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Dual Infection with *Mycobacterium tuberculosis* and *Pneumocystis jiroveci* Lymphadenitis in a Patient with HIV Infection: Case Report and Review of the Literature

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ABSTRACT

We report a case of dual *Mycobacterium tuberculosis* (TB) and *Pneumocystis jiroveci* (*carinii*) (PCP) lymphadenitis in a patient with HIV who had been receiving trimethoprim-sulfamethoxazole (TMP-SMX) as systemic prophylaxis for PCP. This patient was successfully treated with antituberculosis medications and TMP-SMX. Our review of the literature identified this as the first reported case of dual TB and PCP lymphadenitis in an HIV-infected host and highlights the potential limitations of TMP-SMX prophylaxis.

INTRODUCTION

THE HIV PANDEMIC has been accompanied by a dramatic increase in opportunistic infections in this patient population. Despite the availability of combination antiretroviral therapy (ART) and effective opportunistic infection prophylaxis, HIV-related opportunistic infections are prevalent in developing countries where ART access is considerably difficult. In Thailand, the three most common opportunistic infections are tuberculosis, *Pneumocystis jiroveci* (*carinii*) pneumonia (PCP) and cryptococcosis, respectively.[1–3] Reports of extrapulmonary pneumocystosis are relatively rare with an incidence of 0.5%–2.5% in HIV-infected patients.[4,5] The most common reported sites for disseminated pneumocystosis are the spleen, lymph system, and liver. Less common sites include the eye, ear canal, gastrointestinal tract, and skin.[4,5] Concern has been raised that the incidence of extrapulmonary pneumocystosis might increase with continued use of aerosolized pentamidine for prophylaxis, although whether this is an associated risk remains inconclusive.[4,6] We report a case of abdominal lymphadenitis caused by *Mycobacterium tuberculosis* (TB) and PCP coinfection in an HIV-infected patient who had been receiving systemic prophylaxis for PCP. Furthermore, we report a review of the literature on

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PCP lymphadenitis in the HIV-infected population.

CASE REPORT

A 30-year-old woman, diagnosed 1 month earlier with HIV infection was admitted to our hospital with 1 week of intermittent high-grade fever, night sweats, and generalized abdominal pain without nausea, vomiting, or diarrhea. In the initial outpatient work-up, her CD4 count was 61 cells/mm^3 and the HIV RNA was 150,000 copies per milliliter. She was started on GPOvir (stavudine, 30 mg; lamivudine, 150 mg; and nevirapine, 200 mg) every 12 hours and trimethoprim-sulfamethoxazole (TMP-SMX) (160 mg/d of TMP) daily. On presentation to our hospital 1 month later, her temperature was 40°C, heart rate 90 beats per minute, respiratory rate 20 breaths per minute, and blood pressure 110/70 mm Hg. There was generalized abdominal tenderness without guarding or rebound tenderness. Data revealed a normal chest radiograph, total white blood cell count of 12,100/mm^3 (73% neutrophils, 13% lymphocytes, 12% monocytes, and 2% eosinophils), hemoglobin 10.6 g/dL (reference, 12–14 g/dL), aspartate aminotransferase 88 U/L [reference, 15–37 U/L], alanine aminotransferase 55 U/L [reference, 30–65 U/L], alkaline phosphatase of 263 U/L [reference, 50–136 U/L] and lactate dehydrogenase of 335 U/L [reference, 100–190 U/L.]. Serum amylase and lipase were normal. Repeat CD4 count was 61 cells/mm^3 and the HIV RNA was 10^4 copies per milliliter. She reported complete adherence to GPOvir and TMP-SMX and pill counts by our pharmacist confirmed an accurate number of remaining pills. In the initial work-up, a computed tomography (CT) scan of the abdomen showed matted mesenteric and retroperitoneal lymphadenopathy (Fig. 1). A fine-needle aspiration (FNA) of the retroperitoneal lymph nodes was performed and aspirates were submitted for mycobacterial and fungal cultures, histopathology, and polymerase chain reaction (PCR) for PCP. Initial acid fast bacilli (AFB) staining revealed multiple AFB, with negative Gram's and Wright's stains. Other special stains were pending. She was initially treated with isoniazid (5 mg/kg per day), rifampicin (10 mg/kg per day), pyrazinamide (25 mg/kg per day), ethambutol (20 mg/kg per day) and azithromycin (500 mg/day). Because of the potential of drug interaction between rifampicin and nevirapine, the ART regimen was switched to stavudine 30 mg every 12 hours, lamivudine 150 mg every 12 hours and efavirenz 600 mg daily. Two weeks into treatment, she had high fevers, night sweats, and abdominal pain. The Gomeri methenamine silver (GMS) stains from the initial lynph node FNA became available,

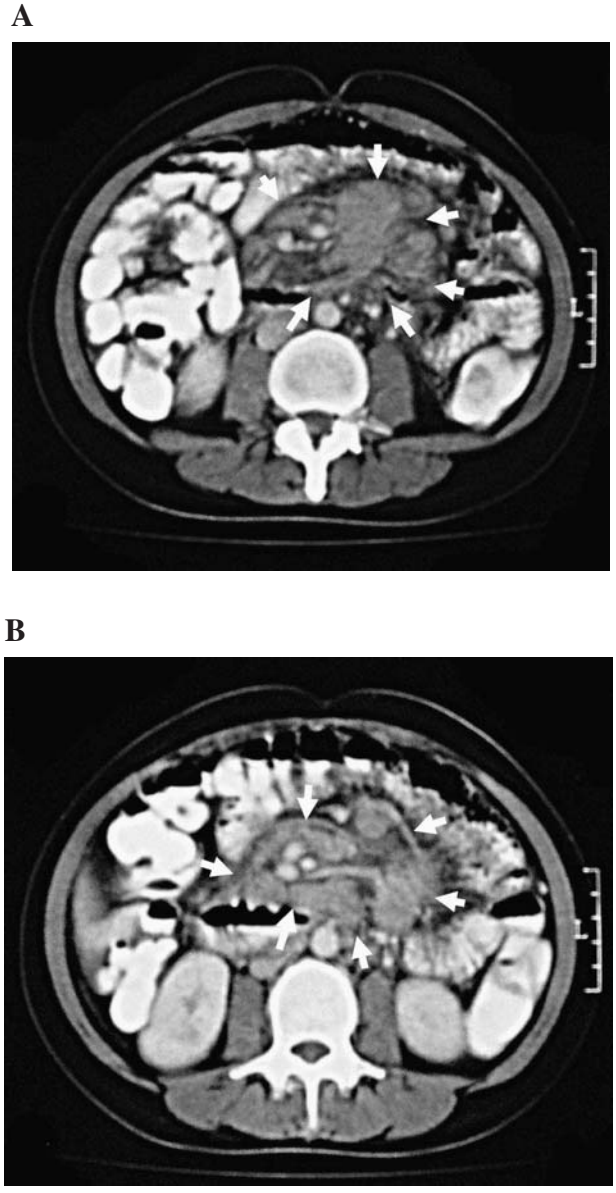

FIG. 1. Abdominal computed tomography of this patient on admission revealed matted mesenteric and retroperitoneal lymph nodes (arrows).

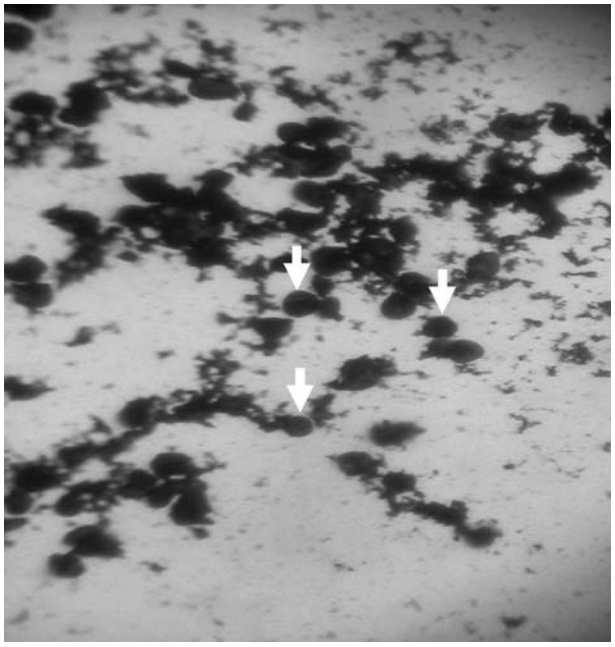

FIG. 2. The cystic forms of *Pneumocystis jiroveci* (arrows) are recognized from the foamy material stained with Gomeri methenamine silver (GMS).

remarkable for multiple PCP cystic forms (Fig. 2) and TMP-SMX (15 mg/kg per day of TMP divided every 6 hours) was initiated. Over the next 4 days, the patient achieved dramatic clinical improvement and was discharged home on isoniazid (5 mg/kg per day), rifampicin (10 mg/kg per day), pyrazinamide (25 mg/kg per day), ethambutol (20 mg/kg per day), TMP-SMX (15 mg/kg per day of TMP) divided every 6 hours, stavudine (300 mg every 12 hours), lamivudine (150 mg every 12 hours), efavirenz (600 mg daily), and azithromycin (500 mg/day). The lymph node aspirate's culture grew *Mycobacterium tuberculosis* susceptible to isoniazid, rifampicin, pyrazinamide, ethambutol, streptomycin, quinolones, and other aminoglycosides. PCR for PCP was positive. Cultures for bacteria and fungi and pathology for malignancy were all negative, and azithromycin was discontinued. At follow-up 6 months after the completion of therapy, there was no evidence of ongoing infection and a repeat CT scan of the abdomen revealed a significant reduction in of the size and amount of intra-abdominal and retroperitoneal lymphadenopathy.

DISCUSSION

Globally, PCP has been the most frequent cause of HIV-related opportunistic infections since the pandemic began; consistently the most common clinical presentation remains pneumonia.[7] In Thailand, where the prevalence of TB is 0.5–2.0 per 1000 population, TB is the most common HIV–related comorbid infection with an incidence of 30%, followed by PCP (20%) and cryptococcosis (15%).[2] Coinfection with TB and PCP has been rarely reported, and when reported, is most often pulmonic.[7] To our knowledge, this case is the first report ¡of dual infection with TB and PCP lymph-

TABLE 1. CLINICAL FEATURES OF PREVIOUSLY PUBLISHED CASES OF *PNEUMOCYSTIS JIROVECI* LYMPHADENITIS AMONG PATIENTS WHO HAD PRIOR HISTORY OF PCP AND THOSE WITHOUT A PRIOR HISTORY OF PCP

Characteristic	*Patients with a prior history of PCP (n = 15)*	*Patients without a prior history of PCP (n = 10)*
Diagnosis of AIDS	15 (100)	10 (100)
Median CD4 counts (cells/mm^3)[a]	19	17
Clinical presentations		
Chest symptoms[b]	7 (47)	4 (40)
Abdominal symptoms[c]	4 (26)	3 (30)
Nonspecific symptoms[d]	2 (13)	2 (20)
Asymptomatic	2 (13)	1 (10)
Survive	3 (20)	2 (20)

Data are number (%) of patients unless noted otherwise.
[a]Data were available for 9 patients.
[b]Including the combinations of fever, cough, chest pain and/or dyspnea.
[c]Including the combinations of fever, abdominal pain, diarrhea, and/or abdominal distention.
[d]Including the combinations of fever, night sweat, weight loss.
PCP, *Pneumocystis jiroveci (carinii)* pneumonia.

adenitis and is most noteworthy given that the patient had been receiving systemic TMP-SMX PCP prophylaxis for the prior 30 days.

The diagnosis in this case was established after FNA, by demonstration of PCP cysts in the aspirated lymph node, and by PCR. Recent studies have identified that the most common infectious causes of lymphadenopathy in HIV-infected patients were TB and *Mycobacteriun avium* complex in 50%–60% of cases; malignancy, mainly lymphoma, Kaposi's sarcoma and PCP comprise the remainder of cases.[8] In dual PCP and HIV infection, the most common extrapulmonary site of PCP is the intrathoracic lymph nodes.[8] PCP presenting as intra-abdominal lymphadenitis, as in our case, has rarely been reported. Autopsy findings suggest that dissemination of the extrapulmonary pneumocystosis has most likely occurred by either direct spread, hematogenously or the lymphatic routes.[9] Furthermore, PCR studies in animal models have shown that extrapulmonary dissemination during the course of pneumocystosis is common.[10]

Atypical extrapulmonary pneumocystosis have been reported with increasing frequency since the onset of HIV/AIDS pandemic and an increased frequency of extrapulmonary pneumocystosis has been noted among users of aerosolized pentamidine.[4] It has been suggested that aerosolized pentamidine distributes locally in the lungs and does not protect against the systemic spread of PCP infection.[8] To date, only two cases of extrapulmonary pneumocystosis have been reported in patients with AIDS who received systemic prophylaxis for PCP with dapsone (100 mg/d) and pyrimethamine (25 mg/d).[8] As the third case, this patient had received TMP-SMX and reported excellent ART and TMP-SMX adherence.

Per our literature review, we identify 24 additional cases of PCP lymphadenitis.[8–29] All cases had the diagnosis of AIDS, had CD4 counts less than 100 cells/μL, and had multiple concurrent infectious sites, including the lung, liver, spleen, kidney, adrenal glands, pituitary, choroid plexus, skin, and bone marrow. The majority of cases had a prior history of PCP (15/25; 60%), and were treated with intravenous pentamidine (8/25; 32%) and TMP-SMX (7/25; 28%). Twelve patients (12/25; 48%) had a prior history of receiving aerosolized pentamidine. Five patients had survived (5/25; 20%). There was no difference in the characteristics among those who had a prior history of PCP and those without a prior history of PCP (Table 1).

As a recognized limitation, we cannot exclude the possibility of existent indolent subclinical PCP infection at the time of TMP-SMX initiation or drug malabsorption due to mesenteric TB. Although the patient developed PCP and TB lymphadenitis within 1 month of initiating ART, because there was delay in immune recovery, noted by the relatively unchanged CD4 count and persistent HIV RNA, immune reconstitution was unlikely.[30]

In summary, coinfection of TB and PCP lymphadenitis in HIV-infected patients is rare. The diagnosis of concurrent infection of these two organisms should be considered for patients who have either one of these infections diagnosed and in whom lack of improvement or clinical deterioration occurs despite appropriate treatment. This report is instructive for clinicians in that atypical presentations of PCP do occur and emphasize the need for further evaluations in persistently ill hosts with advanced HIV infection.

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