Case report

Pneumocystis pneumonia in an immunocompetent patient developing a subacute disease course with central consolidation

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ARTICLE INFO

Keywords:
Central consolidation
Immunocompetent
Pneumocystis jirovecii
Pneumocystis pneumonia

ABSTRACT

Pneumocystis pneumonia (PCP) typically occurs in immunocompromised individuals and rarely presents in immunocompetent individuals. A 55-year-old man was referred to our hospital with cough and anorexia that persisted for 2 months. Chest computed tomography revealed bilateral central consolidation. He was diagnosed with PCP via bronchoscopy. His symptoms and imaging findings improved with the administration of only trimethoprim and sulfamethoxazole. Although he had non-alcoholic fatty liver disease, there were no other complications that could potentially cause immunodeficiency. It should be noted that PCP in immunocompetent individuals can have a subacute disease course presenting with bilateral central consolidation.

1. Introduction

Pneumocystis pneumonia (PCP) is a common opportunistic infection in patients with certain predisposing conditions such as acquired immunodeficiency syndrome (AIDS), underlying malignancies, post-organ transplantation, and use of immunosuppressive medication [1]. Although PCP in patients infected by human immunodeficiency virus (HIV) usually progresses along a subacute disease course, PCP in non-HIV-infected immunocompromised patients is characterized by rapid progression with a higher risk of respiratory failure and higher mortality rate than that observed with PCP in HIV-infected patients [2]. Furthermore, PCP rarely occurs in immunocompetent individuals; such cases are often severe. However, the clinical characteristics of PCP in immunocompetent individuals are unclear.

Herein, we report a case of PCP that had a subacute disease course with central consolidation in an immunocompetent patient.

2. Case presentation

A 55-year-old man was admitted to our institution for the assessment of abnormal chest shadows. He had non-alcoholic fatty liver disease and visited the gastroenterologist regularly. He complained of dry cough, dyspnea on exertion, and anorexia for the preceding
2 months. A chest radiograph revealed bilateral central consolidation (Fig. 1A).

On admission, his vital signs were as follows: blood pressure, 115/96 mmHg; pulse rate, 94 beats/min; respiratory rate, 18 breaths/min; SpO₂, 93% in room air; and body temperature, 36.4 °C. Auscultation revealed fine crackles in the right upper chest at the end of inspiration. Blood examination results revealed that the lymphocyte and serum immunoglobulins were nearly normal, and the anti-HIV antigen/antibody test was negative. Serum Krebs von den Lungen-6 (KL-6) and β-(1,3)-β-D-glucan levels were elevated (4007 pg/mL and 73–109 mg/dL, respectively) (Table 1).

Chest computed tomography (CT) revealed bilateral central consolidation with peripheral sparing, some accompanied by cysts and traction bronchiectasis (Fig. 1B and C). Bronchoscopy performed under mild sedation using midazolam and pethidine without intubation revealed fine cracks in the right upper chest at the end of inspiration. Blood examination results revealed that the lymphocyte and serum immunoglobulins were nearly normal, and the anti-HIV antigen/antibody test was negative. Serum Krebs von den Lungen-6 (KL-6) and (1–3)-β-D-glucan levels were elevated (4007 U/mL and 217.1 pg/mL, respectively) (Table 1).

Chest computed tomography (CT) revealed bilateral central consolidation with peripheral sparing, accompanied by cysts and traction bronchiectasis (Fig. 1B). Bronchoscopy performed under mild sedation using midazolam and pethidine without intubation revealed fine cracks in the right upper chest at the end of inspiration. Blood examination results revealed that the lymphocyte and serum immunoglobulins were nearly normal, and the anti-HIV antigen/antibody test was negative. Serum Krebs von den Lungen-6 (KL-6) and (1–3)-β-D-glucan levels were elevated (4007 U/mL and 217.1 pg/mL, respectively) (Table 1).

The peripheral blood CD4⁺ lymphocyte count was 508/µL. No signs of neoplastic disease were detected during full-body contrast-enhanced CT, ¹⁸F-fluorodeoxyglucose positron emission tomography/CT, upper gastrointestinal endoscopy, and bone marrow puncture. In addition, the patient had no history of recurrent infections or family history of immunodeficiency. Thus, there was no suspicion of primary immunodeficiency or secondary immunodeficiency such as malignancy, HIV infection, or drug-induced immunodeficiency. Therefore, the patient was diagnosed as an immunocompetent patient with PCP. Trimethoprim (960 mg/day) and sulfamethoxazole (4800 mg/day) were administered for 3 weeks without steroids. The patient’s symptoms and chest radiograph findings improved with treatment (Fig. 3). His serum KL-6 and (1–3)-β-D-glucan levels, which were elevated at diagnosis, continued to decrease to normal

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![Fig. 1. Imaging findings on admission. (A) Chest radiograph taken upon admission reveals bilateral central consolidation. (B, C) Chest computed tomography images reveal bilateral central consolidation with peripheral sparing, accompanied by cysts and traction bronchiectasis.](image-url)
ranges after treatment; no recurrence occurred during the 18 months following the discontinuation of trimethoprim and sulfamethoxazole.

3. Discussion

There were three notable clinical findings in this case. First, PCP can occur even in immunocompetent individuals. Second, PCP in immunocompetent individuals can present as central consolidation. Third, PCP in immunocompetent individuals can progress along a subacute disease course and respond well to antibiotic therapy.

PCP can occur in patients without underlying risk factors. Known potential risk factors include low CD4⁺ lymphocyte count (≤200/µL) in HIV infection [2], hematological malignancies, organ transplantation, inflammatory diseases, history of solid tumors, and use of steroids and/or other immunosuppressive drugs [3]. PCP occurring in immunocompetent individuals has been recognized previously, and 14 cases have been reported to date, as shown in Table 2 [4–10].

These previous reports showed no clear clinical features by sex or age that resulted in the onset of immunocompetent PCP. While five cases suggested mild local or systemic immunosuppression, such as chronic obstructive pulmonary disease or diabetes mellitus, another five cases had no underlying disease. Moreover, of the 14 cases, nine cases had acute onset (acute was defined as an onset course of less than 1 month), while two cases had subacute onset (subacute was defined as a course of onset within 3 months), and one case was asymptomatic. In contrast, the other two cases were detected incidentally during examinations of a traumatic injury. None of the patients had a significant decrease in CD4⁺ lymphocyte count (≤200/µL) at the time of diagnosis. Eleven patients were treated with antimicrobial therapy as the initial treatment for bacterial pneumonia. Our patient had no history of smoking or pulmonary disease. Although complications of immunodeficiency might be discovered in the future, they were not evident at the time of this report. PCP can occur in patients without local or systemic immunodeficiency.

Fig. 2. Pathological images of transbronchial lung biopsy (TBLB) specimens. (A) A TBLB specimen of the right upper and lower lobe shows highly granulomatous inflammation infiltrated with inflammatory cells, mainly macrophages, obscuring the alveolar structure (×200, hematoxylin-eosin staining). (B) Accumulation of periodic acid-Schiff-positive foamy eosinophilic material in the alveolar spaces of the TBLB specimen (×400, periodic acid-Schiff staining). (C) A large number of cysts suspected to be Pneumocystis jirovecii are visible within the foamy exudate of the TBLB specimen (×400, Grocott methenamine silver (GMS) stain).

Fig. 3. Chest radiographs taken during and after the course of treatment. Chest radiographs obtained (A) on admission; (B) a week following the administration of trimethoprim and sulfamethoxazole; (C) at the end of the treatment; and (D) 5 weeks following treatment completion.
| No | Report (year) | Age | Sex | Complications and past medical history | Symptoms | Disease course | CD4+ lymphocyte count (/μL) | Radiological findings | Respiratory failure | Initial treatment | Means of diagnosis of PCP | Outcome |
|----|---------------|-----|-----|-----------------------------------------|----------|----------------|-----------------------------|------------------------|-------------------|----------------|---------------------|---------------------|----------|
| 1  | Jacobs et al., 1991 [4] | 78  | F   | Chronic obstructive pulmonary disease, congestive heart failure | A minor trauma | Unknown | 428 | Left pleural effusion, bilateral increased bronchovascular markings | + | Penicillin, vancomycin, and gentamycin | Microscopic visualization of BALF specimen | Died |
| 2  | Jacobs et al., 1991 [4] | 66  | M   | None | Fever, malaise, headache Malaise, lethargy, anorexia | Acute | 347 | Infiltration of the right lower lobe with airbronchogram | + | Erythromycin and cefuroxime | Microscopic visualization of BALF specimen | Survived |
| 3  | Jacobs et al., 1991 [4] | 73  | F   | Diabetes mellitus, asthma, gastritis | Acute | N/A | Diffuse alveolar infiltrate | + | Ceftazidime | Microscopic visualization of BALF specimen | Died |
| 4  | Jacobs et al., 1991 [4] | 78  | F   | Valvular disease of the heart | A traumatic head injury | Unknown | 847 | Pulmonary vascular congestion without focal infiltration | + | Clindamycin and cefuroxime | Microscopic visualization of BALF specimen | Survived |
| 5  | Cano et al., 1993 [5] | 39  | M   | None | Chest pain, fever, dyspnea | Acute | 1755 | Left pleural effusion, bilateral interstitial infiltrate | + | Erythromycin, tobramycin, rifampin, and isoniazid | GMS stain of TNA specimens | Survived |
| 6  | Cano et al., 1993 [5] | 30  | M   | None | Fever, cough, Dyspnea, thoracic pain | Acute | 1080 | Diffuse alveolar infiltrate | + | Erythromycin and tobramycin | GMS stain of BALF specimens | Survived |
| 7  | Cano et al., 1993 [5] | 37  | F   | None | Fever, cough, malaise, dyspnea | Acute | 1176 | Bilateral alveolo-interstitial infiltrate | + | Cefotaxime, erythromycin, and tobramycin | GMS stain of BALF specimens | Survived |
| 8  | Cano et al., 1993 [5] | 37  | M   | Chronic bronchiectasis | Cough, fever, chest pain | Acute | 1220 | Bilateral alveolar infiltrate | Unknown | Erythromycin | GMS stain of TNA specimens | Survived |
| 9  | Cano et al., 1993 [5] | 55  | M   | Chronic obstructive pulmonary disease | Fever, dyspnea | Acute | 1435 | Bilateral alveolar infiltrate in the middle and lower fields | + | Trimethoprim and sulfamethoxazole | GMS stain of induced sputum | Survived |
| 10 | Nejmi et al., 2010 [6] | 21  | F   | None | Dyspnea, cough, sputum | Acute | 1417 | Bilateral alveolo-interstitial infiltrate | + | Amoxicillin and rovamine | GMS stain of BALF specimens | Survived |

(continued on next page)
| No | Report (year) | Age | Sex | Complications and past medical history | Symptoms | Disease course | CD4+ lymphocyte count (/μL) | Radiological findings | Respiratory failure | Initial treatment | Means of diagnosis of PCP | Outcome |
|----|---------------|-----|-----|----------------------------------------|----------|---------------|---------------------------|-----------------------|-------------------|-----------------|--------------------------|--------|
| 11 | Harris et al., 2012 [7] | 51 | M   | Peripheral vascular disease, depression, hepatitis C | None | Asymptomatic | 1510 | A nodule in the right upper lobe | – | Atovaquone | Open lung biopsy | Survived |
| 12 | Koshy et al., 2015 [8] | 56 | M   | Hypertension, diabetes mellitus, tuberculoid leprosy | Cough, dyspnea, hemoptysis | Subacute | 296 | Bilateral ground-glass opacities | – | Treatment for community acquired pneumonia and atypical pneumonia and influenza A | GMS stain of induced sputum | Survived |
| 13 | Ide et al., 2019 [9] | 37 | M   | Right hemiparesis, intellectual disability, symptomatic epilepsy caused by intracerebral hemorrhage | Cough | Acute | N/A | Bilateral airspace consolidation, ground-glass opacities | + | Levofoxacin and corticosteroids | Post-mortem lung biopsy | Died |
| 14 | Olutobi et al., 2020 [10] | 53 | M   | Hypertension, dyslipidemia, gastroesophageal reflux disease | Cough, shortness of breath | Subacute | 759 | Multiple lung nodules, some with central cavitation | – | Trimethoprim and sulfamethoxazole | Pneumocystis jirovecii PCR of BALF | Survived |
| 15 | Present case | 55 | M   | Non-alcoholic fatty liver disease | Dry cough, anorexia | Subacute | 508 | Bilateral central infiltration | – | Trimethoprim and sulfamethoxazole | GMS stain of BALF specimens | Survived |

N/A, not assessed; F, female; M, male; BALF, bronchoalveolar fluid; GMS, Grocott’s methanamine silver; TNA transthoracic needle aspiration.
PCP in immunocompetent individuals can show central consolidation with peripheral sparing on chest CT images. While the radiographic features of PCP are typically bilateral ground-glass opacities (GGOs) [11], our case presented with predominantly central consolidation. In the reported cases of PCP in immunocompetent individuals, image findings were bilateral or localized consolidations or nodular shadows in addition to GGOs (Table 2). Tasaka et al. [12] compared the CT findings of PCP between cases of malignancy and AIDS. In their report, although all cases presented with GGOs, consolidation, in addition to GGOs, were observed more often in cases with malignancy compared to cases with AIDS. Furthermore, Hartel et al. [13] evaluated PCP cases with single or multiple nodules or consolidation and reported that P. jirovecii was present in necrotic or non-necrotic granulomas in most cases. They also reported foam-like neoplasms containing P. jirovecii in intact alveolar spaces in rare cases. In our case, the pathology of the TBLB specimen showed a high degree of inflammatory cell infiltration and granulomas. The relatively preserved host immunity in our case may have promoted granuloma formation for containment, resulting in consolidation. PCP may yield different imaging findings depending on the immunocompetence of the host. Moreover, according to Woon et al.’s review on subpleural sparing in chest CT [14], subpleural sparing patterns are observed in various pulmonary diseases such as nonspecific interstitial pneumonia, pulmonary alveolar proteinosis, inhalational injury, and infections including PCP and coronavirus disease 2019. Although the subpleural sparing pattern is not specific to any disease, it can be an important finding in narrowing the differential diagnoses. In cases with central consolidation and peripheral sparing on chest CT images, PCP with relatively preserved immunocompetence can be considered in the differential diagnosis.

While most PCP in immunocompetent patients develops acutely, this case showed a subacute progression with a good response to treatment. In the existing cases of PCP in immunocompetent individuals, 10 cases among the 14 total cases (71%) presented with respiratory failure, three of which were fatal (Table 2). Generally, PCP in non-HIV-infected immunocompromised patients is more critical than that in HIV-infected patients [15]. Increasing evidence indicates that lung damage occurring during PCP is a result of the extent of the host inflammatory response to P. jirovecii rather than a result of direct damage by P. jirovecii [16]. The symptoms in our patient were of slow onset and were mild with no fever or hypoxemia, although the imaging findings were extensive. Furthermore, the symptoms and imaging findings improved rapidly following the administration of sulfamethoxazole and trimethoprim without steroids. The clinical course in our case was similar to that of PCP in patients with HIV infection. Therefore, the clinical course of PCP in immunocompetent individuals may not be determined by the host’s immunity and is quite diverse. The disease course of PCP in immunocompetent individuals does not always correspond to the host’s immunity; thus, further accumulation of studies and reports involving similar cases is needed.

4. Conclusion

PCP can occur in immunocompetent individuals and has a variable clinical course. It should be borne in mind that PCP in immunocompetent individuals could present as a subacute disease course with central consolidation.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare no conflicts of interest associated with this manuscript.

Acknowledgments

Not applicable.

References

[1] L. Cooley, C. Dendale, J. Wolf, et al., Consensus guidelines for diagnosis, prophylaxis and management of Pneumocystis jirovecii pneumonia in patients with haematological and solid malignancies, Intern. Med. J. 44 (2014) 1350–1363, https://doi.org/10.1111/imj.12599, 2014.
[2] H.J.F. Salzer, G. Schäfer, M. Hoenigl, et al., Clinical, diagnostic, and treatment disparities between HIV-infected and non-HIV-infected immunocompromised patients with Pneumocystis jirovecii pneumonia, Respirion 96 (2018) 52–65, https://doi.org/10.1159/000487713.
[3] Y. Liu, L. Su, S.J. Jiang, H. Qu, Risk factors for mortality from pneumocystis carinii pneumonia (PCP) in non-HIV patients: a meta-analysis, Oncotarget 8 (2017) 59729–59739, https://doi.org/10.18632/oncotarget.19927.
[4] J.L. Jacobs, D.M. Libby, R.A. Winters, et al., A cluster of Pneumocystis carinii pneumonia in adults without predisposing illnesses, N. Engl. J. Med. 324 (1991) 246–250, https://doi.org/10.1056/NEJM199110243240407.
[5] S. Cano, F. Capote, A. Pereira, E. Calderon, J. Castillo, Pneumocystis carinii pneumonia in patients without predisposing illnesses. Acute episode and follow-up of five cases, Chest 104 (1993) 376–381, https://doi.org/10.1378/chest.104.2.376.
[6] H. Nejmi, J. Zlati, A. Tijani, et al., [Pneumocystis jiroveci pneumonia in an immunocompetent female patient], Med. Mal. Infect. 40 (2010) 241–242, https://doi.org/10.1016/j.medmal.2009.08.006.
[7] K. Harris, R. Maroun, M. Chalhoub, D. Elsayegh, Unusual presentation of pneumocystis pneumonia in an immunocompetent patient diagnosed by open lung biopsy, Heart Lung Circ 21 (2012) 221–224, https://doi.org/10.1016/j.hlc.2011.10.006.
[8] J. Koshy, M. John, D. Deodhar, G. Koshy, Pneumocystis jirovecii pneumonia in an immunocompetent host, Ann. Trop. Med. Public Health. 8 (2015) 122–124.
[9] H. Ide, Y. Yamaji, K. Tobino, et al., Pneumocystis jirovecii pneumonia in an immunocompetent Japanese man: a case report and literature review, Case Rep. Pulmonol. 2019 (2019) 224, https://doi.org/10.1155/2019/224.
[10] O. Ojuawo, T. Hwe, O.S. Thien, A. Sahal, Pneumocystis pneumonia causing cavitating lung nodules in an immunocompetent individual, BMJ Case Rep 14 (2021), https://doi.org/10.1136/bcr-2020-241061.
[11] E.M. Carmona, A.H. Limper, Update on the diagnosis and treatment of Pneumocystis pneumonia, Ther. Adv. Respir. Dis. 5 (2011) 41–59, https://doi.org/10.1177/1753465810380102.
[12] S. Tasaka, H. Tokuda, F. Sakai, et al., Comparison of clinical and radiological features of pneumocystis pneumonia between malignancy cases and acquired immunodeficiency syndrome cases: a multicenter study, Intern. Med. 49 (2010) 273–281, https://doi.org/10.2169/internalmedicine.49.2871.

[13] P.H. Hartel, K. Shilo, M. Klassen-Fischer, et al., Granulomatous reaction to pneumocystis jirovecii: clinicopathologic review of 20 cases, Am. J. Surg. Pathol. 34 (2010) 730–734, https://doi.org/10.1097/PAS.0b013e3181d9f16a.

[14] W.H. Chong, B.K. Saha, A. Chopra, et al., The significance of subpleural sparing in CT chest: a state-of-the-art review, Am. J. Med. Sci. 4 (2021) 427–435, https://doi:10.1016/j.amjms.2021.01.008.

[15] S.A. Gilroy, N.J. Bennett, Pneumocystis pneumonia, Semin. Respir. Crit. Care Med. 32 (2011) 775–782, https://doi.org/10.1055/s-0031-1295725.

[16] F. Gigliotti, T.W. Wright, Immunopathogenesis of Pneumocystis carinii pneumonia, Expert Rev. Mol. Med. 7 (2005) 1–16, https://doi.org/10.1017/S1462399405010203.