ventilated (3 days)<br>Non-invasive ventilation 17 days<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: 1 Red cell transfusion | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (10 days)<br>Adjunctive therapy:<br>Nil | PICU LOS: 20 days<br>Total LOS:20 days<br>Discharge destination:<br>Transfer to another hospital<br>Follow up duration:<br>3 years<br>Discharge outcome:<br>Chronic lung disease with an oxygen requirement |
| **Neurology** | | | | | |
| 11 year 2 months<br>Male | 3 day history of vomiting, | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 19.2 | Respiratory support:<br>Intubated and ventilated (4 days)<br>Ionotropic support: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (21 days) | PICU LOS: 4 days<br>Total LOS:65 days |

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| Ornithine transcarbamolase deficiency<br><br>Diagnosis: Encephalitis | increasing lethargy and seizures | Blood PCR; Not detected<br>CSF PCR; Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Normal<br>CT Brain: Cerebral oedema<br>MRI Brain: Subtle and patchy areas of diffusion restriction in the frontal cortex. | Renal replacement therapy: No<br>Blood products: No | Adjunctive therapy:<br>Methylprednisolone (20mg/kg x 5 doses), IVIG (0.4mg/kg x 2 doses), Plasma exchange (5 cycles) | Discharge destination:<br>Discharged home<br>Follow up duration:<br>3 months<br>Discharge outcome:<br>Basal ganglia injury with residual movement disorder |
| 13 years 11 months<br>Male<br>No co-morbidities<br><br>Diagnosis: Gullian Barre Syndrome | 14 day history of fever, vomiting, diarrhoea, abdominal pain followed by acute lower limb weakness | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 34.9<br>CSF PCR; Not detected<br>Brain biopsy PCR: Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>MRI Brain: Bilateral white matter changes, patchy swelling of the cortex and deep brain structures, some restricted diffusion seen. | Respiratory support: No<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (7 days)<br>Adjunctive therapy:<br>IVIG (0.4mg/kg x 5 doses) | PICU LOS: 1 day<br>Total LOS: 30 days<br>Discharge destination:<br>Discharged home<br>Follow up duration:<br>4 years<br>Discharge outcome:<br>Full recovery |
| 8 years<br>Female<br>No Co-morbidities<br><br>Diagnosis: Encephalitis | 2 day history of fever, vomiting, headache followed by altered consciousness | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 35.2<br>CSF PCR; Not detected<br>Brain biopsy PCR: Not detected<br>Blood culture: Negative<br>Co-infection: Pseudomonas UTI<br>Diagnostic imaging:<br>CXR: Patchy airspace consolidation<br>MRI Brain: Diffuse cerebral and cerebellar swelling and hyperintensity with diffuse white matter diffusion restriction. | Respiratory support: Intubated and ventilated (5 days), supplemental oxygen (6 days)<br>Ionotropic support: Yes<br>LV ejection fraction on echo: Day 0 - 25% -> Day 2 - 40% -> Day 164 - 51%<br>Renal replacement therapy: Yes<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (7 days)<br>Adjunctive therapy:<br>Methylprednisolone (10mg/kg x 3 doses, 2mg/kg x 2 doses)<br>IVIG (0.4mg/kg x 2 doses) | PICU LOS: 6 days<br>Total LOS: 50 days<br>Discharge destination:<br>Discharged home<br>Follow up duration:<br>6 months<br>Discharge outcome:<br>Full recovery |
| 3 years 6 months<br>Male<br>No co-morbidities | 1 day fever and diarrhoea followed by | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 34.6 | Respiratory support: Intubated and ventilated (2 days), supplemental oxygen (2 days) | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (10 days) | PICU LOS: 2 days<br>Total LOS: 3 days |

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| Diagnosis:<br>Encephalitis | generalised tonic clonic seizure | CSF PCR; Not detected<br>Blood culture: Negative<br>Co-infection: SARS-CoV-2<br>Diagnostic imaging:<br>Nil | Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | Adjunctive therapy:<br>Nil | Discharge destination:<br>Transferred to another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Unknown |
| 14 yeas 11 months<br>Male<br>No co-morbidities<br><br>Diagnosis;<br>Encephalitis, hypoxic respiratory failure | 2 day history of fever, vomiting, lethargy followed by altered consciousness | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 26.7<br>CSF PCR; Not detected<br>Blood culture: Negative<br>Co-infection: Influenza B virus<br>Diagnostic imaging:<br>CXR: Normal<br>MRI Brain: Normal | Respiratory support: Intubated and ventilated (2 days), supplemental oxygen (2 days)<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (14 days)<br>Adjunctive therapy:<br>Nil | PICU LOS: 2 days<br>Total LOS: 5 days<br>Discharge destination:<br>Transferred to another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Full recovery |
| 6 year 3 months<br>Female<br>Sensorineural hearing loss<br><br>Diagnosis:<br>Meningo-encephalitis | 1 day history of vomiting and lethargy followed by altered consciousness and generalised tonic clonic seizure | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 25.5<br>CSF PCR; Not detected<br>Blood culture: Negative<br>Co-infection: Nil<br>Diagnostic imaging:<br>CXR: Normal<br>MRI Brain: Supratentorial cerebral oedema with sulcal effacement | Respiratory support: Intubated and ventilated (2 days), supplemental oxygen (1 day)<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (9 days)<br>Adjunctive therapy:<br>Dexamethasone (0.6mg/kg x 1 dose) | PICU LOS: 2 days<br>Total LOS: 9 days<br>Discharge destination:<br>Transferred to another hospital<br>Follow up duration:<br>1 month<br>Discharge outcome:<br>Clinically well, normal hearing |
| 6 weeks<br>Male<br>Osteopetrosis<br><br>Diagnosis:<br>Cerebellitis | 3 day history of coryza and cough followed by apnoea and altered consciousness | Mycoplasma PCR<br>NPA: DNA Detected, CT Value 29.6<br>Blood PCR: Not detected<br>CSF PCR:<br>Blood culture: Negative<br>Co-infection: Rhino/Enterovirus<br>Diagnostic imaging:<br>CXR: Normal<br>MRI Brain: Oedema of the cerebella hemispheres with mass effect and tonsillar herniation | Respiratory support:<br>Intubated and ventilated (6 days)<br>Supplemental oxygen ( 1 day)<br>Ionotropic support: No<br>Renal replacement therapy: No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (7 days)<br>Adjunctive therapy:<br>Dexamethasone (0.5mg/kg 8 hourly x 3 days followed by wean over 2 days) | PICU LOS: 1 days<br>Total LOS: Remained an inpatient for bone marrow transplant<br>Discharge destination:<br>Home<br>Follow up duration:<br>1 year<br>Discharge outcome:<br>Hearing and visual impairment, iatrogenic adrenal suppression |

| **Other** | | | | | |
|---|---|---|---|---|---|
| 9 years 9 month<br>Female<br>No co-morbidities<br><br>Diagnosis:<br>Mycoplasma induced rash and mucositis | 10 day history of cough, coryza, 4 day history of conjunctivitis, fever, pharyngitis followed by 1 day of widespread maculopapular rash with mucosal involvement | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 34.5<br>Blood culture: Negative<br>Co-infection: SARS-CoV-2<br>Diagnostic imaging:<br>CXR: Normal | Respiratory support:<br>Intubated and ventilated (2 days)<br>Ionotropic support: Yes<br>Renal replacement therapy: No<br>Blood products: 1 Red cell transfusion | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (Uncertain, course completed in another hospital)<br>Adjunctive therapy:<br>IVIG (1g/kg x 3 doses), Plasma exchange (5 cycles) | PICU LOS: 2 days<br>Total LOS: 2 days<br>Discharge destination:<br>Transferred to another PICU<br>Follow up duration:<br>4 months<br>Discharge outcome:<br>Required amniotic membrane transplant to conjunctivae bilaterally. Bowel ischaemia and abdominal compartment syndrome requiring significant small and large bowel resection and ileostomy. |
| 3 years 9 months<br>Female<br>No Co-morbidities<br><br>Diagnosis: Steroid refractory nephrotic syndrome | 1 day history of fever, vomiting, abdominal pain and altered level of consciousness | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 29.9<br>Blood culture: Negative<br>Co-infection: Rhino/Enterovirus, Adenovirus<br>Diagnostic imaging:<br>CXR: Patchy perihilar consolidation. | Respiratory support:<br>Supplemental oxygen (2 days)<br>Ionotropic support: No<br>Renal replacement therapy No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (7 days)<br>Adjunctive therapy:<br>Prednisolone (60mg/m2 daily x 5 days followed by wean) | PICU LOS: 2 days<br>Total LOS: 11 days<br>Discharge destination:<br>Discharged home<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Unknown |
| 6 years 7 months<br>Male<br>No co-morbidities<br><br>Diagnosis: Sepsis, fluid refractory shock | 7 days history of fever, rash, conjunctivitis, pharyngitis followed by 2 days of diarrhoea | Laboratory<br>Mycoplasma PCR<br>NPA: DNA Detected, CT Value 33.1<br>Blood culture: Negative<br>Co-infection: SARS-CoV-2<br>Diagnostic imaging:<br>CXR: Normal | Respiratory support:<br>Intubated and Ventilated (1 day)<br>Ionotropic support: Yes<br>LV ejection fraction on echo: 54% (M-mode)<br>Renal replacement therapy No<br>Blood products: No | *M. pneumoniae* directed antibiotic management<br>Clarithromycin (7 days)<br>Adjunctive therapy:<br>IVIG (2g/kg 1 dose), Methylprednisolone (10mg/kg x 3 doses), Prednisolone (2mg/kg x 7 doses) | PICU LOS: 5 days<br>Total LOS: 9 days<br>Discharge destination:<br>Transferred to another hospital<br>Follow up duration:<br>Nil<br>Discharge outcome:<br>Unknown |
| BAL: Bronchoalveolar lavage, CSF: Cerebrospinal fluid, CT value: Cycle threshold value, CT Brain: Computed tomography brain, CXR: Chest X ray, DNA: Deoxyribonucleic acid, VV ECMO: Venovenous Extra Corporeal Membrane Oxygenation, HFOV: High frequency oscillatory ventilation, IVIG: Intravenous immunoglobulin, LOS: Length of stay, mg/kg: Milligrams | | | | | |

per kilogram, LV: left ventricle, MRI: Magnetic resonance imaging, *M. pneumoniae*: *Mycoplasma pneumoniae*, NPA: Nasopharyngeal aspirate, PCR: Polymerase chain reaction, PICU: Paediatric Intensive care unit, RSV: Respiratory syncytial virus, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, UTI: Urinary tract infection.

**Table 1: Summary of severe cases and clinical characteristics**