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# Human metapneumovirus pneumonia in a renal transplant recipient: A therapeutic challenge

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## Abstract

Treatment of human metapneumovirus (hMPV) infection in immunocompromised patients is not established yet. In this case report we describe a renal transplant recipient who was under immunosuppressive therapy and suffered an acute pneumonia. He was initially treated with meropenem and teicoplanin, without response. PCR of nasopharyngeal and BAL samples came positive for hMPV and thus ribavirin was started, with a successful clinical and radiological response one week after the beginning of this treatment.

## Keywords

hMPV; Pneumonia; Immunocompromised; Ribavirin; Renal transplant.

## Introduction

Human metapneumovirus (hMPV) is an enveloped virus with a negative-sense single-stranded RNA chain [1]. Its clinical pattern is similar to that of respiratory syncytial virus (RSV). It causes upper and lower respiratory infections, being a concern at extreme ages of life and in immunocompromised patients [2]. It is also frequent as an opportunistic infection, causing around 9% of lower respiratory tract infections in Hematopoietic Stem Cell Transplantation (HSCT) recipients in some series and it is also a common cause of infection in lung transplant recipients [3]. Treatment of hMPV infection in immunocompromised patients is, though, not established yet [4].

## Case Presentation

We describe a clinical case of a 70-year-old man that attended the Emergency Department after 48 h of dyspnea and low-grade fever. He did not refer cough or expectoration. He was under immunosuppressive therapy with prednisone 2.5 mg and tacrolimus 4 mg once a day and mycophenolate mofetil 500 mg twice

a day, since 16 years ago he received a kidney transplant due to a non-filiated chronic kidney disease. His past medical history was also remarkable for having atrial fibrillation and coronary artery disease.

On admission, the patient was lethargic. His temperature was 37.3ºC, and his blood pressure and heart rate were 113/67 mmHg and 57 bpm, respectively. His basal peripheral oxygen saturation ($SpO_2$) was 89%. Cardiopulmonary auscultation was anodyne and he had no peripheral edema. A SARS-CoV-2 RT-PCR test was performed, which was negative.

His blood tests showed lymphopenia (440 /µL), normal leukocyte and neutrophil count and a C-reactive protein (CRP) of 119 mg/dL, as well as respiratory alkalosis. His serum creatine levels had raised to 2.8 mg/dL (from a basal creatine of 2 mg/dL).

The chest X-ray showed a significant left lower lobe consolidation and several opacities in the right lung with discrete pleural effusion. He was empirically treated with meropenem 1 g/12 h and teicoplanin 200 mg/24 h.

After four days of hospitalization he continued with fever and dyspnea, so the Infectious Disease Unit was consulted. Blood and urine cultures came negative, as well as serology tests for detecting *Coxiella burnetii*, *Mycoplasma pneumoniae*, *Toxoplasma gondii*, *Chlamydia sp* and *Leishmania*. Urine antigen tests for *Legionella pneumophila* and *S. pneumoniae*, RT-PCR for Influenza A, Influenza B and RSV, a serum galactomannan test and a blood CMV viral load were all negative.

In the absence of clinical improvement, our request was expanded with a complete panel of respiratory viruses, which was only positive for hMPV. A chest X-ray and a thorax CT-scan were performed on day six, showing areas of ground glass opacities and consolidation, predominantly in the left lung, with discrete right pleural effusion (Figures 1A and 1B).

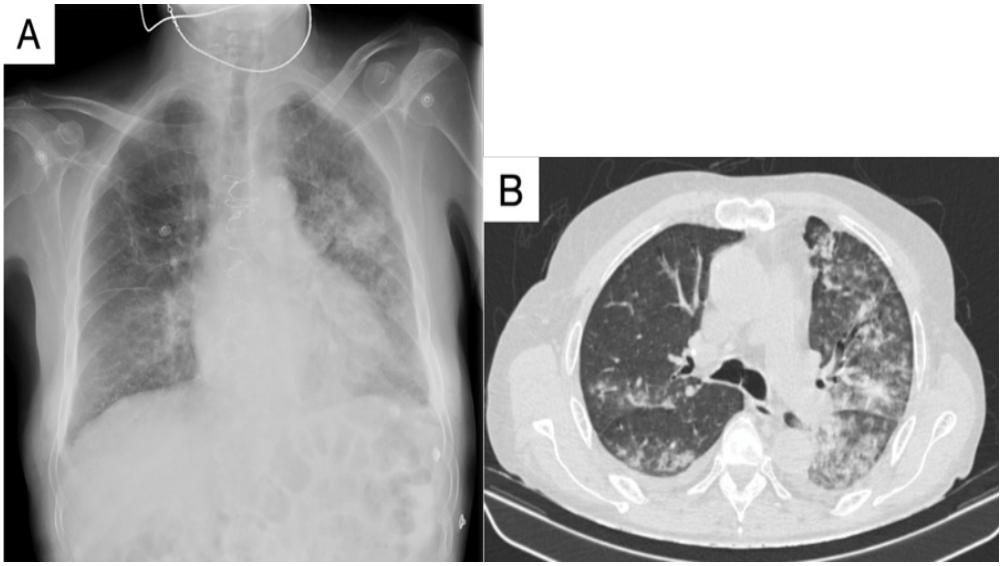


**Figure 1: (A):** Chest X-ray showing bilateral opacities in both lungs. **(B):** CT scan frame showing bilateral ground glass opacities and consolidations, as well as discrete right pleural effusion.

After six days of antibiotic treatment, the patient showed no clinical improvement. At this point, we decided discontinued meropenem and teicoplanin and started oral ribavirin (200 mg/24 h) to treat hMPV.

Microbiological tests were also carried out in Bronchoalveolar Lavage (BAL) samples. Conventional and fungical cultures were negative, as well as qPCR (quantitative polymerase chain reaction) for *Pneumocystis jirovecii* and viruses, except for hMPV that was positive. A galactomannan test in BAL was also negative.

Seven days after starting treatment with ribavirin, the patient showed significant improvement. He was asymptomatic and no longer needed supplemental oxygen therapy and analytically the CRP progressively decreased and the lymphocyte count raised over 500 /mL. The chest X-ray also confirmed significant improvement with respect to previous radiological studies, since only subtle residual opacities were present at this point.

## Discussion

HMPV infection is a challenging disease in immunocompromised patients. In those who present as an upper respiratory tract infection, up to 49% can progress to pneumonia and mortality reaches 54.5% in HSTC recipients [5,6].

It is important to notice that the diagnosis of hMPV infection requires both clinical suspicion and a positive RT-PCR test, preferably not only in nasopharynx samples, since those may not represent active disease [7]. Coinfection is very common in respiratory infections in Solid Organ Transplant (SOT) recipients in which hMPV is involved, being *S. pneumoniae* the most frequent pathogen [5]. In our patient, however, all microbiological test came negative except for hMPV.

Nowadays, clinical support therapy still remains the basis of treatment of hMPV infection [8]. Ribavirin is approved for treatment of hepatitis C virus and RSV [9] and it has been proved effective against experimental hMPV infection in mice, but no convincing evidence is available about its use in humans [10]. Its mechanism of action consists of purine metabolism disruption and RNA-polymerase inhibition, which leads to an upregulation of certain type 1 helper T cell cytokines such as IL-2, TNF-alpha, IFN-gamma and downregulation of regulatory T cell cytokines such as IL-10 [10].

## Conclusion

To our knowledge, this is the first case described in literature of a hMPV pneumonia infection in a kidney transplant recipient successfully treated with ribavirin. Our patient suffered an acute pneumonia and he was treated with broad-spectrum antibiotics without success, but once we confirmed that the causative agent was hMPV and switched to ribavirin the clinical improvement was dramatic.

The use intravenous ribavirin has already been reported as an experimental therapy against a hMPV pneumonia in a lung transplant recipient with a successful outcome [1]. A recent study also suggest that the oral formulation is as effective as the aerosolized formulation against RSV [11]. Oral ribavirin seemed

also effective to treat a small number of HSCT patients with hMPV respiratory infections, according to a retrospective study [12].

This case suggests that ribavirin, a drug with a long history that has been proved effective against other viral pathogens, could be an appropriate treatment for hMPV pneumonia in immunocompromised patients and in particular in SOT recipients, but more studies are needed to prove the effectiveness of this treatment.

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