



Case report

Cavitary lung lesions caused by *Pneumocystis jirovecii* in setting of common variable immune deficiencyZhenmei Zhang^a, Ryan M. Kern^a, Avni Y. Joshi^b, Vivek N. Iyer^a, Patricio Escalante^{a,*}^a Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, USA^b Division of Pediatric Allergy and Immunology, Mayo Clinic, Rochester, MN, USA

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ABSTRACT

Pneumocystis pneumonia affects immunocompromised hosts. The typical imaging finding is bilateral diffuse ground glass opacities. Here we presented a case of *Pneumocystis* causing biopsy-confirmed cavitary lung lesions in a patient with a predominant B cell defect with common variable immune deficiency.

1. Introduction

Pneumocystis is a ubiquitous pathogen found in the environment and was originally discovered in rodents and thought to be a protozoan. In the 1980s it was reclassified as a fungus [1] and the human form was renamed *Pneumocystis jirovecii* in 1999 [2].

Pneumocystis jirovecii pneumonia (PJP) causes a severe respiratory infection that frequently affects individuals with immunosuppressive conditions, such as patients with acquired immunodeficiency syndrome (AIDS), organ transplantation, or on immunosuppressive agents [3].

The clinical presentation of PJP is different between patients with HIV and those without: HIV infected patients often have a subacute onset of dyspnea, nonproductive cough and low-grade fever. On the other hand, immunocompromised patients without HIV typically have a more acute presentation with significant dyspnea, fever, and chills [4]. Radiographic findings are nonspecific and can range from normal chest radiograph to bilateral pulmonary infiltrates and occasionally multiple cysts of various sizes and shapes [5].

2. Case

A 24 year old man with common variable immune deficiency (CVID) on immunoglobulin infusions and granulomatous lymphocytic interstitial lung disease presented to pulmonary clinic with one month of worsening dyspnea and 20 pound weight loss. He also reported night sweats, fevers and fatigue. He denied recent corticosteroid use. On exam, he was a well-nourished male with normal respiratory effort and no respiratory distress. Crackles were auscultated in both lung fields,

most significant at the bases. There was no cervical, submandibular or supraclavicular lymphadenopathy. Mild tachycardia was also noted. There was significant bilateral finger clubbing. Vital signs demonstrated a pulse of 128/min, blood pressure 95/63, tympanic temperature 39.1 Fahrenheit, and oxygen saturation 87% on room air.

Laboratory studies showed: hemoglobin 12.7 g/dL, platelet $223 \times 10^9/L$, white blood cell $14.9 \times 10^9/L$ with neutrophils $11.74 \times 10^9/L$. Immunoglobulin A was low at 3 (normal range, 61–356 mg/dL), immunoglobulin M was undetectable < 5 (37–286 mg/dL), and immunoglobulin G was normal at 1200 (767–1590 mg/dL), on supplemental IgG therapy. Immunophenotyping showed marginally low CD4⁺ T cell count at 434 (365–1437 cells/mcL) and CD8⁺ T cell count at 649 (199–846 cells/mcL), and deficient CD19⁺ B cell count at 1 (91–409 cells/mcL). Chest computed tomography (CT) without intravenous contrast showed interval development of large indeterminate cavitary mass-like consolidative processes in the central left upper lobe and lingula (Fig. 1), and multifocal cavitary masses and nodules with scattered ground glass opacities in both lungs. There was also interval enlargement of mediastinal, hilar and supraclavicular lymph nodes. The overall picture was concerning for development of lymphoma in the left upper lobe/lingula with concomitant multifocal infection/inflammation changes.

Patient was directly admitted to the hospital and started on broad spectrum antibiotics with intravenous vancomycin, cefepime and metronidazole. Sputum and blood cultures were obtained prior to initiation of antibiotics, and fungal serologies for blastomycosis, histoplasma, cryptococcus and coccidioides, and aspergillus antigen were drawn. He underwent flexible bronchoscopy with bronchoalveolar

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lavage (BAL) with immunocompromised protocol on hospital day 2. The small bronchoscope (Olympus P190) was advanced inside the lingular lung cavity which did not show significant purulent materials and biopsies of the cavity wall were obtained due to a concern of lymphoma or invasive fungal infection (Fig. 2). His BAL studies returned positive for pneumocystis PCR and negative testing for other pathogens and opportunistic infections including aspergillus antigen (galactomannan), legionella antigen PCR, nocardia stain, adenovirus PCR, influenza A and B PCR, respiratory syncytial virus PCR, acid fast smear, and bacterial, fungal and mycobacterial cultures were negative. Nasal swab for methicillin-resistant *Staphylococcus aureus*, blood cultures, urinary antigen for pneumococcus and legionella antigens, serum fungal serologies and HIV testing were also negative. He was started on high dose sulfamethoxazole/trimethoprim therapy with weight based dosing of 20 mg/kg trimethoprim daily with subsequent improvement in his respiratory status, and broad spectrum antibiotics were discontinued on hospital day 4. The biopsy from the mass-like lesion in the lingula showed necrotizing granulomatous inflammation with pneumocystis organism on Grocott methenamine silver (GMS) stain (Fig. 3). He was prescribed 21 days of sulfamethoxazole/trimethoprim therapy with chronic suppression dose afterwards, and did not need supplemental oxygen at time of hospital discharge. He recovered well from his illness at 1 month follow-up after hospital discharge, and follow up chest x-ray at 10 month showed improvement in his pulmonary opacities, probably related to residual pulmonary scarring after recovering from his severe PJP.

3. Discussion

Radiological findings of PJP can be nonspecific. Chest X-ray can be normal or have a variable degree of pulmonary infiltrates [6]. CT is more sensitive than chest X-ray at detecting abnormalities in patients with PJP. The classic findings are bilateral diffuse ground glass opacities and patchy consolidations and early and mid-stage of the disease, which can progress to bilateral diffuse consolidations at late stage [6]. Atypical radiological findings have also been reported, including cysts of variable wall thickness [5] and pneumatoceles [7], both occur more frequently in HIV-positive patients. Rarely, PJP can present as pulmonary nodules or focal masses, which may progress to cavitation [5]. Our patient presented with multiple cavitary lesions with biopsy showing *Pneumocystis* organisms on GMS stain with exuberant granulomatous inflammation, which is a very rare presentation of PJP, especially in HIV-negative patients. One potential limitation in our case report is that BAL cultures were obtained after 1 day of broad spectrum antibiotics which could lower the yield of bacterial culture. However, the possibility of co-existing bacterial co-infection to explain his cavitary lesions seems unlikely because of the initial negative nasal swab for methicillin-resistant *Staphylococcus aureus*, negative blood cultures, negative urinary antigens for bacterial infections, lack of purulent bronchial secretions on bronchoscopy, and successful de-escalation of broad spectrum antibiotics after 4 days of therapy, which will be insufficient to treat severe bacterial pneumonia with cavitary or

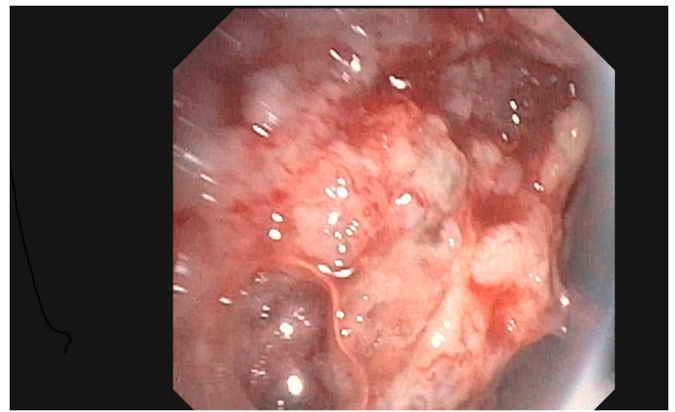


Fig. 2. Bronchoscopic view inside the cavitary lesion in the lingula. This showed an irregular gray appearance inside the cavity and six biopsies were taken.

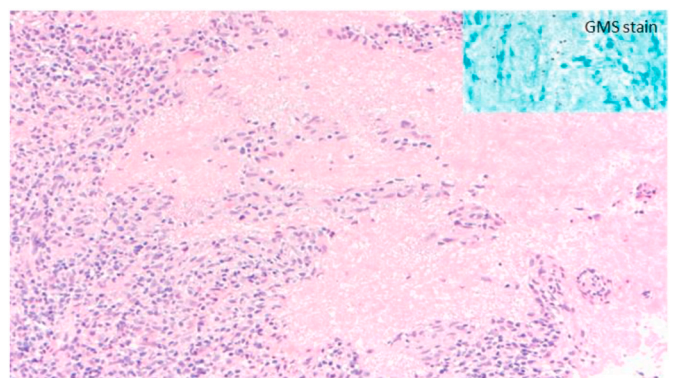


Fig. 3. Exuberant necrotizing granulomatous inflammation associated eosinophilic materials (hematoxylin and eosin stain, 200x original magnification) containing many *Pneumocystis jirovecii* organisms shown by Grocotts Methenamine Silver (GMS) stain (inlet; 400x original magnification).

necrotizing features in an immunosuppressed host. Another interesting aspect in this case is the development of PJP in a patient with CVID. CVID is a heterogeneous group of immune deficiencies characterized by low immunoglobulin levels thought to be secondary to failure in B cell differentiation and in activation of antibody secretion [8]. Common respiratory complications in CVID patients include pneumonia, sinusitis and bronchiectasis [9]. With regards to PJP, there only have been several case reports of patients with CVID and concomitant lymphopenia who were found to have *Pneumocystis* pneumonia [10,11]. However, our patient had a normal serum lymphocyte count, specifically T cell count at time of diagnosis. T cell lymphopenia is one of the most important risk

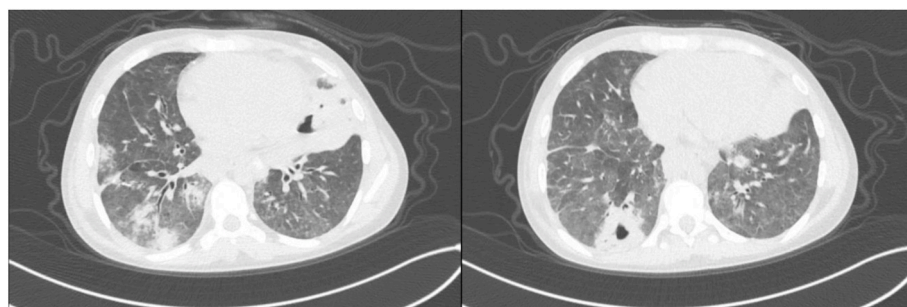


Fig. 1. High resolution chest CT showing multiple cavitary lesions in bilateral lung fields with scattered ground glass opacities in a background of underlying granulomatous lymphocytic interstitial lung disease.

factors for *Pneumocystis* infection because CD4⁺ T cells play an essential role in the clearance of the organisms after inhalation from the environment [3]. CVID is not classically associated with T cell immunodeficiency, but there have been studies showing T cell proliferation and subsequent cytokine release can be affected in CVID patients [8], which might put our patient at increased risk for PJP.

4. Conclusion

In this case, we reported an unusual presentation for PJP, which commonly presents as diffuse, bilateral, ground glass pulmonary infiltrates. On occasion, nodules and masses can develop and evolve into cavitary lesions. It is important to recognize a broad spectrum of possible imaging findings in PJP, especially in immunocompromised hosts. This case also raises awareness of PJP in patients with CVID which is a B cell predominant immune deficiency and is rarely associated with PJP infections.

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Declaration of competing interest

None.

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