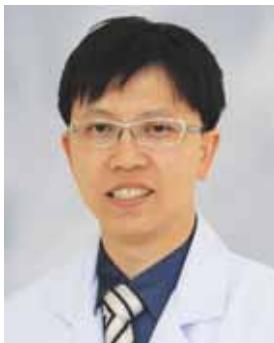


## Noteworthy Cases of Viral Pneumonia



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**C**ommunity-acquired pneumonia (CAP) is an important cause of morbidity and mortality in all age groups throughout the world. Bacterial pneumonia is the most described, with *Streptococcus pneumoniae* being the most important pathogen in all age groups. Viruses are also recognised as important causes of CAP both in children and adults. Viral pneumonia account for 13 - 50% of single pathogen diagnosed community-acquired pneumonia cases and 8 -27% of mixed bacterial-viral pneumonia.<sup>1-4</sup>

In the past there were relatively limited ranges of diagnostic tools for viral pneumonia such as antibody detection only, thereby compromising the ability to identify the causative virus in the CAP cases. With the outbreaks of severe acute respiratory syndrome (SARS) and pandemic flu many more studies have focused their attention on the causative viruses in severe viral pneumonias. Developments in diagnostic tests (particularly nucleic acid amplification tests) have improved the ability to detect and clarify the culprit viruses and allow clinicians to understand and characterise the epidemiology of respiratory virus infections better. Significantly, these tests have illustrated how the role of viruses in CAP has been previously underestimated. Influenza virus type A&B are the most common aetiology of viral pneumonia in adults.<sup>4</sup> The other common pathogens are Respiratory syncytial virus (RSV), Adenovirus, Parainfluenza virus (PIV), Coronavirus, and human Metapneumovirus (hMPV). Among these groups the RSV, PIV and hMPV are part of Paramyxoviridae family.

We describe two cases that developed severe viral pneumonia associated with the novel virus in Paramyxoviridae family. These patients were admitted to the intensive care unit (ICU) at Bangkok Hospital Hua Hin because of severe respiratory failure. We hope that these two cases will raise awareness among clinicians to consider other significant causes of viral pneumonia other than Influenza.

### Case Report # 1

A 59-year-old Thai man was transferred from the local hospital in Prachuap Khiri Khan Province with worsening respiratory failure. He initially presented to the local hospital with a history of hemoptysis, shortness of breath and low grade fever for 3 days. Five days earlier the only leading symptom was cough. The patient was an ex-smoker. He worked as a civil servant and only drank alcohol occasionally for social purposes. He incorporated a chicken farm into his garden at home. His previous medical history included asthma, hypertension, hypercholesterolemia, benign prostatic hypertrophy and gout. His regular medications were Symbicort, Perindopril, Rosuvastatin, Ezetimibe, Alfuzosin, Aspirin, Allopurinol and Colchicine.

At a local hospital he was treated for community acquired pneumonia with Ceftriaxone and Clarithromycin. Despite treatment with antibiotics, his condition had further deteriorated and he developed respiratory failure.

On arrival at Bangkok Hospital Hua Hin he was in distress with respiratory failure. His lips were dry. He was afebrile at 36.6 °C, tachypnea at 28 breaths per minute and had a blood pressure of 157/84 mmHg. His pulse rate was normal at 74 beats per minute. His oxygen saturation was 94% despite 10 LPM of oxygen supplement via a non re-breathing mask.

Chest auscultation revealed bilateral crepitation. There was bilateral diffuse patchy infiltration which predominated over the right side on the initial chest x-ray. Completed blood count showed Hb 14 g/dL, WBC 7430 cells/cm<sup>3</sup> (81 % Polymorphonuclear cells and 14% lymphocytes), and platelets 239000/mm<sup>3</sup>. Other blood test results were Cr 0.77 mg/dL, ALT 66 U/L, AST 56 U/L, total bilirubin 0.6 mg/dL, total protein 7.29 g/dL, albumin 4.13 g/dL. His prothrombin time was only 13.1 sec. He had a low NT-ProBNP at 108 pg/mL. The anti-HIV antibody was non reactive. The nasopharyngeal swab for influenza type A/B screening test was also negative by Immunofluorescence immunoassay technique. Arterial blood gases analysis was obtained while the patient was on 10 LPM of Oxygen supplement via a non re-breathing mask. The results were pH 7.43, PaO<sub>2</sub> 83.0 mmHg, PaCO<sub>2</sub> 42.4 mmHg, HCO<sub>3</sub> 27.4 mmol/l (PF ratio is 138.3). The sputum gram stain only showed a few white blood cells, gram positive cocci and gram negative bacilli. The sputum acid fast bacilli smear was negative.

Non invasive ventilation (NIV) was initiated and the patient was given Imipenem, Levofloxacin and Oseltamivir while the team was waited for the rest of the septic screening

results. An echocardiogram was requested and this showed good left ventricular systolic function with left ventricular ejection fraction of 60%. There was no regional wall motion abnormality. Mild mitral regurgitation, trivial aortic regurgitation and trivial. Tricuspid regurgitation were detected. The estimated right ventricular systolic pressure was 39 mmHg. There was no pericardial effusion. The early and late ventricular filling velocities ratio was 1.15. Inferior Venacava had normal diameter at 1.6 cm with a caval index of less than 50%.

On the second day following the ICU admission a repeated chest x-ray showed no improvement. A high resolution computerized tomography (HRCT) was arranged within the next 48 hours. In the meantime a trial of high dose dexamethasone was given. The patient made a transient improvement in his symptoms with the first dose of dexamethasone but not with further doses. The HRCT revealed asymptomatic patchy consolidation which were more prominent at both upper lobes and at the left lower lobe. There was also diffuse ground-glass appearance over both lungs field without pleural effusion. At 96 hours post admission the hemoculture as well as sputum culture results were available and there was no growth on both tests. The polymerase chain reaction (PCR) test for tuberculosis was also negative. The respiratory panel test was carried out and this revealed a positive result for human Metapneumovirus.

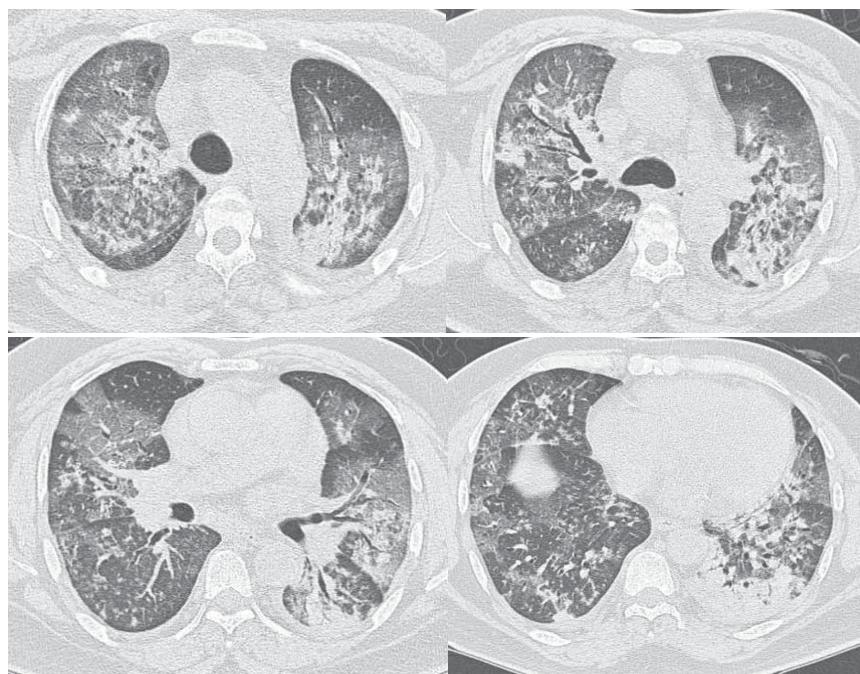
Following the respiratory panel test result the antibiotics were stopped after a completion of 7 days course on the basis that a mixed bacterial and viral infection was still a possibility. The patient continued supportive treatment and made a reasonable recovery over the next 7 days of his hospital stay. The patient was discharged after a total of 15 hospital admission days. He came back to the follow up clinics and remained well in himself.



**Figure 1:** Day 1, Bilateral diffuse patchy infiltration which predominated the right side.



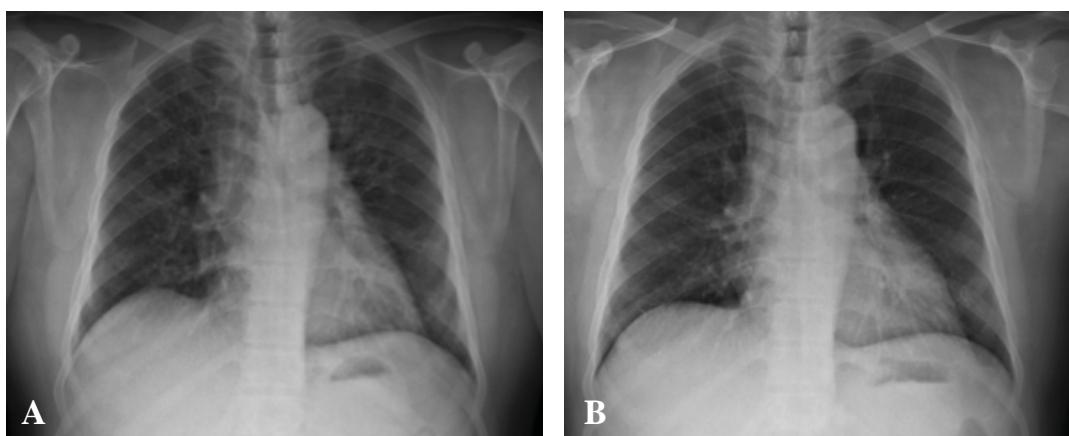
**Figure 2:** Day 2, Unchanged infiltration in both lungs.



**Figure 3:** The high resolution computerized tomography (HRCT) of chest shows asymmetrical patchy consolidation. The change predominates over both upper lobes and the left lower lobe. There are diffuse ground-glass opacities at both lungs without pleural effusion.



**Figure 4:** Day 7, Decreased infiltration in both lungs.



**Figure 5:** A. Day 21, Further reduction in bilateral infiltration in comparison to the third chest x-ray.  
B. Day 50, Significant improvement of both lung fields in comparison with previous chest x-rays.

## Case Report # 2

A 66-year-old British man presented to the emergency room with shortness of breath for 2 days. The patient had been travelling in Thailand for a month before developing unusual chesty symptoms. He described fever, rigor, productive cough with greenish yellow sputum and difficulty in breathing for 48 hours before attending the hospital. His medical background included hypertension, chronic hypersensitivity pneumonitis with pulmonary fibrosis which was diagnosed in 2001. Prior to his trip he had fitness to fly test in the United Kingdom (UK). His baseline oxygen saturation in room air was 96% and he was prescribed an oxygen supplement to be used in the cabin during the flight.

The patient was an ex-smoker with only a 5 pack a year history. He only drank alcohol occasionally for social events. His regular medications were Bendroflumethiazide, Valsartan, Aspirin, and Simvastatin.

On examination the patient was significantly dyspnea with respiratory rate of 44 breaths per minute. He had a fever of 38.5 °C. His blood pressure and heart rate were stable at 161/91 mmHg and 75 beats per minute consequently. His oxygen saturation was 97% despite 10 LPM of oxygen supplement via a non re-breathing mask. His chest x-ray revealed bilateral diffuse patchy infiltration. Complete blood count showed Hb 13.9 g/dL, WBC 8120 cells/cm<sup>3</sup> (83.4 % Polymorphonuclear cells and 12.3% lymphocytes), and platelets 192000/mm<sup>3</sup>. Other blood test were Cr 0.96 mg/dL, ALT 20 U/L, AST 25 U/L, total bilirubin 0.8 mg/dL, total protein 7.43 g/dL, albumin 4.21 g/dL, NT-ProBNP 251 pg/mL, Procalcitonin 0.06 ng/ml.

The nasopharyngeal swab for influenza type A/B screening test was also negative by Immunofluorescence immunoassay technique. The sputum gram stain showed a moderate amount of white blood cells, few gram positive cocci and a very small number of gram negative bacilli.

Non invasive ventilation (NIV) was initiated and the patient was given Ceftazidime and Levofloxacin. The patient was transferred to ICU for close monitoring. Bedside echocardiogram revealed good left ventricular systolic function with a left ventricular ejection fraction of 72%. There was no regional wall motion abnormality. Trivial Tricuspid regurgitation was detected. The estimated right ventricular systolic pressure was 41 mmHg. There was no pericardial effusion.

The early and late ventricular filling velocities ratio was 0.96. Inferior Venacava had normal diameter at 1.56 cm with a caval index of less than 50%.

On the grounds of interstitial lung disease the patient was given dexamethasone in parallel with a broad antibiotic regime. The patient made a remarkable recovery despite a transient atrial fibrillation episode. He was weaned off the NIV within 48 hours of admission and became oxygen independent within 3 days. His hemoculture and sputum culture were reported as no growth. The respiratory panel test revealed a positive result for human Metapneumovirus.

The patient was safely discharged from the hospital on the fifth day of hospital admission. The patient returned to our follow-up clinic at day 10 and appeared to be very well in himself. The follow-up chest x-ray demonstrated a significant improvement of the bilateral infiltration in comparison to the first chest x-ray on admission.



**Figure 7:** Day 1, Bilateral diffuse patchy infiltration which predominate over both lower lungs zone.



**Figure 8:** On day 2, Unchanged bilateral infiltration appearance.



**Figure 9:** Day 3, Decreased infiltration of both lungs in comparison to the previous films.



**Figure 10:** Day 10, Further improvement in both lung fields.

## Discussion

Human Metapneumovirus (hMPV) was first discovered in the Netherlands in 2001. The virus is classified as the first human member of the Metapneumovirus genus in the subfamily Pneumovirinae of the family Paramyxoviridae. Retrospective serologic studies demonstrated the presence of hMPV antibodies in humans more than 50 years earlier.<sup>5</sup> In their initial 2001 report, van den Hoogen et al demonstrated 100% seropositivity by age 10 years in 28 young children in the Netherlands. Similar studies worldwide have confirmed this high rate of seroprevalence in early childhood.<sup>6,7</sup>

hMPV is distributed worldwide and there is extensive evidence of previous exposure to the virus from various studies around the world. Although there is a high prevalence of antibodies against the virus in all age groups the peak incidence is found in pediatric and elderly patients. hMPV is the second most common cause of lower respiratory tract infection in young children after RSV. However it is worth noting that the group of patients with chronic pulmonary disease such as COPD tend to develop more severe feature of hMPV infection.<sup>8-10</sup> The cases of severe respiratory failure or even death from hMPV are reported.

hMPV is genetically most similar to the virus in the Pneumoviridae subfamily, of which RSV is a prominent member. hMPV has an identical gene order to the avian pneumovirus (aMPV), which also belongs to the Metapneumovirus genus in Pneumoviridae subfamily.<sup>5</sup> The virus was therefore named human Metapneumovirus after its close relatives in birds. It is an enveloped, negative single-strand RNA virus. Phylogenetic analysis identified

two subgroups of hMPV, subgroup A and B. Both subtypes can co-circulate simultaneously, but during an epidemic one subtype usually dominates. hMPV also has a seasonal distribution comparable to that of the influenza virus which tends to strike in the late winter and early spring.<sup>11</sup>

Like many other viruses, hMPV infection produces incomplete immunity therefore re-infection is not uncommon and can occur at all ages. Transmission is by direct or close contact with contaminated secretions, which may involve saliva, droplets, or large particle aerosols. The incubation period is approximately 3 to 6 days.<sup>12</sup>

The signs and symptoms of hMPV infection are generally indistinguishable from those caused by RSV. Like RSV, hMPV has a tropism for the respiratory epithelium. The patient may be asymptomatic. The symptoms may range from mild upper RTI symptoms to severe pneumonia. Most patients present with cough, dyspnea, and fever. Some studies also described a symptom of mono-nucleosis-like illness. Other symptoms such as productive cough, sore throat, conjunctivitis, and otitis media are also reported.<sup>13</sup> Interestingly RSV or Influenza-infected adults are likely to experience fever more than adults with hMPV infection. In contrast, the patients with hMPV infection are more likely to experience hoarseness and wheezing symptom than the other 2 viruses.<sup>10</sup> However compared to RSV and influenza, adults with hMPV infection have similar rates of ICU admission, mechanical ventilation, length of stay for hospitalization and length of stay in ICU.

A general respiratory virus culture obtained by nasal wash or nasopharyngeal swab should be performed in concerned patients with clinical symptoms of LRTI.

Virus culture, however, is relatively difficult, because hMPV grows slowly in conventional cell culture.<sup>14</sup> The rapid culture technique known as shell vial amplification can produce results within 72 hours. The other detection techniques that have been developed include identification by reverse transcriptase-polymerase chain reaction (RT-PCR) assay, enzyme immunoassay (EIA), and enzyme-linked immunosorbent assay (ELISA). Among the antigen detection test RT-PCR is the most sensitive method for diagnosis of hMPV infection.

## Conclusion

In summary, hMPV tends to cause only mild illnesses which are self-limiting, but the infections can be severe in high risk groups (elderly patients over 65 years, patients with cardiac or pulmonary diseases and immunocompromised patients). hMPV infection has been increasingly more acknowledged over the last few years; this virus should be considered as a causative agent in patients with respiratory failure in the ICU.

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