Human metapneumovirus treated with inhaled ribavirin: A case report

Monica Khunger, Ellen F. Eaton, Craig Hoesley

ABSTRACT

Introduction: Human metapneumovirus is a new pulmonary pathogen in the Paramyxoviridae family. It is increasingly associated with respiratory illnesses particularly in immunocompromised patients. We report a case of a multiple myeloma patient diagnosed with human metapneumovirus pneumonia and successfully treated with inhaled ribavirin.

Case Report: A 56-year-old white female previously diagnosed with multiple myeloma presented with fever, non-productive cough, dyspnea and new onset ground glass opacities on computed tomography scan. Human metapneumovirus was detected in bronchoalveolar lavage specimen with direct fluorescent antibody testing. Marked clinical improvement was observed following a five-day course of inhaled ribavirin.

Conclusion: Human metapneumovirus can cause community acquired pneumonia in immunocompromised patients presenting with lower respiratory tract illness. It is associated with significant morbidity and mortality in this population. Early diagnosis and prompt treatment with inhaled ribavirin may improve outcomes in immunocompromised patients.

International Journal of Case Reports and Images (IJCRI)

International Journal of Case Reports and Images (IJCRI) is an international, peer reviewed, monthly, open access, online journal, publishing high-quality, articles in all areas of basic medical sciences and clinical specialties.

Aim of IJCRI is to encourage the publication of new information by providing a platform for reporting of unique, unusual and rare cases which enhance understanding of disease process, its diagnosis, management and clinico-pathologic correlations.

IJCRI publishes Review Articles, Case Series, Case Reports, Case in Images, Clinical Images and Letters to Editor.

Website: www.ijcasereportsandimages.com

CASE REPORT

OPEN ACCESS

Human metapneumovirus treated with inhaled ribavirin: A case report

Monica Khunger, Ellen F. Eaton, Craig Hoesley

ABSTRACT

Introduction: Human metapneumovirus is a new pulmonary pathogen in the Paramyxoviridae family. It is increasingly associated with respiratory illnesses particularly in immunocompromised patients. We report a case of a multiple myeloma patient diagnosed with human metapneumovirus pneumonia and successfully treated with inhaled ribavirin. **Case Report:** A 56-year-old white female previously diagnosed with multiple myeloma presented with fever, non-productive cough, dyspnea and new onset ground glass opacities on computed tomography scan. Human metapneumovirus was detected in bronchoalveolar lavage specimen with direct fluorescent antibody testing. Marked clinical improvement was observed following a five-day course of inhaled ribavirin. **Conclusion:** Human metapneumovirus can cause community acquired pneumonia in immunocompromised patients presenting with lower respiratory tract illness. It is associated with significant morbidity and mortality in this population. Early diagnosis and prompt treatment with inhaled ribavirin may improve outcomes in immunocompromised patients.

Keywords: Bone marrow transplant, Human metapneumovirus, Immunocompromised, Ribavirin

How to cite this article

Khunger M, Eaton EF, Hoesley C. Human metapneumovirus treated with inhaled ribavirin: A case report. Int J Case Rep Images 2014;5(12):813–817.

doi:10.5348/ijcri-2014139-CR-10450

INTRODUCTION

Human metapneumovirus (hMPV) was first identified in 2001 from 28 nasopharyngeal isolates from Dutch children with upper respiratory infections symptom. Its electron micrographic structure, biochemical properties and cytopathic effects position hMPV in the Paramyxoviridae family [1]. No similar virus was identified in 400 children without respiratory symptoms suggesting its role in symptomatic upper respiratory tract infection (URI). Reverse transcriptase PCR (RT-PCR) and direct fluorescent antibody (DFA-Abs) testing proved this was a novel virus. Its RNA did not amplify with primers associated with other members of Paramyxoviridae family. In addition, anti-sera of animals exposed to hMPV did not react with viral particles of known members of Paramyxoviridae family. A year after its discovery, Boivin et al. studied 11 nasopharyngeal and bronchoalveolar lavage (BAL) specimens and isolated hMPV for the first time in adults [2]. This study also demonstrated the first evidence of re-infection when the investigators found a single child had two different hMPV strains in two different winter seasons.

The clinical manifestations relate to hMPV-infected dendritic cells (DCs) releasing soluble matrix proteins from virus. These matrix protein bind activated DCs

Monica Khunger¹, Ellen F. Eaton², Craig Hoesley³

Affiliations: ¹MBBS, All India Institute of Medical Sciences; ²MD, Fellow, Division of Infectious Disease, University of Alabama at Birmingham; ³MD, Professor, Division of Infectious Disease, University of Alabama at Birmingham.

Corresponding Author: Craig J. Hoesley, MD, Professor, Division of Infectious Disease, University of Alabama at Birmingham; Email: choesley@uab.edu

Received: 31 July 2014
Accepted: 18 August 2014
Published: 01 December 2014

inducing their maturation and production of cytokines and subsequent activation of T lymphocytes. In addition, hMPV causes hyperplasia of the respiratory epithelium resulting in airway obstruction and hyper responsiveness to methacholine challenge. This suggests the possibility of asthma exacerbation with hMPV infection similar to other respiratory tract viral infections [3]. The clinical manifestations of hMPV infection in adults and children are identical. The infection usually presents with cough, nasal congestion, rhinorrhea, dyspnea, hoarseness and wheezing. Immunocompromised hosts present similarly but may also have fever [1].

There are two major modalities for the diagnosis of hMPV: Reverse transcription (RT-PCR) and (Direct fluorescent antibody assay). Though RT-PCR is the most sensitive method of diagnosis, it has limitations including the possibility of false positive results in asymptomatic carriers. The other method for diagnosis is antibody assay which detects hMPV antigens by immunofluorescence on nasopharyngeal or bronchoalveolar lavage specimen. This assay uses a blend of three fluorescein labeled murine monoclonal antibodies (MAbs). Though not successful in detecting new antigenic variants, this test has a very high specificity and can be performed rapidly [1].

Supportive therapy is the main stay of treatment for hMPV. To date, there are no FDA-approved treatment options for individuals with hMPV infection. Hamelin et al. compared intraperitoneal ribavirin and glucocorticoids in hMPV infected mice and found ribavirin significantly decreased both hMPV replication in lungs and pulmonary inflammation on postinfection day five whereas glucocorticoids only reduced alveolar and interstitial inflammation [4].

There is little data on successful treatment of human metapneumovirus with ribavirin in the immunocompromised patients, including multiple myeloma patients. We report a case of human metapneumovirus pneumonia with successful symptom resolution after a five-day course of inhaled ribavirin.

CASE REPORT

A 56-year-old white female with multiple myeloma presented to outpatient clinic with low grade fever, non-productive cough and chest congestion. She also had progressive dyspnea on exertion with minimal exertion. She denied chest pain, dysuria, orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema, rash and oral lesions. She had no recent travel or sick contacts. She had a past medical history of lambda light chain multiple myeloma complicated by acute kidney injury, diffuse bone involvement and plasmacytoma of the right iliac crest one year prior to arrival. This was treated with successful autologous bone marrow transplant one year ago, and since then she had been managed on prednisone 20 mg/day. She received levofloxacin at an outside hospital

before presentation with slight improvement in her fever curve but not complete resolution. Her temperature was 100.6°F, heart rate was 120 beats per minute, blood pressure was 110/70 mmHg, and oxygen saturation was 93% on 2L nasal cannula. On examination she was in no acute respiratory distress. Fine bibasilar crackles were heard, and her examination was otherwise unremarkable. Her laboratory were significant for absolute neutrophil count of 143. The hemoglobin levels, platelet count, renal and liver function tests were within normal limits. Conventional radiographic findings (Figure 1) and subsequent computed tomography (CT) scan (Figure 2) on admission and hospital day-2, respectively, revealed bilateral patchy lung infiltrates, right lower lobe atelectasis with discrete ground-glass opacification. On admission blood and sputum samples were obtained for routine microscopy and culture, including bacterial, fungal and mycobacterial cultures, and were unrevealing. Nasal washings were also negative for respiratory syncytial virus (RSV), influenza, para-influenza and fungal assay were all negative. She underwent a bronchoscopy with bronchoalveolar lavage (BAL). The BAL fluid was also cultured for bacteria, fungi and mycobacteria and all were negative. Additional diagnostic testing of the BAL fluid for *Pneumocystis jirovecii* and other respiratory viruses (influenza A and B, RSV, parainfluenza virus, adenovirus, and enterovirus) remained negative but hMPV type B was detected using direct fluorescent antibody testing.

The patient remained symptomatic and febrile even on broadspectrum anti-bacterial agents. Her initial antibiotic regimen included cefepime 2 g IV BID, vancomycin 1 g IV q18 hours, trimethoprim/sulfamethoxazole 25 mL IV q8 hours and azithromycin 250 mg IV daily. Based on the results of BAL fluid testing a five-day course of inhaled ribavirin, 2 g q8 hours, was initiated. Her neutropenia resolved with administration of filgrastim at a dose of 5 µg/kg/day. With ribavirin treatment, her shortness of breath and respiratory distress gradually improved, and her oxygen was weaned off. She also showed marked improvement in her physical examination within 48 hours. As a result she was discharged home within three days of completion of her inhaled ribavirin treatment. A computed tomography scan of thorax performed two months after her discharge showed complete resolution of ground glass opacities (Figure 3). Incidentally, she was noted to have elevated lambda light chain and beta-2 microglobulin levels, with a low free lambda/kappa light chain concerning for multiple myeloma recurrence. Bone marrow biopsy confirmed a relapse of her multiple myeloma. This, in addition to her acute illness, was a probable reason for her neutropenia at presentation. The patient developed further complications of recurrent multiple myeloma. She presented four months later with acute renal failure and cord compression related to spinal metastases. When she became uremic and obtunded, her family decided to pursue palliative care measures and withdrew aggressive resuscitation. She died five months after metapneumovirus diagnosis.

Figure 1: Conventional radiographic imaging on admission revealed bilateral patchy lung infiltrates, right lower lobe atelectasis with discrete ground-glass opacification.

Figure 2: Computed tomography imaging on hospital day-2, revealed bilateral patchy lung infiltrates, right lower lobe atelectasis with discrete ground-glass opacification.

Figure 3: Computed tomography scan of chest performed two months after treatment with inhaled ribavirin showing resolution of ground glass opacities.

DISCUSSION

The development of fever with pulmonary infiltrates is a frequent life-threatening complication in immunocompromised patients, requiring early diagnosis and treatment. Our patient's acute respiratory illness was consistent with hMPV infection based on her clinical presentation, hMPV direct fluorescent antibody testing result, and the absence of alternate explanation for her symptoms. She had an indolent but progressive respiratory illness consistent with hMPV. Her history of multiple myeloma and corticosteroid treatment resulted in immunosuppression and likely contributed to her prolonged course. Respiratory infections due to hMPV, like RSV are more severe in immunocompromised patients [1]. CT scan also showed bilateral ground glass opacities not present on CT scan performed five months prior to presentation consistent with a viral etiology.

An hMPV associated respiratory disease occurs in all age groups. It is found in 3.4% of adult population with respiratory tract infection [1, 5]. The hMPV infections may be more severe and the course more prolonged in immunocompromised patients due to poor clearance of virus.

In a study by William et al., 251 episodes of respiratory tract infections were studied in patients with hematological malignancies [6]. Twenty-two (9%) of these episodes were found to be associated with hMPV infection. Of these, 16 occurred in hematopoietic cell transplant recipients and three of nine patients with lower respiratory tract disease died.

Ribavirin is a synthetic guanosine nucleoside analog with in vitro activity against hMPV [7]. Its mechanism of action involves inhibition of viral RNA polymerase. Data on ribavirin treatment of hMPV in immunocompromised hosts are limited. Englund et al. detected hMPV in bronchoalveolar lavage specimens from 5 of 163 (3.0%) HSCTs patients [8]. Four of the five patients died with acute respiratory failure. The one patient treated with inhaled ribavirin had a fatal outcome. Another case report by Kamble et al. reported successful treatment in a hematopoietic stem cell transplant patient with a four-day course of intravenous ribavirin and immunoglobulins [9]. In another case series by Shahda et al., nine immunocompromised patients with hMPV pneumonia were studied—two were successfully treated with oral and aerosolized ribavirin along with intravenous immunoglobulins (IVIg) [10]. In another case series, Egli et al., described two multiple myeloma patients with hMPV pneumonia [11]. Of these two, one was treated with IVIg and oral ribavirin while the other was treated with IVIg alone.

We report the first case of successful outcome and improved respiratory distress with inhaled ribavirin alone without oral antiviral therapy or IVIg in a multiple myeloma patient. In the absence of data on hMPV treatment outcomes, experience with inhaled ribavirin in immunocompromised RSV patients led us to select inhaled

rather than oral or IV administration [12]. Likewise, there are no studies of optimal ribavirin dosing in human metapneumovirus pneumonia. However, randomized controlled multicenter trials of inhaled ribavirin in RSV infection suggested the use of 6 g/24 h of aerosolized ribavirin at a rate of 2 g/8h, the dose selected for our patient [13]. We believe the early recognition of hMPV pneumonia and timely therapy with inhaled ribavirin contributed to the successful outcome. Inhaled ribavirin is an expensive and cumbersome treatment modality but may be appropriate in heavily immunocompromised population like current patient. However, multi-center case series are needed to shed light on the long-term safety and efficacy of inhaled ribavirin. From the time our patient was diagnosed and treated new research has suggested that oral ribavirin may be an option for patients with RSV and moderate to severe immunosuppression, a finding that may hold promise in hMPV [14].

CONCLUSION

The goals of this case report are:

- (1) to alert clinicians to the possibility of hMPV as a cause of severe community acquired pneumonia in immunocompromised hosts
- (2) to highlight the importance of early suspicion of viral infection and rapid diagnostic testing
- (3) to suggest the use of inhaled ribavirin as a possible treatment modality. Prompt administration of inhaled ribavirin should be considered in immunocompromised patient population with established hMPV infection.

Author Contributions

Monica Khunger – Data acquisition, Analysis and interpretation of data, Drafting of the manuscript, Final approval of the version to be published

Ellen F. Eaton – Data acquisition, Analysis and interpretation of data, Drafting of the manuscript; Final approval of the version to be published

Craig Hoesley – Case report concept and design, Analysis and interpretation of data, Critical revision of the manuscript for important intellectual content, Administrative, technical, or material support; case report supervision, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2014 Monica Khunger et al. This article is distributed under the terms of Creative Commons Attribution

License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited.

REFERENCES

1. Williams JV, Harris PA, Tollefson SJ, et al. Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children. *N Engl J Med* 2004 Jan 29;350(5):443–50.
2. Boivin G, Abed Y, Pelletier G, et al. Virological features and clinical manifestations associated with human metapneumovirus: A new paramyxovirus responsible for acute respiratory-tract infections in all age groups. *J Infect Dis* 2002 Nov 1;186(9):1330–4.
3. Hamelin ME, Prince GA, Gomez AM, Kinkead R, Boivin G. Human metapneumovirus infection induces long-term pulmonary inflammation associated with airway obstruction and hyperresponsiveness in mice. *J Infect Dis* 2006 Jun 15;193(12):1634–2.
4. Hamelin ME, Prince GA, Boivin G. Effect of ribavirin and glucocorticoid treatment in a mouse model of human metapneumovirus infection. *Antimicrob Agents Chemother* 2006 Feb;50(2):774–7.
5. Falsey AR. Human metapneumovirus infection in adults. *Pediatr Infect Dis J* 2008 Oct;27(10 Suppl):S80–3.
6. Williams JV, Martino R, Rabella N, et al. A prospective study comparing human metapneumovirus with other respiratory viruses in adults with hematologic malignancies and respiratory tract infections. *J Infect Dis* 2005 Sep 15;192(6):1061–5.
7. Wyde PR, Chetty SN, Jewell AM, Boivin G, Piedra PA. Comparison of the inhibition of human metapneumovirus and respiratory syncytial virus by ribavirin and immune serum globulin in vitro. *Antiviral Res* 2003 Sep;60(1):51–9.
8. Englund JA, Boeckh M, Kuypers J, et al. Brief communication: Fatal human metapneumovirus infection in stem-cell transplant recipients. *Ann Intern Med* 2006 Mar 7;144(5):344–9.
9. Kamble RT, Bollard C, Demmler G, LaSala PR, Carrum G. Human metapneumovirus infection in a hematopoietic transplant recipient. *Bone Marrow Transplant* 2007 Oct;40(7):699–700.
10. Shahda S, Carlos WG, Kiel PJ, Khan BA, Hage CA. The human metapneumovirus: A case series and review of the literature. *Transpl Infect Dis* 2011 Jun;13(3):324–8.
11. Egli A, Bucher C, Dumoulin A, et al. Human metapneumovirus infection after allogeneic hematopoietic stem cell transplantation. *Infection* 2012 Dec;40(6):677–84.
12. Hynicka LM, Ensor CR. Prophylaxis and treatment of respiratory syncytial virus in adult immunocompromised patients. *Ann Pharmacother* 2012 Apr;46(4):558–66.
13. Boeckh M, Englund J, Li Y, et al. Randomized controlled multicenter trial of aerosolized ribavirin for respiratory syncytial virus upper respiratory tract infection in hematopoietic cell transplant recipients. *Clin Infect Dis* 2007 Jan 15;44(2):245–9.

14. Marcelin JR, Wilson JW, Razonable RR. Oral ribavirin therapy for respiratory syncytial virus infections in moderately to severely immunocompromised patients. *Transpl Infect Dis* 2014 Apr;16(2):242–50.

Access full text article on
other devices

Access PDF of article on
other devices

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.

Mentored Review Articles (MRA)

Our academic program "Mentored Review Article" (MRA) gives you a unique opportunity to publish papers under mentorship of international faculty. These articles are published free of charges.

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US