A RARE COMPLICATION: ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) INDUCED BY SEVERE PNEUMOCYSTIS CARINII PNEUMONIA (PCP)

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ABSTRACT

Introduction: Pneumocystis pneumonia (PCP) represents a prevalent opportunistic infection among individuals with HIV, posing a significant risk of mortality. The occurrence of acute respiratory distress syndrome (ARDS) as a consequence of PCP further accentuates the gravity and intricacy of this pulmonary infection.

Objective: This case report aims to discuss the management of the rare complication of ARDS induced by severe PCP in a 36-year-old man with HIV.

Case Presentation: A 36-year-old male teacher, presented with worsening dyspnea, intermittent fever, and a productive cough persisting for two weeks, along with weight loss and fatigue. Initial diagnostic impressions included pulmonary tuberculosis with pneumonia. Treatment involved oxygen therapy, fluid administration, and medication. Laboratory tests showed leukocytosis, elevated blood glucose, and abnormal liver function. Subsequent investigations confirmed HIV infection. Chest X-ray revealed severe bilateral pneumonia and possible ARDS, leading to transfer to the Intensive Care Coronary Unit for further management.

Discussion: The diagnosis of severe Pneumocystis jirovecii pneumonia (PCP) underscores the importance of recognizing PCP as a significant clinical concern, especially in HIV patients. Diagnostic challenges, such as late HIV diagnosis, highlight the need for timely screening and intervention. Management involved a multidisciplinary approach, including pulmonologists and cardiologists. Despite treatment adjustments, some patients experience clinical deterioration, necessitating careful management strategies like antiretroviral (ARV) therapy and respiratory support. This case underscores the complexity of managing PCP-related ARDS and the crucial role of timely intervention and comprehensive care.

Conclusion: Severe PCP led to ARDS in an HIV-infected patient due to inflammation and lung damage, exacerbated by the immunocompromised state. Timely diagnosis and treatment are crucial to prevent complications and improve outcomes in such cases.

Keywords: Pneumocystis pneumonia, acute respiratory distress syndrome, HIV/AIDS
INTRODUCTION

Pneumocystis carinii pneumonia (PCP), also known as Pneumocystis jirovecii pneumonia (PJP), is a fungal infection primarily affecting the lungs. It is caused by the fungus Pneumocystis jirovecii, previously known as Pneumocystis carinii. Initially thought to be caused by a protozoan, it was later classified as a fungus. PCP rarely occurs in healthy individuals who do not have HIV/AIDS.\textsuperscript{1,2}

PCP is a common opportunistic infection (OI) in HIV-infected patients, with a higher risk of mortality compared to other OIs like tuberculosis or cryptococcal pneumonia. It was first reported in the USA in 1980 in an HIV-infected individual. PCP significantly impacts HIV-infected patients within the first six months of initiating Highly Active Antiretroviral Therapy (HAART), with a mortality hazard ratio of 2.36. However, recent literature suggests a broader spectrum of PCP occurrence, extending beyond the HIV-infected population to encompass individuals with various forms of immunosuppression or underlying respiratory conditions. Weakened immune systems due to conditions like cancer or medications like high-dose corticosteroids can predispose individuals to PCP.\textsuperscript{3,4}

The emergence of cute Respiratory Distress Syndrome (ARDS) as a complication of PCP underscores the severity and complexity of this pulmonary infection. Symptoms include difficulty breathing, low oxygen levels in the blood, and an increased alveolar-arterial oxygen tension gradient. ARDS represents a clinical syndrome characterized by acute and severe hypoxemic respiratory failure, often precipitated by diverse pulmonary insults. When ARDS complicates PCP, it further exacerbates respiratory compromise and escalates the risk of adverse outcomes, necessitating prompt recognition and intervention.\textsuperscript{5,6}

Despite advancements in medical care and preventive strategies, the incidence of PCP-associated ARDS remains relatively low, contributing to its diagnostic and therapeutic challenges. Clinicians must maintain a high index of suspicion for PCP in patients presenting with respiratory distress, particularly in the context of immunocompromise or predisposing respiratory conditions.\textsuperscript{7,8} This case report aims to discuss the management of the rare complication of ARDS induced by PCP in a 36-year-old man with HIV.

Case Presentation

A 36-year-old male teacher sought medical attention at Luwuk Regional Hospital's Emergency Room on September 13, 2023. He presented with a chief complaint of having trouble breathing that had intensified over the past day, accompanied by symptoms of intermittent fever and a persistent productive cough. He reported experiencing this discomfort for the past two weeks, describing the fever as sporadic and not severe, with temperatures remaining within the normal range. Additionally, he noted the presence of clear sputum in his cough, a symptom he had been experiencing for the last five months, which had failed to improve despite conservative measures. Alongside these respiratory symptoms, he also reported a gradual decline in weight and persistent fatigue. Patient reported no signs of mouth ulceration or chest pain.

The patient has no previous history of illness like this. He does not have diabetes (DM) but has high blood pressure (HT) and takes amlodipine 5 mg regularly. He does not have asthma. There is no family history of similar illness. He occasionally takes Paratusin tablets. The patient works as a lecturer at a private college. His relationship history is unknown. He denies using illicit drugs and does not smoke.

Upon examination, the patient appeared in moderate distress due to his respiratory symptoms. His vital signs showed a blood pressure of 126/76 mmHg, a pulse rate of 134 x/minute, a respiratory rate of 27 x/minute, a temperature of 37.1°C, and an oxygen saturation of 70%. Auscultation revealed normal breath sounds with vesicular breath sounds present bilaterally, along with normal heart sounds (S1S2) and no murmurs. The initial diagnostic impression suspected of pulmonary tuberculosis with pneumonia, with differentials such as bronchitis, bronchial asthma, or chronic obstructive pulmonary disease (COPD) being considered.

The treatment plan included administering oxygen via a non-rebreather mask at 15 liters per minute, intravenous fluid infusion with Ringer's lactate at a rate of 20 drops per minute, administering Farbion intravenously every 24 hours, injecting Methylprednisolone at a dose of 62.5 mg, and administering Omeprazole intravenously at a dose of 40 mg every 12 hours. Laboratory tests included routine blood work, blood sugar levels (GDS), urine analysis (UR/CR), and liver function tests (OT/PT). Additionally, a chest X-ray and EKG was ordered.

The results of the blood tests revealed a leukocyte count of 11.7, with elevated levels of blood glucose at 146. Additionally, the liver function tests showed elevated levels of SGOT (52) and SGPT (23). The chest X-ray (Figure 1) revealed bilateral infiltrates and opacities scattered throughout both lungs. Furthermore, it indicated a shift of the heart towards the right side, with no enlargement noted. There was sharp visualization of the right and left costophrenic angles. The diaphragm on the right appeared normal, while the left diaphragm showed elevation. The overall impression included findings of dextrocardia, severe bilateral pneumonia, and possible acute respiratory distress syndrome (ARDS). Additionally, there was evidence of eversion of the left diaphragm.
Within 3 days of admission, recommendations were made by pulmonologist for consultation with a cardiologist to evaluate for possible acute respiratory distress syndrome (ARDS) and concurrent cardiogenic pulmonary edema. The patient was transferred to the Intensive Care Coronary Unit for closer monitoring. Treatment included intravenous administration of Ceftriaxone 2g every 24 hours, along with Levofoxacin tablets (750 mg) and nebulized Respivent. Consultation with a cardiologist led to additional measures such as intravenous Furosemide 40 mg every 8 hours and continuation of care in the ICCU.

Table 1. The results of laboratorium analysis

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Results</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>Leukocyte</td>
<td>11.7</td>
<td>Normal</td>
</tr>
<tr>
<td>Urem</td>
<td>29</td>
<td>Normal</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.0</td>
<td>Normal</td>
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<tr>
<td>SGOT</td>
<td>52</td>
<td>High</td>
</tr>
<tr>
<td>SGPT</td>
<td>23</td>
<td>Normal</td>
</tr>
<tr>
<td>RBS</td>
<td>146</td>
<td>Normal</td>
</tr>
<tr>
<td>HIV 1</td>
<td>Reactive</td>
<td>HIV positive</td>
</tr>
<tr>
<td>HIV 2</td>
<td>Reactive</td>
<td>HIV positive</td>
</tr>
<tr>
<td>HIV 3</td>
<td>Reactive</td>
<td>HIV positive</td>
</tr>
<tr>
<td>Na</td>
<td>133</td>
<td>Low</td>
</tr>
<tr>
<td>K</td>
<td>4.5</td>
<td>Normal</td>
</tr>
<tr>
<td>Cl</td>
<td>100</td>
<td>Normal</td>
</tr>
<tr>
<td>PaO₂</td>
<td>7</td>
<td>Low</td>
</tr>
<tr>
<td>SaO₂</td>
<td>90%</td>
<td>Low</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.6</td>
<td>Normal</td>
</tr>
<tr>
<td>CD4</td>
<td>15</td>
<td>Low</td>
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Additional investigations, including HIV testing, CD4 count determination, and a thoracic computed tomography (CT) scan, were ordered to confirm the diagnosis and assess the extent of lung involvement. Laboratory results revealed reactive findings for HIV 1, HIV 2, and HIV 3. Additionally, electrolyte analysis showed decreased sodium levels and a decreased CD4 count, indicating immunocompromise. A CT scan of the thorax (Fig 3) revealed extensive ground glass opacity scattered throughout both lungs, along with multiple nodular lytic/cystic lesions. Extensive interstitial shadowing with alveolar shadowing was observed. Clear air bronchograms were observed, and there were no abnormalities in the heart or trachea. From the blood gas analysis, thoracic CT scan, and oxygen saturation levels, a final diagnosis of severe Pneumocystis jirovecii pneumonia (PCP) were made.

Within four days of admission, the pulmonologist continued to manage the patient's respiratory symptoms in the ICCU, with treatment adjustments such as increased oxygen and intravenous medications failing to yield improvement, indicating possible severe respiratory failure and bilateral pneumonia. Concurrently, the cardiologist maintained diuretic therapy for fluid overload. Subsequent follow-ups on the fifth and sixth days post-admission showed improvement in the patient's condition, with the pulmonologist adjusting respiratory support and medications, while the cardiologist continued diuretic therapy for fluid management.

Transitioning to room-based care within 7 days of admission, the pulmonologist continued to monitor the patient's progress, noting further improvement in symptoms. Treatment plans remained focused on supportive care and initiation of antiretroviral therapy (ART) for HIV. Additionally, an internal medicine specialist contributed to the patient's care, ensuring appropriate ARV therapy and supportive management. Throughout subsequent room-based follow-ups until 14 days after admission, the pulmonologist continued to oversee the patient's care, with a gradual improvement in symptoms observed over time.

Treatment plans were adjusted as necessary, with a focus on maintaining respiratory support, managing underlying conditions, and optimizing medication regimens. Throughout his hospitalization, the patient responded positively to the treatment regimen, with notable improvements in his respiratory symptoms and overall condition observed during follow-up assessments.

**DISCUSSION**

Pneumocystis pneumonia (PCP) is an infection caused by *Pneumocystis jirovecii* or previously *Pneumocystis carinii*. PCP emerges as a significant clinical concern, especially for primary care physicians, often marking the initial HIV-related clinical presentation for patients. Clinical manifestations typically include exertional dyspnea, malaise, dry cough, and, less commonly, symptoms like haemoptysis or pleuritic chest pain. This case presents a case of 36-year-old male teacher with initial complaint of difficulty breathing, accompanied by intermittent fever, productive cough, weight loss, and fatigue, hence warranted thorough evaluation and management.

PCP is a respiratory tract infection caused by a unicellular fungus that affects both humans and mammals. The organism was first introduced by Chagas in 1909, initially named Pneumocystic carinii after being isolated from infected rats by Dr. Carni. Later, Dr. Otto Jirovec and colleagues discovered its presence in humans, leading to its renaming as Pneumocystis jirovecii. This dual nomenclature results in the terms PCP and PJP being used interchangeably. Initially debated as belonging to the protozoa or trypanosome groups, biochemical analysis of *Pneumocystis* RNA and mitochondrial DNA categorizes it as a unicellular fungus. Further research reveals three structural forms of the organism: trophozoite,
Pneumocystis pneumonia (PCP) is a global infectious fungal disease, primarily affecting children aged 3 to 4 years. Studies indicate airborne transmission of PCP spores, particularly in individuals with compromised immunity, such as those with HIV/AIDS. Defective cellular and humoral immunity contribute to PCP pathogenesis, with low CD4+ T cell counts (<200 cells/microliter) predisposing individuals to infection. Several risk factors increase susceptibility to PCP, including HIV/AIDS, immunodeficiency, long-term immunosuppressive therapy, malnutrition, organ transplantation with corticosteroid therapy, and hematologic or non-hematologic malignancies. The incidence of PCP is higher in immunocompromised patients, particularly those receiving corticosteroids or undergoing organ transplantation.\(^5\)\(^6\) In this patient, the count of CD4 upon diagnosis is significantly low on 15 cells/mm\(^3\) and electrolyte analysis showed decreased sodium, indicating immunocompromise.

The prognosis of PCP is intricately linked with early identification and prompt initiation of treatment. The diagnosis of HIV was previously unknown in this patient which caused a late management of HIV infection. Late diagnosis of HIV is alarmingly common, underscoring the critical need for early detection facilitated by diagnostic vigilance and opportunistic screening strategies informed by prevalence data. However, challenges persist in HIV testing due to stigma and societal factors, hindering efforts to reach high-risk populations effectively. Various testing approaches, including opt-out testing, have been advocated to enhance uptake and identify undiagnosed cases promptly. Despite a decline in the number of new HIV diagnoses, a substantial proportion of infections remain undiagnosed, posing risks of opportunistic infections, transmission, and mortality.\(^3\)\(^5\)

Diagnosing PCP often involves a combination of radiographic imaging and laboratory investigations such as serum lactate dehydrogenase levels. High-resolution CT scans play a crucial role in diagnosis, offering characteristic findings like patchy areas of ground-glass opacity.\(^7\)\(^10\) In this case, the thoracic CT scan presented with extensive bilateral scattered ground glass opacity and extensive interstitial and alveolar shadowing. Blood gas analysis showed low PaO\(_2\) and SaO\(_2\) with oxygen saturation levels <91%. These results indicated a conclusive diagnosis of severe PCP. The interdisciplinary approach involving pulmonologists, cardiologists, and internal medicine specialists ensured comprehensive care tailored to the patient's complex presentation and underlying conditions.\(^1\)

Despite advancements in HIV management, PCP remains a significant concern, emphasizing the ongoing necessity for healthcare providers to maintain a high index of suspicion for PCP, ensuring timely recognition and appropriate intervention to optimize patient outcomes.\(^7\) Upon examination, the patient displayed vital signs indicative of respiratory distress, prompting further investigation into the underlying cause. Differential diagnoses including pulmonary tuberculosis, pneumonia, bronchitis, bronchial asthma, or chronic obstructive pulmonary disease (COPD) were considered based on the clinical presentation and initial assessment. Treatment initiation, including oxygen therapy, intravenous fluids, and medications targeting potential respiratory and systemic infections, was crucial for stabilizing the patient's condition. However, the subsequent deterioration and suspicion of acute respiratory distress syndrome (ARDS) and cardiogenic pulmonary edema necessitated collaboration with a cardiologist for comprehensive management.

The diagnosis of acute respiratory distress syndrome (ARDS) in this study followed the 2012 Berlin definition criteria. These criteria include acute onset or exacerbation of respiratory symptoms within 1 week, respiratory failure not attributable to cardiac dysfunction or fluid overload, bilateral infiltration shadows on chest X-ray radiographs not fully explained by other factors such as pleural effusion, nodules, or masses, and oxygenation indices categorizing severity as mild, moderate, or severe based on values of 200–300, 100–200, and <100, respectively.\(^11\) The patient in this study met all the diagnostic criteria for ARDS.

Despite advancements in intensive care medicine and standardized approaches to ARDS, PCP remains a significant cause of morbidity and mortality. ARDS is a severe and potentially reversible clinical condition associated with mortality rates as high as 30% to 40%. Standard management involves addressing infections, providing respiratory support, careful fluid management, and general supportive measures like nutrition.\(^12\)

The management of ARDS in this case involved administering oxygen, intravenous fluid infusion, and medications including Farbion, Methylprednisolone, and Omeprazole. Further investigations were conducted, including blood tests, chest X-ray, and EKG, which revealed findings suggestive of severe bilateral pneumonia and possible ARDS. Consultations with pulmonologists and cardiologists led to adjustments in treatment, with additional medications such as Ceftriaxone, Levofloxacin, and Furosemide administered. HIV testing was performed, revealing reactive results, and a thoracic CT scan confirmed the diagnosis of Pneumocystis jirovecii pneumonia. Treatment continued in the Intensive Care Coronary Unit (ICCU), with respiratory support and diuretic therapy managed by pulmonologists and cardiologists, respectively.

Despite these therapies, some patients deteriorate clinically. Extracorporeal membrane oxygenation (ECMO) is considered a rescue therapy, allowing time for lung recovery. However, its use in immunocompromised patients, including those with immunocompromise.
HIV/AIDS, has been avoided due to concerns about further immune suppression, and no specific clinical indications have been established for this population. In the reported case, ECMO was not administered to the patient.

Transitioning to room-based care, antiretroviral therapy (ART) for HIV was initiated, and supportive management continued under the oversight of internal medicine specialists. ART therapy is pivotal in managing HIV, aiming to suppress viral replication, reduce viral load, maintain immune function, and improve patient outcomes. The specific ART regimen selected is tailored to factors like viral load, CD4 cell count, potential drug interactions, and patient history. Typically, ART therapy involves a combination of drugs from different classes, including nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase inhibitors, and entry/fusion inhibitors. The initiation of ART therapy in this case involves selecting an appropriate combination regimen to achieve and maintain viral suppression, prevent drug resistance, restore immune function, and reduce the risk of HIV-related complications.

Regular monitoring of viral load, CD4 cell count, and medication adherence is crucial to assess ART therapy's effectiveness and make necessary adjustments. Patient education and support are essential to ensure understanding of medication adherence and management of potential side effects. Overall, ART therapy plays a critical role in comprehensive HIV management, aiming to control disease progression and improve long-term prognosis.

In this case, severe PCP led to the development of ARDS in the patient with HIV. PCP is known to cause severe inflammation and damage to the lung tissue, resulting in impaired gas exchange and respiratory failure. The infection leads to diffuse alveolar damage, with widespread inflammation and fluid accumulation in the lungs. This inflammatory response can progress rapidly, leading to the development of ARDS, a severe and potentially life-threatening complication characterized by widespread inflammation in the lungs and impaired oxygenation.

In the present case, the patient's chest X-ray revealed severe bilateral pneumonia, indicative of extensive lung involvement due to PCP. The progression to ARDS likely occurred due to the severe inflammatory response triggered by the underlying infection, leading to increased permeability of the alveolar-capillary membrane and subsequent pulmonary edema. Additionally, the patient's immunocompromised state as a result of HIV infection may have contributed to the severity of the inflammatory response and the development of ARDS.

Throughout hospitalization, the patient showed improvement in respiratory symptoms and overall condition, with treatment plans adjusted as necessary to optimize outcomes. Overall, this case underscores the importance of a multidisciplinary approach, timely interventions, and ongoing assessment in managing complex respiratory and systemic illnesses, leading to positive patient outcomes and improved quality of care.

**CONCLUSION**

PCP-induced inflammation and lung damage led to impaired gas exchange and respiratory failure characteristic of ARDS. Severe and extensive lung involvement observed on chest X-ray combined with the patient's immunocompromised state due to HIV infection exacerbated the inflammatory response that caused ARDS development. Recognizing PCP as a significant risk factor for ARDS in HIV-infected individuals underscores the importance of timely diagnosis and treatment initiation to prevent complications and improve outcomes.

**REFERENCE**


