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# *Hemophilus influenzae* and Parainfluenza Virus Pneumonia in a Patient with AIDS

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NJ, U.S.A.**Corresponding Author:** Sandhya Nagarakanti, e-mail: [Sandhya.nagarakanti@rwjbh.org](mailto:Sandhya.nagarakanti@rwjbh.org)**Conflict of interest:** None declared

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**Patient:** Male, 64-year-old  
**Final Diagnosis:** *Hemophilus influenzae* and parainfluenza virus pneumonia in a patient with AIDS  
**Symptoms:** Shortness of breath  
**Medication:** —  
**Clinical Procedure:** Bronchoalveolar lavage  
**Specialty:** Infectious Diseases**Objective:** Rare disease**Background:** Parainfluenza viruses (PIV) are known to cause mild respiratory tract infections in immunocompetent patients but can cause severe infections in immune-compromised patients such as transplant recipients and children with HIV. PIV infection in HIV-infected adults has rarely been reported. We report a case of PIV pneumonia in an adult with AIDS who was successfully treated with oral ribavirin.**Case Report:** A 64-year-old man with history of acquired immune deficiency syndrome (AIDS) was admitted to the hospital with shortness of breath that began 3 days before. He was in respiratory distress and required mechanical ventilation on arrival. A bronchoalveolar lavage (BAL) culture was positive for *Hemophilus influenzae* and a respiratory viral panel was positive for Parainfluenza virus. The patient was initially started on Cefepime and Trimethoprim- Sulfamethoxazole and later changed to Ceftriaxone based on culture results. As the patient's condition did not improve after 48 h, oral ribavirin was added to treat PIV. The patient subsequently improved and was extubated after 72 h.**Conclusions:** Oral ribavirin can have a beneficial effect in AIDS patients who have PIV-associated pneumonia. Further investigation of the benefit of oral ribavirin in similar cases is warranted.**MeSH Keywords:** Haemophilus Infections • HIV • Parainfluenza Virus 1, Human • Parainfluenza Virus 2, Human • Parainfluenza Virus 3, Human • Ribavirin**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/923132>

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## Background

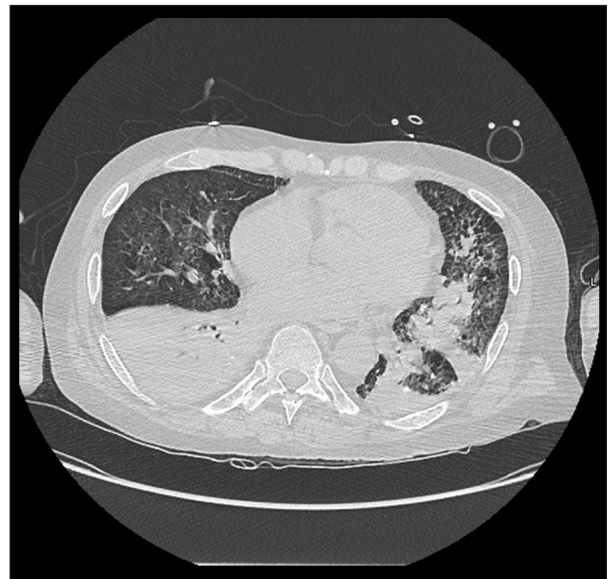
Parainfluenza virus (PIV) is single-stranded, enveloped RNA virus causing respiratory infections in children and adults. PIV are known to cause severe infections in immune-compromised patients such as transplant recipients and children with HIV. *Haemophilus influenzae* (*H. influenzae*) is a frequent cause of bacterial pneumonia in HIV-infected people and is also known to be colonizer in chronic obstructive pulmonary disease (COPD) patients, causing challenges in distinguishing between true infections vs. colonization in patients with HIV and COPD. PIV infection in HIV-infected adults has rarely been reported. There are no approved treatment options to treat PIV infections.

## Case Report

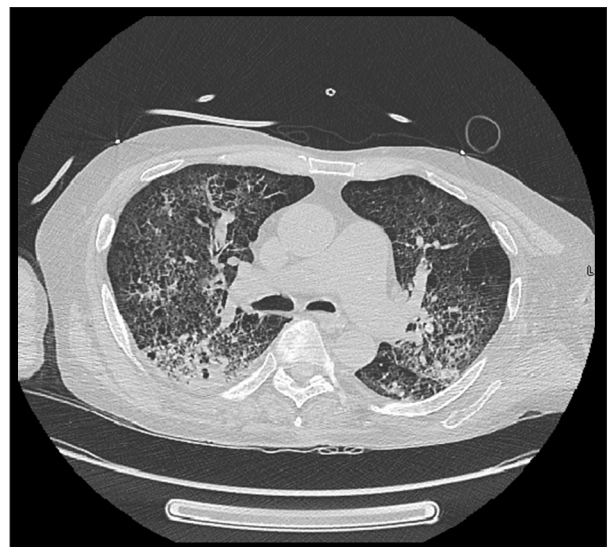
A 64-year-old man was admitted with shortness of breath for 3 days prior to admission. The patient's history was significant for acquired immune deficiency syndrome (AIDS), with a CD4 of 34  $\mu\text{L}$ ; he was maintained on antiretroviral therapy with abacavir/lamivudine and dolutegravir. The patient had a history of COPD and renal insufficiency. On admission, his temperature was 97.4°F (36.3°C), blood pressure 114/68 mmHg, heart rate 94 beats/min, and respiratory rate 20/min. A cardiac examination revealed normal heart sounds. His lungs were clear to auscultation, with bilateral rhonchi. The abdomen was soft, with no organomegaly. Results of a neurological exam were normal.

A laboratory examination revealed a white blood cell (WBC) count of  $14.2 \times 10^3/\mu\text{L}$ , hemoglobin 13.8 g/dL, platelets  $268 \times 10^3/\mu\text{L}$ , sodium 140 mmol/L, blood urea nitrogen 14 mg/dL, creatinine, 0.73 mg/dL, procalcitonin 6.43 ng/mL, and serum LDH 306 Unit/L. A urine drug toxicity study was positive for benzodiazepines and cocaine. Arterial blood gas showed a pH of 7.17,  $\text{PCO}_2$  92 mmHg,  $\text{PO}_2$  58 mmHg, oxygen saturation of 81%, CD4 37 cells/ $\mu\text{L}$  (6%), and HIV viral load 32 copies/mL. A chest X-ray showed bilateral lung consolidations without effusion or pneumothorax, and a CT chest showed extensive diffuse bilateral interstitial opacities with multifocal areas of consolidation, most prominent in the right lower lobe, compatible with multifocal pneumonia and pulmonary arterial hypertension (Figures 1, 2).

In the emergency room, the patient was in respiratory distress, and because of his diagnosis of COPD, he was given intravenous solumedrol 125 mg and albuterol nebulizer treatment and was placed on BiPAP. His clinical condition worsened; he was intubated and required mechanical ventilation, and then was transferred to the Intensive Care Unit. The diagnoses of *Pneumocystis jirovecii* pneumonia (PJP) vs. community-acquired



**Figure 1.** CT chest showing diffuse bilateral interstitial opacities and multifocal consolidation.



**Figure 2.** CT chest showing consolidation in multiple areas and pulmonary hypertension.

pneumonia were considered. The patient was placed on IV trimethoprim/sulfamethoxazole 450 mg q6hrs (trimethoprim dose) and cefepime 2 gm Q 12hrs. Serum beta D glucan was  $<31$  pg/mL. The patient underwent bronchoalveolar lavage (BAL), which revealed a WBC count of 19 800 CU/MM with 92% neutrophils and RBC 4478 CU/MM. The respiratory virus panel from BAL using target-enriched multiplex polymerase chain reaction (PCR) assay (BioMérieux easy MAG, Life Tech Veriti, Sensovation Sensospot) was positive for PIV, and BAL culture grew *Hemophilus influenzae* (*H. influenzae*). Cytology from BAL showed rare pulmonary alveolar macrophages in a background of purulent exudate. No *Pneumocystis*, fungal organisms, or



**Figure 3.** CT chest 30 days after treatment showing significantly decreased bilateral interstitial opacities.

viral inclusions were seen on Papanicolaou and Gomori methenamine-silver stains. Intravenous Ceftriaxone 1 gram every 24 h was initiated and cefepime and trimethoprim-sulfamethoxazole were discontinued. The patient's clinical condition did not improve and he remained intubated, requiring mechanical ventilation. Due to the finding of PIV on BAL, a decision was made to start oral ribavirin 600 mg every 12 h.

The patient improved clinically over the next 48 h after starting ribavirin and he was extubated after 72 h. A chest X-ray after 7 days of treatment with ribavirin showed improving bibasilar opacities, and the patient was discharged home and continued to do well. A follow-up CT scan done 30 days after discharge revealed significantly decreased bilateral interstitial opacities (Figure 3).

## Discussion

PIV is an enveloped, single-stranded, negative-sense RNA virus belonging to the genus Paramyxoviridae. The PIV are distributed worldwide and are important respiratory pathogens in adults and children. There are 4 known PIV serotypes: 1–4. PIV 1–3 are implicated in most infections, both in children and adults, whereas serotype 4 is less common [1].

Host defense against PIV is mediated by both humoral and cellular immunity. Antibodies against the 2 main viral surface glycoproteins, F and HN, are neutralizing. Secretory IgA develops after natural infection, while cytotoxic T lymphocytes have been shown to have a role in clearance of PIV in hamster and mouse models [1].

PIV can cause severe clinical syndromes in immunocompromised hosts; children with severe combined immunodeficiency syndrome (SCID) were described with giant cell pneumonia, and with a fulminant course [2]. Infections have been described in inpatients who underwent bone marrow and lung transplant. Most of these infections start with an initial upper-respiratory tract infection (URI) which progresses to become a lower-respiratory tract infection (LRTI), progressing to pneumonitis and often leading to respiratory failure [3–5]. Progression from URI to LRTI was described in 18–77% of immunosuppressed patients [5–7]. Srinivasan et al. [8] noted that PIV infection was the most commonly encountered symptomatic respiratory viral infection. Risk factors for PIV progression to LRTI were thought to be lymphopenia, steroid use, and co-infections with other respiratory agents [9]. The virus has also been implicated in COPD exacerbation [10].

The natural history of PIV infection in HIV-infected children is not well characterized, but it seems that severe disease does not appear until they develop significant T cell depletion [11,12].

Cohen et al. [13] studied the incidence of PIV pneumonia and found that it was higher in HIV-infected children and adults compared to the HIV non-infected population. Madhi et al. prospectively studied the clinical manifestations of 80 hospitalized children with severe respiratory tract infection caused by PIV and noted that the clinical features were similar between HIV-infected and non-infected children [14]. HIV-infected children with PIV had increased rates of hospitalization and increased morbidity [3,4,14].

Garbino et al. [15] screened 59 BAL samples from HIV-infected patients suspected of having an opportunistic infection by using real-time reverse transcriptase PCR assays, finding that 11 samples had at least 1 respiratory virus, and 3 were found to have 1 each of the PIV serotypes 2, 3, and 4.

Other viral infections can mimic PIV infection. Cunha et al. described a patient diagnosed as having PIV; the patient presented with influenza-like illness but with negative rapid influenza diagnostic tests. A viral respiratory fluorescent antigen panel and reverse transcriptase PCR for influenza (H1N1) were negative [16]. Another case report described an adult HIV-infected patient who was hospitalized with influenza-like illness suspected of having influenza and PCP pneumonia. The patient was eventually diagnosed as having RSV pneumonia [17].

*H. influenzae* is a frequent cause of bacterial pneumonia in HIV-infected patients, with an incidence of 15–27% [18]. Invasive disease with this pathogen has been described to be 100-fold higher in HIV-infected patients than in non-infected patients [18]. Caiaffia et al. noted that CD4 lymphocyte count less than 200  $\mu$ L, previous episode of PJP, age 30–40 years, and

smoking illicit drugs were associated with higher incidence of bacterial pneumonia in HIV-infected patients [19].

*H. influenzae* is a frequent colonizer in COPD patients' airways and has been implicated as a cause of intermittent exacerbations [20,21].

Currently there are no FDA-approved treatments for PIV. Ribavirin is active against Paramyxoviruses through the depletion of intracellular guanosine triphosphate pools secondary to inhibition of inosine monophosphate dehydrogenase. Aerosolized ribavirin has been tried, but it is costly and causes many aerosol-related adverse effects, including bronchospasm and teratogenic effects on health care workers [22]. In addition, the administration of aerosolized ribavirin through a ventilator can crystallize in the ventilator circuit. The alternative intravenous ribavirin is not currently approved for use in the USA.

Oral ribavirin has been suggested as an option for treatment of patients with PIV and RSV infections. The drug has shown favorable results in some small case series and case reports. The benefit of using oral ribavirin has been described in children with HSCT and lung transplant recipients, and both RSV and PIV infections were included in these series [3,23,24]. However, it is difficult to draw a conclusion about the benefit of oral ribavirin, as these reports did not have a comparator treatment arm. In a study by So-Youn Park et al. [25], the authors compared oral ribavirin-treated patients with hematological diseases to patients receiving only supportive care. The authors used a propensity-matched case control analysis and logistic regression with co-variable adjustments in order to compensate for biases inherent in observational studies. The authors concluded that oral ribavirin was not associated with better outcome than supportive care [25]. To the best of

our knowledge, there are no published case reports of PIV infection in AIDS patients who were successfully treated with oral ribavirin.

In summary, our patient was initially diagnosed and treated as having COPD exacerbation. When his respiratory condition deteriorated, he was considered to have PJP and was treated with trimethoprim/sulfamethoxazole, but this diagnosis was later ruled out. BAL culture showed *H. influenzae*, and respiratory panel PCR was positive for PIV. The patient was initially treated with ceftriaxone, but when no improvement was noted, oral ribavirin was initiated, with a significant clinical improvement, allowing extubation and eventual discharge home.

To the best of our knowledge, this is the first published case in which both *H. influenzae* and PIV were isolated from an AIDS patient who had a significant improvement after treatment with oral ribavirin.

## Conclusions

PIV can cause of severe clinical syndromes in immunocompromised hosts and can lead to fulminant pneumonia in this population. There are no FDA-approved therapies for PIV pneumonia. Oral ribavirin may have a beneficial effect in AIDS patients who have PIV-associated pneumonia by the associated decreasing morbidity and mortality. Further investigation of the benefit of oral ribavirin in similar cases is warranted.

## Conflict of interest

None.

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