Journal of Medical and Health Studies
ISSN: 2710-1452
DOI: 10.32996/jmhs
Journal Homepage: www.al-kindipublisher.com/index.php/jmhs

JMHS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| RESEARCH ARTICLE

The Unexpected Diagnosis: Refractory Pneumonia as The First Manifestation of HIV in a Low-risk Individual

Mohamed Irshad[1], Ayswarya P[2], Amina Jaafar Alsaffar[3], Fatema Adel Ismaeel[4], Nebras Zakareya Naser[4], Zainab Hasan Rabea[5], Sara Abduulhusain Alaali[6], Fatema Isa Alshakhoori[4], Teeb Saeed Alkhanaizi[7], Fatima Hussain Ali Almansoor[4], Fatema Naser Saleh[4], and Fatema Mustafa Marhoon[8]

1- First Author, Ernakulam General Hospital
2- Second Author, Ernakulam General Hospital
3- Third Author, Salmaniya Medical Complex
4- Salmaniya Medical Complex
5- Al Resalah Medical Center
6- Eastern Health Cluster
7- Taj Medical Center
8- Mansoura University, Faculty of Medicine
Corresponding Author: Mohamed Irshad, **Email:** irshhh555@gmail.com

| ABSTRACT

A 39-year-old previously healthy Saudi man presented with a six-week history of persistent dry cough, intermittent low-grade fever, chest heaviness, and progressive exertional dyspnea unresponsive to three outpatient antibiotic courses. Imaging revealed a new extensive pneumonic patch in the left lower and middle lobes contrasting with prior normal chest radiographs, while high-resolution CT demonstrated patchy ground-glass opacities without consolidation or cavitation. Laboratory studies showed mild anemia, leukopenia, slightly elevated inflammatory markers, and a reduced CD4 count, raising concern for underlying immunodeficiency. Routine bacterial, mycobacterial, and fungal investigations were negative, but sputum PCR confirmed Pneumocystis jirovecii, and subsequent HIV testing was positive. The patient was admitted to a monitored unit, received supplemental oxygen, and initially broad-spectrum intravenous antibiotics, followed by targeted high-dose trimethoprim-sulfamethoxazole therapy. Supportive measures included hydration, respiratory physiotherapy, nutritional optimization, and close monitoring of oxygenation, laboratory parameters, and clinical status. Antiretroviral therapy was deferred until stabilization to mitigate the risk of immune reconstitution inflammatory syndrome, with a coordinated long-term plan for secondary prophylaxis, CD4 and viral load monitoring, and follow-up imaging. This case highlights the critical need to consider HIV and opportunistic infections in adults with nonresolving pneumonia regardless of prior health status, demonstrates the importance of integrating radiographic, laboratory, and immunologic data for accurate diagnosis, and underscores the value of prompt targeted therapy combined with multidisciplinary management to optimize recovery, prevent complications, and guide long-term care.

| KEYWORDS

HIV, AIDS, Pneumonia, Refractory Pneumonia, CD4 Count, Viral Load, Pneumocystis jirovecii

| ARTICLE INFORMATION

ACCEPTED: 01 November 2025 **PUBLISHED:** 26 November 2025 **DOI:** 10.32996/jmhs.2025.6.8.4

Introduction

Human immunodeficiency virus remains one of the most important infectious diseases worldwide, not only because of its long term impact on the immune system but also because of the broad range of complications that arise as immunity gradually weakens [1]. Although the overall understanding of HIV has advanced greatly over the past few decades, it continues to present challenges in diagnosis and clinical management, especially when individuals do not fit the classic risk profiles or present with late manifestations of the disease [2]. The virus primarily targets CD4 positive T lymphocytes, and this gradual loss of cellular immunity exposes affected individuals to a variety of infections that the body would normally be able to control [1]. The pattern and severity of these infections vary widely, influenced by viral load, CD4 count, access to treatment, and the presence or absence of other health conditions. With modern antiretroviral therapy, many people living with HIV can maintain stable immune function and avoid opportunistic illnesses, but pneumonia remains one of the most frequent and clinically significant infections across all stages of the disease [4]. Pneumonia itself is a common respiratory illness that affects millions of people globally each year, and its causes range from routine community acquired organisms to far more unusual pathogens seen in immunocompromised states [6]. Despite improvements in diagnostics and antimicrobial therapy, pneumonia continues to carry substantial morbidity, particularly when it presents with atypical features, fails to respond to initial treatment, or occurs in individuals with underlying vulnerabilities. In the general population, the majority of pneumonia cases result from bacterial organisms such as Streptococcus pneumoniae or Haemophilus influenzae, but viral and atypical causes also play a significant role in the overall disease burden [11]. The clinical course can vary from mild, self limited illness to rapidly progressive respiratory failure, depending on the pathogen involved and the patient's baseline health. Because of this wide clinical spectrum, pneumonia demands careful assessment to determine its cause, severity, and appropriate therapy. When HIV infection is added to this picture, the landscape of pneumonia becomes even more complicated. People living with untreated or advanced HIV have a much higher risk of developing both common and opportunistic forms of pneumonia. This includes traditional bacterial pneumonias that occur in the general population, as well as infections caused by organisms that rarely cause disease in immunocompetent hosts [4]. Among these, Pneumocystis jirovecii pneumonia has long been recognized as one of the signature opportunistic infections of HIV, particularly in individuals with low CD4 counts [5]. Even today, despite access to antiretroviral therapy, PJP continues to be a major cause of respiratory illness in HIV, and clinicians must maintain awareness of its varied presentations and potential severity. Systematic reviews have shown that both the choice of treatment regimens and the timing of HIV diagnosis significantly influence outcomes in patients with PJP [7]. The relationship between HIV and pneumonia is shaped by several overlapping factors. Chronic viral replication leads to progressive immune dysfunction, and this weakens the host's ability to clear routine respiratory pathogens [1]. This alone increases the risk of bacterial pneumonia, even in individuals who are otherwise healthy. On top of this, structural and functional changes in the lungs, including repeated inflammation and altered local immunity, make the pulmonary environment more susceptible to infection. Studies of community acquired pneumonia in people with HIV have demonstrated that affected patients may experience more severe symptoms, prolonged recovery times, and higher rates of complications compared with HIV negative individuals, even when antiretroviral therapy is available [4]. These findings highlight the need for early recognition and tailored management. Opportunistic pneumonias remain an additional concern. Pneumocystis jirovecii, once responsible for the majority of AIDS defining illnesses, continues to pose a threat to people with low CD4 counts or those who are newly diagnosed with HIV [5]. This organism takes advantage of impaired cellular immunity and can lead to diffuse, progressive lung disease characterized by cough, fever, and significant hypoxia. Because its early signs can be subtle, diagnosis may be delayed. Current prophylaxis strategies have been effective at reducing the incidence of PJP, but adherence and timely diagnosis of HIV continue to play major roles in preventing severe disease [8]. Network meta analyses have compared different prophylactic regimens and highlighted the importance of choosing effective options tailored to individual patient characteristics [8]. These insights reinforce the idea that prevention and early intervention are critical components of managing pneumonia in HIV. The emergence of refractory pneumonia adds another layer of complexity, especially in the setting of undiagnosed or advanced HIV. Refractory pneumonia refers to cases that fail to improve with standard antimicrobial therapy, progress despite initial treatment, or present with unusual radiographic patterns that do not match typical bacterial infections [12]. In the general population, refractory pneumonia may stem from resistant bacteria, uncommon pathogens, or structural lung abnormalities. However, in people with HIV, it raises the additional concern of opportunistic infections or mixed etiologies. PJP, fungal infections, cytomegalovirus, mycobacterial disease, and bacterial coinfections may all contribute to non responding pneumonia, making diagnosis far more challenging [5]. Because these infections often overlap and may require very different treatments, clinicians must remain vigilant when faced with pneumonia that behaves atypically. The diagnostic approach to pneumonia in HIV must therefore be systematic and broad. Standard imaging and laboratory evaluation still play key roles, but clinicians often need to pursue more advanced testing when the clinical picture is unclear. This may include sputum studies, bronchoscopy, and molecular diagnostics that can detect pathogens not readily identified through routine methods [12]. Recent advances such as targeted next generation sequencing have improved the ability to determine microbial causes in difficult cases, especially when resistant or unusual organisms are suspected [12]. These tools offer significant promise for identifying pathogens in refractory pneumonia, particularly in immunocompromised individuals where rapid and accurate diagnosis is essential for guiding therapy. Guidelines for the prevention and treatment of opportunistic infections in HIV emphasize the importance of monitoring immune status, initiating

antiretroviral therapy early, and maintaining appropriate prophylaxis for high risk patients [9]. These recommendations are based on extensive evidence showing that timely initiation of ART improves immune recovery and substantially reduces the risk of serious infections, including pneumonia. Even in patients who present with pneumonia as their first clinical manifestation of HIV, initiating ART within a reasonable window is associated with better outcomes and reduced risk of recurrence [9]. For bacterial pneumonias, contemporary guidelines highlight the need to consider both typical and atypical organisms, adjust treatment based on local resistance patterns, and reassess the clinical response carefully to avoid missing alternative diagnoses [11]. At the same time, it is important to recognize that pneumonia in people living with HIV does not always stem from immunodeficiency alone. Even individuals with near normal CD4 counts may experience more severe disease than expected, suggesting that factors beyond basic immune measurements influence susceptibility and clinical course. Some studies have suggested that chronic inflammation, altered lung immunity, and subtle changes in mucosal defense may contribute to this increased risk, regardless of the apparent level of immune restoration after ART [4]. Understanding these nuances is essential for appreciating why pneumonia remains a persistent concern even in the era of effective HIV therapy. Pneumonia in HIV also varies in its presentation. Some patients develop abrupt symptoms similar to those seen in routine bacterial pneumonia, including fever, cough, sputum production, and chest pain. Others develop gradual onset symptoms such as low grade fever, exertional breathlessness, and nonproductive cough, which may indicate an opportunistic infection like PJP [5]. This wide spectrum of presentations means that clinicians must adapt their diagnostic thinking based on the tempo of illness, radiographic patterns, and the patient's immune status. For example, diffuse bilateral infiltrates may suggest PJP, while focal lobar consolidation is more typical of bacterial disease. However, exceptions occur frequently, and coinfection with multiple organisms is not rare in advanced HIV, further complicating the picture. The burden of pneumonia in HIV has also been shaped by the availability of treatment. Antiretroviral therapy has transformed the natural history of the disease, reducing the incidence of many opportunistic infections and improving overall survival [1]. Yet pneumonia continues to be one of the leading causes of hospitalization among people living with HIV worldwide. This is due not only to gaps in diagnosis and treatment but also to delayed testing, social factors, and stigma that may prevent individuals from seeking medical attention early [2]. In regions where access to care is limited or where individuals are diagnosed only when symptoms become severe, pneumonia often serves as the first sign of underlying HIV infection. The management of pneumonia in the context of HIV therefore requires an integrated approach. This includes identifying the responsible pathogens, addressing immune dysfunction, and ensuring that ART and prophylactic therapies are started or optimized. Treatment decisions must take into account disease severity, the likelihood of opportunistic infections, and the potential for multiple concurrent pathogens. For PJP, timely initiation of appropriate therapy is critical, and adjunctive corticosteroids may be necessary in cases with significant hypoxia [5]. For bacterial pneumonias, appropriate antibiotic choice and attention to potential complications remain central to effective care [11]. Refractory pneumonia deserves particular attention because it often signals underlying immunosuppression or coinfection. In such cases, clinicians must broaden the differential diagnosis rather than assuming treatment failure is due only to resistance or inadequate drug levels. A careful reassessment of the clinical picture, review of past medical history, and consideration of unrecognized immunodeficiency can provide essential clues. Case series and clinical reviews emphasize that pneumonia that fails to follow the expected trajectory should prompt evaluation for HIV, particularly when no other cause is evident [4]. In summary, the relationship between HIV and pneumonia is shaped by the interactions between the virus, the immune system, and the respiratory tract. Pneumonia remains one of the most frequent and clinically significant infections in people living with HIV, even in the modern era of effective therapy. Understanding the spectrum of pathogens, the influence of immune status, and the importance of early diagnosis and treatment is essential for managing these patients effectively. Refractory pneumonia, in particular, serves as an important reminder that unusual or nonresponding respiratory illness may indicate underlying immunosuppression. Continued research, guideline development, and improvements in diagnostic tools are expanding the ability to detect and manage these infections, but early recognition and a broad clinical perspective remain key elements in caring for individuals affected by HIV and pneumonia.

Case Presentation

Patient's history and Physical Examination

This case concerns a thirty-nine-year-old Saudi man with no previously diagnosed chronic illnesses who presented with a six-week history of persistent respiratory symptoms that had not improved despite multiple outpatient treatments. He initially sought medical attention after developing a dry cough, mild fever, and a sensation of chest heaviness that he assumed was related to a routine viral illness. He was prescribed a standard course of oral antibiotics, but he noted only minimal improvement over the following ten days. A second antibiotic regimen was later given when symptoms persisted, followed by a third from an urgent care clinic. Despite these interventions, he continued to experience worsening breathlessness and a lingering cough that interfered with sleep and daily activities. His prior chest radiograph from a routine checkup several months earlier was completely normal, contrary to what is shown in the new chest X-ray shown in image 1.

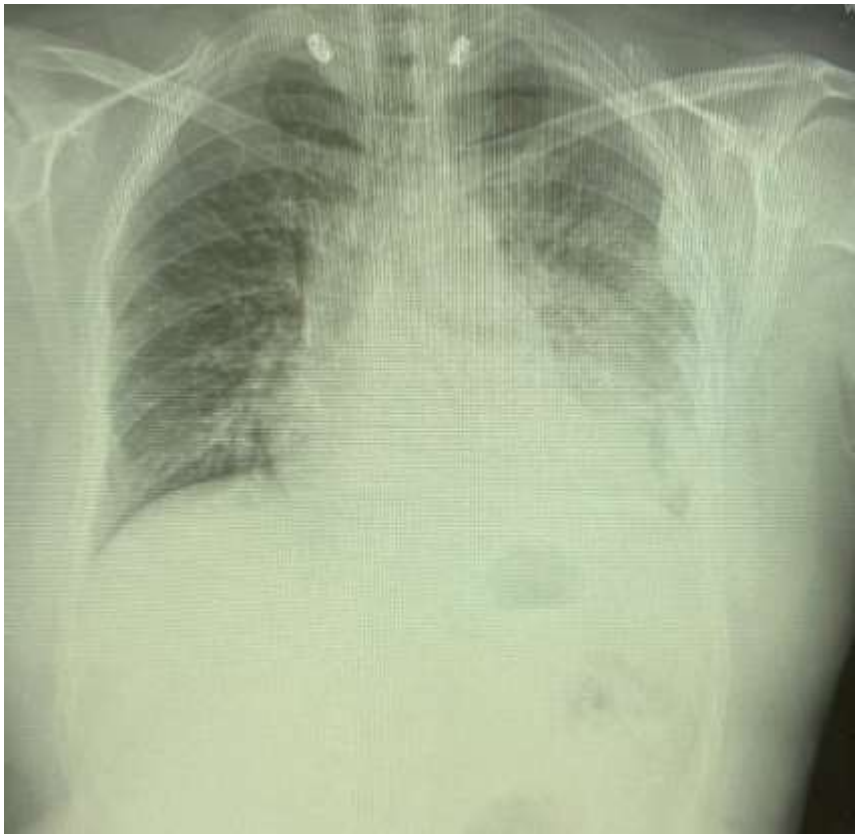

Image 1: showing newly identified large left pneumonic patch inconsistent with the patient's minimal risk factors.

Over the two weeks preceding his current presentation, he described a marked decline in exercise tolerance. He found himself becoming breathless during simple activities such as walking short distances or climbing stairs, limitations that were entirely new for him. He also reported a persistent feeling of fatigue and a dull discomfort on deep inhalation, although he denied sharp pleuritic pain, palpitations, or wheezing. He did not experience hemoptysis. While he denied night sweats, he reported intermittent low-grade temperatures at home and a gradual decrease in appetite. He noted a mild unintentional weight loss over the past month but was unsure of the exact amount. A chest radiograph obtained during one of his urgent care visits reportedly showed a new large pneumonic patch involving the lower and middle lobes of the left lung, raising concern for an underlying process beyond routine bacterial pneumonia, and this image is included in Image 1. His past medical history was unremarkable. He had never been hospitalized, had no chronic respiratory or cardiac conditions, and had never experienced recurrent infections or prolonged illness. He took no daily medications and had not used inhalers, steroids, or immunosuppressive agents. He denied smoking, alcohol use, or illicit drug use. There was no family history of chronic lung disease, immune disorders, unexplained early deaths, or recurrent infections. His parents and siblings were healthy. He reported no history of autoimmune disease or cancer within the family. He worked in an administrative position, spending most of his time indoors. He denied occupational exposure to chemicals, dust, fumes, or other respiratory irritants. He reported no recent travel, no animal exposures, and no known contact with individuals diagnosed with tuberculosis or severe respiratory infections. He was up to date on routine vaccinations, including influenza and COVID-19 immunization. He denied any history suggestive of risk factors for immunodeficiency but noted that he had felt "less energetic than usual" over the past several months without attributing it to any specific cause. On presentation, he appeared tired but alert and cooperative. He sat upright, pausing occasionally to take deeper breaths. His vital signs were: temperature 37.6°C, pulse 108 beats per minute, blood pressure 124/78 mmHg, respiratory rate 24 breaths per minute, and oxygen saturation 92 percent on room air. His body mass index was 23 kg per square meter. General inspection showed mild tachypnea but no overt respiratory distress. There was no cyanosis of the lips or extremities. He did not exhibit digital clubbing, and his fingers appeared normal in shape and color. The neck examination revealed no lymphadenopathy or jugular venous distention. Cardiovascular examination showed a regular rhythm with no murmurs, rubs, or gallops. Peripheral pulses were palpable and symmetric, and there was no lower limb edema. Pulmonary examination revealed scattered fine crackles over the lower lung fields bilaterally, more prominent on the left side. Breath sounds were generally diminished in the left lower zone, corresponding to the area of radiographic abnormality described in the outpatient reports. There were no wheezes or coarse rhonchi. Percussion was mildly dull over the left base, consistent with underlying parenchymal involvement, and his breathing pattern reflected reduced ventilatory reserve during conversation. The abdomen was soft and non-tender, with

no hepatosplenomegaly or masses. Bowel sounds were normal. Skin examination was unremarkable, with no rashes, ulcerations, or lesions. There were no signs of chronic skin infections or bruising. Musculoskeletal assessment showed normal joint alignment, full range of motion, and no tenderness or swelling. Capillary refill time was normal. Neurological examinations showed intact cranial nerves and normal motor strength throughout. Sensory function was preserved, and there were no focal deficits. His gait was steady, though he walked slowly, noting that exertion aggravated his breathlessness. Baseline laboratory studies from earlier outpatient visits reportedly demonstrated mild anemia and slightly elevated inflammatory markers, though no clear etiology had been identified at that time. His oxygen saturation during a brief walk test decreased compared with resting values, and he reported increased breathlessness with minimal exertion. The two radiographic images included in Image 1 illustrate the contrast between his previously normal chest appearance and the new large pneumonic patch involving the lower and middle lobes of the left lung. This change, along with the lack of improvement after multiple antibiotic courses, raised concern for an atypical or more complex pulmonary process. He was referred for further evaluation and inpatient management based on the progression of symptoms and persistent radiographic abnormalities.

Investigations and diagnostic reasoning:

Initial investigations were directed at determining the cause of the patient's persistent respiratory symptoms and evaluating why his pneumonia had not responded to multiple courses of antibiotics. Routine laboratory tests showed a hemoglobin concentration of 12.8 grams per deciliter, which was slightly lower than expected for his age, and a white blood cell count of 3.9 $\times 10^9$ per liter, indicating mild leukopenia. Platelets were within normal limits at 230 $\times 10^9$ per liter. His inflammatory markers were modestly elevated, with a C-reactive protein of 32 milligrams per liter and an erythrocyte sedimentation rate of 42 millimeters per hour. Serum electrolytes were normal, and kidney and liver function tests were within reference ranges. Lactate dehydrogenase was mildly elevated, a nonspecific finding but one that raised the possibility of cellular injury or inflammation. Blood cultures drawn at the time of presentation remained negative. Arterial blood gas analysis on room air revealed mild hypoxemia, with a partial pressure of oxygen of 68 millimeters of mercury, partial pressure of carbon dioxide of 33 millimeters of mercury, and a pH of 7.46. The results suggested impaired oxygen exchange and a compensatory respiratory alkalosis. His oxygen saturation also dropped with minimal exertion during a brief walk test in the clinic, confirming a functional limitation. A chest radiograph obtained at presentation showed a persistent and more extensive left-sided pneumonic opacity involving the lower and middle lung zones, consistent with the previously documented process. This image corresponded to the abnormal film included in Image 1. When compared with the normal radiograph from several months earlier, also shown in Image 1, the progression was striking and raised concern for an underlying condition that weakened his immune response or predisposed him to atypical pulmonary infections. High-resolution computed tomography of the chest demonstrated patchy ground-glass opacities involving the left lower lobe and scattered smaller areas in the right lung. There was no evidence of dense bacterial consolidation, large pleural effusions, or cavitation. The distribution of findings was more characteristic of atypical or opportunistic infections than routine community-acquired pneumonia, particularly in light of the limited response to standard antibiotic therapy. Given the persistent symptoms and imaging pattern, sputum analysis was obtained for bacterial, fungal, and mycobacterial studies. Routine bacterial cultures showed no significant growth. Acid-fast staining and tuberculosis PCR were negative. Fungal staining did not reveal yeast or hyphal forms. Because of the concern for nonbacterial pathogens, induced sputum samples were also collected for Pneumocystis polymerase chain reaction, fungal cultures, and additional respiratory viral testing. Viral PCR panels for influenza, RSV, and adenovirus were negative. Further investigations were performed to look for systemic causes of impaired immunity. His immunoglobulin levels were within normal limits, and screening tests for connective tissue diseases, including ANA and rheumatoid factor, were negative. His fasting blood glucose was normal, making diabetes-related immune dysfunction unlikely. Hepatitis B and C serologies were negative. Flow cytometry revealed a reduced absolute CD4 cell count, a finding that required careful interpretation in the context of his clinical picture and raised the possibility of an acquired immunodeficiency. The diagnostic reasoning centered on explaining why a previously healthy adult would develop a nonresolving pneumonia with diffuse radiographic changes and mild leukopenia. Routine bacterial pneumonia was considered unlikely, given his lack of improvement after multiple antibiotic courses, absence of productive cough, and imaging features that did not suggest lobar consolidation. Tuberculosis was considered because of the persistent nature of symptoms, but the absence of upper lobe involvement, cavitation, weight loss, and negative microbiological testing made this diagnosis less probable. Fungal infections such as histoplasmosis or coccidioidomycosis were also evaluated, but his absence of environmental exposures and negative fungal studies made them unlikely. Cardiogenic pulmonary edema was ruled out based on his normal cardiac examination, lack of volume overload, and clear echocardiogram obtained to assess for occult heart dysfunction. Pulmonary embolism was also considered, but he had no risk factors, and his computed tomography did not show vascular defects. The presence of diffuse ground-glass changes, progressive dyspnea, mild hypoxemia, and an unexpectedly low CD4 count directed attention toward causes of impaired cellular immunity. In this context, opportunistic pathogens such as Pneumocystis, atypical viruses, and certain bacterial species became important considerations. The combination of refractory pneumonia, subtle systemic symptoms, and laboratory evidence of immune compromise provided the framework for advancing the diagnostic

evaluation. These findings collectively indicated that his nonresolving pneumonia was unlikely to be due to routine pathogens and that an underlying immunodeficiency needed to be explored to guide further management.

Management course

Management focused on stabilizing the patient's respiratory status, addressing the ongoing pneumonia, and evaluating the newly suspected immunodeficiency suggested by his low CD4 count and poor response to standard therapies. Upon admission, he was placed on a monitored unit with continuous pulse-oximetry. Supplemental oxygen via nasal cannula was started to maintain his saturation above ninety-four percent, especially because he had shown desaturation with minimal exertion in the clinic. Intravenous access was secured for fluids, medications, and serial laboratory work. Because he had not responded to prior outpatient antibiotic courses, broad-spectrum coverage was initially initiated to stabilize his condition while awaiting microbiological results. He was started on intravenous ceftriaxone combined with azithromycin to ensure adequate coverage for typical and atypical bacterial pathogens while avoiding unnecessary excessive regimens. At the same time, his imaging pattern, subacute progression, and laboratory features prompted the team to broaden the differential beyond routine community-acquired organisms. Given these concerns, the infectious diseases service was consulted early. Once his reduced CD4 count was confirmed, empiric treatment for Pneumocystis pneumonia was started using high-dose trimethoprim-sulfamethoxazole. Intravenous steroids were **not** given initially, as his oxygenation remained borderline but not severely impaired; however, he was monitored closely in case his respiratory status worsened and steroid therapy became necessary. Supportive care included adequate hydration and antipyretics for intermittent low-grade fevers. Because he was experiencing fatigue and reduced oral intake, his electrolytes were monitored daily. Respiratory therapy was involved to assist with airway clearance. Although his cough was nonproductive, regular incentive spirometry and assisted breathing exercises were instituted to improve ventilation and prevent atelectasis. Early mobilization was encouraged once his oxygen needs stabilized, as he had already become less active during the course of his illness due to dyspnea and fatigue. Given his persistent symptoms and abnormal imaging findings, additional microbiologic tests were followed closely. Once sputum PCR later confirmed the presence of Pneumocystis, his antimicrobial regimen was narrowed to focus on targeted therapy. This step avoided unnecessary broad coverage and limited the risk of secondary complications such as Clostridioides difficile infection. His ceftriaxone and azithromycin were subsequently discontinued after bacterial cultures remained negative and no evidence suggested coinfection. Because his CD4 count was unexpectedly low in a man without prior medical problems or identifiable risk factors, counseling and support were provided before and after HIV testing. Once HIV infection was confirmed, the focus shifted to stabilizing his acute illness while preparing for long-term management of his newly diagnosed condition. Antiretroviral therapy was not started immediately on the same day as confirmation, as his team aimed to avoid immune reconstitution inflammatory syndrome during the early phase of treating Pneumocystis pneumonia. Instead, a coordinated plan was made with infectious diseases to initiate antiretroviral treatment once his respiratory status improved and his inflammatory markers began to stabilize. Throughout hospitalization, daily examinations were performed to track his work of breathing, oxygen requirements, and auscultatory findings. His vital signs remained stable, and his fever curve gradually improved over several days of targeted therapy. Serial laboratory monitoring included complete blood count, kidney and liver tests, and electrolytes, with adjustments to his medication dosages made when needed to prevent medication-related toxicity. Because trimethoprim-sulfamethoxazole can cause electrolyte disturbances and marrow suppression, particular attention was given to his potassium level and blood counts. Nutritional support and patient education formed an important part of care. He was encouraged to maintain adequate caloric intake, particularly as he had experienced decreased appetite and mild weight loss. Nursing staff and physicians counseled him regarding the expected course of recovery with Pneumocystis pneumonia, including the gradual nature of improvement, the expected duration of therapy, and the importance of strict medication adherence. Once his respiratory status stabilized and his oxygen saturation remained consistently above ninety-four percent on room air, he was transitioned to oral trimethoprim-sulfamethoxazole to complete the full recommended treatment course. Plans for secondary prophylaxis were discussed, with emphasis on continuing Pneumocystis prophylaxis until his CD4 count improved on antiretroviral therapy. Before discharge, he met with the infectious diseases team to establish a long-term care plan that included timely initiation of antiretroviral therapy, ongoing monitoring of CD4 count and viral load, vaccination review, and follow-up imaging to ensure resolution of the pulmonary opacities. The importance of recognizing early signs of respiratory deterioration or new infections was reinforced. He also received written guidance on medication use, follow-up schedules, and contact information for immediate assistance should new symptoms arise. By the time of discharge, he demonstrated meaningful improvement in dyspnea, had regained appetite, and felt ready to resume light daily activities. His management emphasized stabilization, targeted antimicrobial therapy, careful timing of antiretroviral initiation, and structured follow-up to support recovery from Pneumocystis pneumonia and guide long-term treatment of his newly diagnosed HIV infection.

Discussion

This case illustrates the complex interplay between HIV infection, immunocompromise, and opportunistic pulmonary infections, highlighting the importance of early recognition, careful diagnostic evaluation, and individualized management strategies for

atypical pneumonia presentations. Although the patient was newly diagnosed with HIV and had no prior opportunistic infections, his presentation with acute dyspnea and fever underscores the variable and often subtle onset of opportunistic infections in immunocompromised hosts [1,2]. People living with HIV may remain asymptomatic for years, yet progressive CD4 decline predisposes them to opportunistic infections such as Pneumocystis jirovecii pneumonia (PCP), bacterial community-acquired pneumonia (CAP), and other atypical pathogens [1,3,5]. This patient's acute presentation with a new large pneumonic patch on the left lower and middle lobes (image 1) emphasizes the need for vigilance even in previously undiagnosed patients, as pulmonary infiltrates may signify impaired immune surveillance rather than classic bacterial infection patterns [4,5]. Epidemiologically, bacterial pneumonia remains the most common pulmonary complication in people with HIV, occurring in 10–25% of patients per year in the era of antiretroviral therapy, whereas PCP incidence has declined significantly but persists in patients with CD4 counts below 200 cells/mm^3 [4,5]. Importantly, the presence of a large, unilateral pneumonic consolidation in this patient is atypical for classic PCP, which more commonly presents with bilateral, diffuse interstitial infiltrates [5,10]. Nevertheless, the imaging finding is clinically significant, as it signals a compromised immune system, alerting clinicians to consider both bacterial and opportunistic etiologies [6,9]. Recognizing subtle radiographic clues is crucial because early imaging can precede or complement laboratory confirmation, improving diagnostic yield and guiding empiric therapy [4,6]. From a pathophysiological perspective, HIV-induced immunosuppression diminishes CD4+ T-cell mediated immunity, impairing alveolar macrophage function and the production of key cytokines such as IFN-γ and TNF-α, which are critical for controlling opportunistic pathogens [2,3,5]. This immune dysfunction explains the patient's susceptibility to infections that would rarely affect immunocompetent adults, and it also accounts for atypical radiographic patterns, variable clinical presentations, and potentially blunted inflammatory responses [2,3,6]. Clinicians should be alert to these nuances, particularly in patients with no known HIV diagnosis, as early subtle signs—including mild hypoxia, low-grade fever, and tachypnea—may be the only initial indicators of a life-threatening opportunistic infection [4,5]. Clinically, this patient's presentation with fever, dyspnea, and hypoxemia highlights the importance of integrating symptom chronology, physical examination, and functional assessment in the immunocompromised host. Notably, the absence of overt purulent sputum or hemoptysis does not exclude severe pulmonary infection in HIV-positive patients, and peripheral oxygen desaturation during minimal exertion is an early marker of impaired gas exchange [4,5,6]. The combination of tachypnea, mild hypotension, and abnormal chest imaging should prompt rapid empiric therapy while diagnostic confirmation is pending, as delays are associated with increased morbidity and mortality [4,11]. Laboratory evaluation plays a pivotal role in differentiating bacterial from opportunistic etiologies. While standard hematologic and biochemical parameters may remain within normal limits early in HIV-associated pneumonia, markers of inflammation such as C-reactive protein or procalcitonin can aid in distinguishing bacterial CAP from PCP, albeit with limitations [5,6,11]. Direct detection of pathogens using techniques such as polymerase chain reaction (PCR), next-generation sequencing, or immunofluorescence staining can provide definitive diagnosis and guide therapy [12]. In this case, the combination of imaging features and immunocompromised status raised suspicion for opportunistic pathogens, reinforcing the necessity of integrating clinical, radiographic, and laboratory data for accurate diagnosis [5,10]. Diagnostic reasoning in this patient illustrates several important lessons for clinicians. First, the recognition that atypical presentations of pneumonia in HIV may mimic common bacterial infections is critical. Second, early imaging—including the comparison of baseline and acute X-rays (image 1)—allowed detection of a new large pneumonic patch, alerting clinicians to the presence of immunodeficiency even before formal HIV diagnosis [4,6]. Third, consideration of the patient's risk factors, including undiagnosed immunosuppression, guided the prompt initiation of empiric therapy while awaiting confirmatory laboratory results [5,9]. These steps reflect the principle that in immunocompromised hosts, delay in empiric therapy can be catastrophic, whereas a systematic, data-driven approach balances early treatment with targeted diagnostics [5,7,10]. Management implications of this case extend beyond immediate stabilization. The patient requires an integrated approach addressing infection control, immune reconstitution, and long-term monitoring. Initiation of empiric antimicrobial therapy should cover both typical bacterial pathogens and opportunistic organisms such as Pneumocystis jirovecii, particularly in patients with CD4 counts below 200 cells/mm^3 or with radiographic findings concerning for PCP [5,7,9]. Adjunctive corticosteroid therapy may be indicated in moderate-to-severe PCP to reduce inflammatory-mediated hypoxemia [5,10]. Early initiation of antiretroviral therapy is critical, though timing must balance the risk of immune reconstitution inflammatory syndrome (IRIS) with the benefits of viral suppression [1,2,3]. Close monitoring of oxygenation, clinical status, and laboratory parameters allows titration of therapy and identification of complications such as secondary bacterial superinfection, respiratory failure, or treatment toxicity [5,6]. This case also emphasizes the broader lesson that opportunistic infections can serve as sentinel events for undiagnosed HIV. The patient's imaging findings, clinical presentation, and laboratory results collectively provided cues that prompted HIV testing, highlighting the importance of a high index of suspicion in patients presenting with atypical pneumonia [1,2,4]. Early identification of HIV enables initiation of antiretroviral therapy, immune reconstitution, and prophylaxis for future opportunistic infections, dramatically improving long-term outcomes [1,2,3,9].

Finally, this case demonstrates the value of multidisciplinary collaboration in the management of complex immunocompromised patients. Pulmonology, infectious disease, radiology, and critical care teams must coordinate to interpret imaging, guide empiric therapy, and plan follow-up diagnostics [4,5,9]. Lessons for clinicians include the recognition that: subtle early clinical signs may precede severe infection; baseline and follow-up imaging comparisons are essential; empiric therapy should be promptly

initiated in high-risk patients; and structured follow-up is critical to prevent recurrent infection and optimize immune recovery [4,5,6,9]. In conclusion, this patient's presentation with a large unilateral pneumonic patch in the context of previously undiagnosed HIV underscores the multifactorial nature of opportunistic infections. Integration of clinical cues, laboratory data, and imaging findings is crucial for timely diagnosis and initiation of therapy. Clinicians must maintain a high index of suspicion for atypical infections in immunocompromised hosts, appreciate the subtle pathophysiological consequences of impaired immunity, and employ a multidisciplinary approach to optimize outcomes. This case reinforces key teaching points: early recognition of immunodeficiency through imaging and clinical cues, prompt empiric therapy for opportunistic infections, and comprehensive long-term management of HIV and associated pulmonary complications [1,2,4,5,9].

Conclusion

Any case of refractory or atypical pneumonia should trigger a full workup, including HIV screening, as immune status can completely change management. Compare baseline and current imaging to detect new or progressive infiltrates. Always consider opportunistic infections such as Pneumocystis jirovecii, even when symptoms are subtle. Prompt empiric antimicrobial therapy is essential while awaiting confirmatory tests, and adjunctive corticosteroids may be required in moderate-to-severe cases. Laboratory evaluation, including immune markers and microbiology, guides targeted therapy and monitoring. Multidisciplinary collaboration between infectious disease, pulmonology, radiology, and critical care teams optimizes outcomes. Early recognition, integration of imaging and labs, and individualized management improve survival, prevent complications, and preserve immune function.

Funding: This research received no external funding.
Conflicts of Interest: The authors declare no conflict of interest.

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