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CASE REPORT | LIVER

Pneumocystis Pneumonia in a Patient With Alcoholic Hepatitis

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ABSTRACT

Pneumocystis jirovecii is an opportunistic fungus typically causing pulmonary infection in immunocompromised persons. We present a case of *Pneumocystis jirovecii* pneumonia (PJP) in a patient with alcoholic hepatitis and underlying cirrhosis. PJP in patients with alcoholic hepatitis or cirrhosis is sparsely reported in literature. This condition carries a poor prognosis and high mortality. Clinicians need to recognize alcohol use resulting in liver damage as a significant etiological risk factor for PJP.

KEYWORDS: *Pneumocystis jirovecii* pneumonia; alcohol use disorder; alcohol induced liver injury

INTRODUCTION

Pneumocystis jirovecii pneumonia (PJP) is an opportunistic fungus causing pulmonary infection in immunocompromised persons, most often with AIDS or on immunosuppressive therapy. PJP is a devastating infection with a mortality rate as high as 50% in HIV-negative patients.[1] We present a case of PJP pneumonia in a patient with severe alcohol use disorder. We also review other cases in the current literature. We identify this as the seventh published case of PJP in an HIV-negative patient with alcoholic hepatitis.

CASE REPORT

Our patient was a 36-year-old man presenting with altered mental status, severe sepsis, and progressive abdominal distension. Medical history was significant for alcohol use disorder and recurrent alcohol-related pancreatitis. He was not on any medications, including immunosuppressive therapy, as an outpatient. Laboratory data revealed elevated liver enzymes (Aspartate transaminase 340 (AST) and alanine transaminase 81 (ALT)), a total bilirubin of 18.9 mg/dL, an International Normalized Ratio (INR) of 2.8, and a lactate of 5.2 mmol/L. His presentation was consistent with acute alcoholic hepatitis with ascites, with a Model for End-Stage Liver Disease–Sodium (MELD-Na) score of 30, signifying 27%–32% 90-day mortality risk. Additionally, Maddrey's Discriminant Function (MDF) score was 97, also indicating poor prognosis. He was emergently intubated because of his hypoxic respiratory distress and hypotension necessitating vasopressor support. Chest x-ray showed multifocal pneumonia (Figure 1), and he was started on broad spectrum for pneumonia.

On day 3, he began a 5-day course of hydrocortisone 50 mg every 4 hours for septic shock. Computed tomography of the abdomen showed nodular liver parenchyma, his first radiographic evidence of cirrhosis. Bronchioalveolar lavage analysis grew *Pneumocystis jiroveci*. Antibiotics were then narrowed to a 21-day course of trimethoprim-sulfamethoxazole (TMP-SMX). He self-extubated on day 7, and repeat chest x-ray on day 8 showed resolving infection (Figure 2). He was discharged with only 3 days of TMP-SMX 480 mg left to complete his 21-day course. No prophylactic medications were prescribed. It has been approximately 18 months since the time of his admission. He is still alive with regular paracentesis. Since discharge over 18 months ago, the patient has been admitted several times since for alcohol-related co-morbidities.

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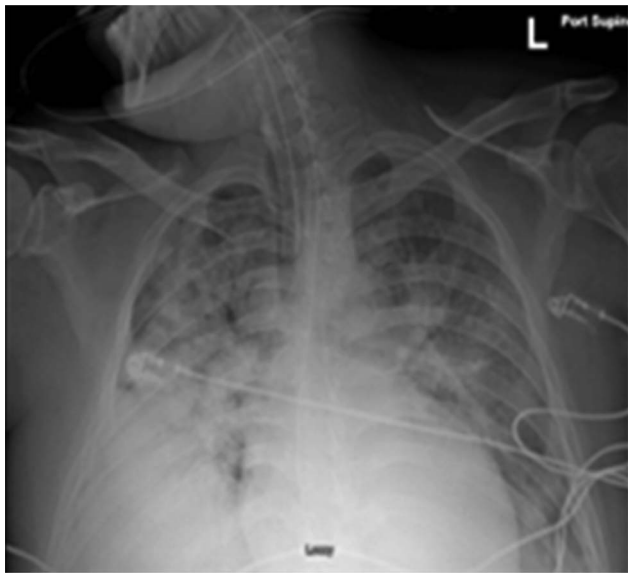

Figure 1. Chest x-ray at admission showing diffuse ground-glass opacities.

DISCUSSION

When the AIDS epidemic began, there were 20,000 cases of PJP annually. Cases began declining with the introduction of antiretroviral therapy and prophylaxis administration for $CD4^+$ counts below 200.[2] PJP has been reported in cases of alcoholic hepatitis, but it is most frequently seen with concomitant immunosuppressive glucocorticoids for treatment of alcoholic hepatitis. A current literature review revealed 20 reported cases from 8 manuscripts of PJP infection associated with alcoholic cirrhosis (Table 1). Of these 20, only 6 did not have concurrent corticosteroid use (30%). Nine had another infection present, such as cytomegalovirus or HIV. In 14 of the 20 cases (70%), PJP infection resulted in death.

Alcohol disrupts the immune system in several ways. It weakens tight junctions between cells in the digestive tract, leading to increased intestinal permeability. This allows bacterial products (such as lipopolysaccharides) to enter the bloodstream. Lipopolysaccharides then activate immune cells in the liver resulting in a chronic inflammatory state.[3] In the respiratory system, alcohol decreases antioxidant levels, leading to oxidative stress and increasing the risk of acute respiratory distress syndrome and bacterial infection.[3] Alcohol affects antigen presentation and $CD4^+/CD8^+$ cell function, which suppresses the Th1 response to IFN-γ and decreases activation of macrophages.[4]

The Infectious Disease Society of America recommends TMP-SMX for treatment and prevention of PJP. TMP-SMX is used in patients with AIDS and confers high prophylactic protection against PJP. In addition, patients with moderate-to-severe disease, defined as room air PO_2 <70 mm Hg or PAO_2-PaO_2 ≥35 mm Hg, should receive corticosteroids within 72 hours of starting TMP-SMX.[5] Prophylactic TMP-SMX is not recommended in these other populations.[3] Research regarding infection in non-HIV persons is limited with no guidelines for prophylaxis.

Other studies demonstrate a higher mortality rate in non-HIV patients than those with it.[5] Some identified risk factors in non-HIV patients include cytomegalovirus coinfection, decreased lymphocyte count, invasive ventilation, and pneumothorax during infection.[6] It is helpful than to think of immunodeficiency as a continuum. Other comorbidities such as liver failure and malnutrition may lead to worse immune function than being HIV-positive status alone. More work is needed to understand the differences in mortality between HIV-infected and -noninfected groups. This understanding will help stratify the risk of opportunistic infections in all susceptible individuals.

Like other reported cases, our patient had acute respiratory distress syndrome and severe advanced chronic liver disease. Unlike the others, he was diagnosed with cirrhosis, based on radiological evidence, during the referenced admission. While several of the other patients required corticosteroids because of the severity of their advanced chronic liver disease, our patient was off steroids at the time of PJP diagnosis. Finally, our patient lacked the presence of other coinfections. These distinctions make our case unique from other reported cases.

Our study is limited by lack of research and reporting. There is no standard for diagnosis of PJP in HIV-negative immunocompromised populations, so it is likely underdiagnosed. There is currently no way to stratify levels of immunosuppression in patients with liver disease alone and without concomitant HIV infection. Liver disease is a form of immunodeficiency, and short courses should be taken whenever possible while prescribing corticosteroids. Although this study has shortcomings, we believe it is the largest literature review of HIV-negative patients with PJP secondary to immunosuppression from decompensated liver disease and marks a compelling case for further research.

In conclusion, our case highlights a rare example of PJP in a patient with acute alcoholic hepatitis. It is important for clinicians to recognize the risk of PJP infection in chronic alcohol users and non-HIV immunocompromised patients.

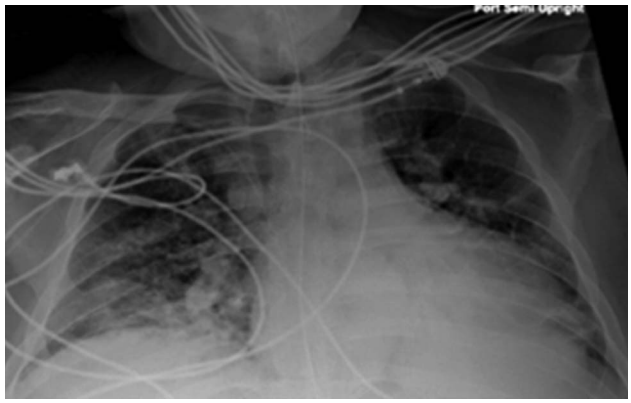

Figure 2. Chest x-ray on day 8 showing resolving infection.

Table 1. Literature review

Author, year	Age, sex (M/F)	Corticosteroid exposure?	Infections	Risk factors besides cirrhosis	Death (Y/N)
Ikawa, 2001[7]	40 yr, M	Y	PJP and CMV	Steroids	Y
Ichai, 2002[8]	2 patients, unknown	Y	PJP and CMV (1 of 2)	HIV, steroids	Y
Faria, 2007[9]	7 patients aged 44–61 yr	Y (6 of 7 cases)	CMV (3 of 7)	n/a	Y (7)
Dodi, 2010[10]	54 yr, F	Y	PJP and CMV	Steroids	Y
Hadfield, 2019[11]	63 yr, M	N	PJP	None	Y
Chung, 2020[12]	43 yr, M	Y	PJP	None	Y
Meyers, 2022[12]	59 yr, M	N	PJP	None	Y
Franceschini, 2023[13]	6 patients, 34–66 yr	Y (2 of 5 cases)	PJP, HBV (1), aspergillosis (2), and CMV (1)	n/a	Y (2), N (6)
Krier, 2023	36 yr	N	PJP	None	N

CMV, cytomegalovirus; HBV, hepatitis B virus.

Additionally, timely therapeutic intervention is warranted because of its high mortality.

DISCLOSURES

Author contributions: Literature search and background: E. Krier and U. Tomczak. Direct patient care: all authors. Drafted manuscript: E. Krier, U. Tomczak, and T. Checketts. Edited and revised manuscript: T. Checketts. Approved final version of manuscript: T. Checketts and S. Chandan. S. Chandan is the article guarantor.

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