Pneumocystis jirovecii pneumonia in a patient receiving chemotherapy for advanced prostatic cancer: a case report

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Abstract

Pneumocystis jirovecii pneumonia (PJP) in advanced prostatic cancer patients not receiving high-dose glucocorticoids has been reported rarely. A 73-year-old man underwent chemotherapy with cisplatin and docetaxel for advanced prostatic cancer. After nine cycles of chemotherapy, he developed a high fever, dry cough, shortness of breath, and severe fatigue, with rapid-onset hypoxic respiratory failure. Investigations demonstrated bilateral ground-glass opacities with positive bronchoalveolar lavage fluid (BALF) for Pneumocystis jirovecii by next-generation sequencing (NGS). The patient recovered well with treatment with trimethoprim-sulfamethoxazole, caspofungin, and corticosteroids. This case report describes a case of PJP in a patient with a solid tumor who did not receive high-dose glucocorticoids and emphasizes the importance of early diagnosis and treatment.

Keywords

Pneumocystis jirovecii, trimethoprim-sulfamethoxazole, advanced prostatic cancer, chemotherapy, respiratory failure, ground-glass opacity, bronchoalveolar lavage fluid, next-generation sequencing

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Background

Chemotherapy is associated with improved survival in advanced prostatic cancer and is a dominant treatment for many patients with this cancer.1 In this article, we present a case of Pneumocystis jirovecii pneumonia,
which is a rare complication with an increasing incidence in cancer patients not receiving high-dose glucocorticoids.2

**Case presentation**

A 73-year-old Chinese man who had undergone prostate cancer surgery in 2017 was diagnosed with advanced prostatic cancer with lumbar invasion in 2019. He then began chemotherapy with the docetaxel plus cisplatin (DP) regimen, consisting of docetaxel 120 mg on day 1 and cisplatin 40 mg on days 1 to 3. The cycle was repeated every 21 days. During the chemotherapy, dexamethasone (15.75 mg on days 0–2) was used to prevent drug allergy. The patient completed six cycles of treatment, followed by docetaxel chemotherapy, only, for the next three cycles. Chemotherapy was completed on 21 February 2020. On 7 March 2020, he was admitted to the hospital because of a high fever, dry cough, shortness of breath, and severe fatigue for 8 days.

On examination, the patient was hypoxic, with an oxygen saturation (SpO2) by pulse oximetry of 63% on room air. Arterial blood gas analysis (ABG) indicated type I respiratory failure (arterial partial pressure of oxygen (PaO2): 5.1 kPa; arterial partial pressure of carbon dioxide (PaCO2): 3.81 kPa). Moist crackles were assaulted over both lower lungs. Baseline blood testing demonstrated an elevated C-reactive protein (CRP) concentration of 6.10 μmol/L (reference range: 0–0.40 μmol/L) and a white blood cell count of 9.84 × 10^9 cells/L (reference range: 3.5–9.5 × 10^9 cells/L). Neutrophilia (neutrophil count: 8.57 × 10^9 cells/L, reference range: 1.8–6.3 × 10^9 cells/L) was also observed; however, the lymphocyte count (0.7 × 10^9 cells/L, reference range: 1.1–3.2 × 10^9 cells/L) was lower than the normal range. The cluster of differentiation 4 (CD4+) T cell and B cell counts were decreased at 417 cells/μL and 74 cells/μL, respectively (reference range: 441–2156 cells/μL and 107–698 cells/μL, respectively). In contrast, the CD8+ T cell and natural killer (NK) cell counts were within their normal ranges (383 cells/μL and 117 cells/μL, respectively; reference range: 125–1312 cells/μL and 95–640 cells/μL, respectively). Furthermore, decreased hemoglobin (Hb: 101 g/L, reference range: 130–175 g/L) and elevated lactate dehydrogenase (LDH: 1524 U/L, reference range: 313–618 U/L) concentrations were observed. The result of human immunodeficiency virus (HIV) testing was negative, and the serum 1,3-β-D-glucan concentration was 1.11 × 10^-3 μmol/mL (reference range: <0.62 × 10^-3 μmol/mL). Computed tomography (CT) revealed extensive bilateral ground-glass opacities (GGO), predominantly in the perihilar region, with peripheral sparing (Figure 1). Blood and sputum were collected for pathogen culture. On 9 Mar 2020, after obtaining the patient’s consent for examination and treatment, bronchoscopy was performed, and bronchoalveolar lavage fluid (BALF) was collected for next-generation sequencing (NGS). While awaiting the NGS results, moxifloxacin, meropenem, and caspofungin were commenced empirically because the patient had been admitted to the hospital. In consideration of the possibility of *Pneumocystis jirovecii* pneumonia (PJP), trimethoprim-sulfamethoxazole (TMP-SMX) (0.96 g q6h, orally) was also prescribed. Combination therapy with methylprednisolone and high-flow nasal cannula oxygen therapy (HFNC) was used to alleviate the patient’s respiratory distress.

On 10 March 2020, after 2 days of treatment, the patient’s fever subsided, and his cough and hypoxemia improved gradually. On 11 March 2020, NGS revealed 36 sequence reads specific for *Pneumocystis jirovecii*, 8182 sequence reads specific for *Candida albicans*, and 275 sequence reads specific for human gammaherpesvirus 4 (EBV). On 12 March 2020, sputum
culture was positive for *Candida albicans* (3+). In accordance with these findings, we discontinued meropenem and added acyclovir. On 17 March 2020, after 7 days of treatment, all of the patient’s clinical manifestations disappeared. Additionally, PaO₂ was 9.7 kPa, and the CD4⁺ T cell and B cell counts had increased (490 cells/μL and 100 cells/μL, respectively). Follow-up CT showed significant improvement in the lung findings (Figure 2). Moxifloxacin and acyclovir were discontinued, and the dosage of methylprednisolone was reduced gradually. On 24 March 2020, the patient had an increased body temperature (axillary temperature, >37.5°C), and the CRP concentration and the neutrophil count were elevated (1.53 μmol/L and 6.77 × 10⁹ cells/L, respectively). Latamoxef was used for 3 days; however, the patient’s body temperature remained elevated. A CT scan showed new lung abnormalities on 27 March (Figure 3). Therefore, higher-dose TMP-SMX (1.44 g q8h, orally) plus clindamycin rather than latamoxef was begun. After 2 days, a skin rash was observed on the patient’s back and legs; therefore, we stopped the clindamycin under the suspicion of a drug allergy. Two days later, the patient’s body temperature was normal, and the skin rash had disappeared. The patient continued treatment with TMP-SMX (0.96 g q8h, orally) after discharge on 5 April 2020, which was the 29th day from the onset of symptoms.

Seven days after discharge, the patient had no complaints, and CT showed that all lung infiltrates had resolved.

**Discussion**

*Pneumocystis jirovecii* is found worldwide, with humans being the main reservoir.³ This organism causes pneumonia (*Pneumocystis jirovecii pneumonia, PJP*) in immunocompromised patients.⁴ With effective treatment for HIV, the PJP incidence in HIV patients has decreased. However, the incidence has increased in HIV-negative patients, namely those with innate or

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**Figure 1.** CT images obtained on 7 March 2020 (a–c) The images show extensive bilateral ground-glass opacities, predominantly in the perihilar region, with peripheral sparing. (d) After treatment, resolution of the ground-glass opacities was apparent. a and b: upper lobes, c and d: lower lobes.

CT, computed tomography.
acquired immunosuppression, such as those receiving long-term or high-dose corticosteroids or immunosuppressive treatment (e.g., monoclonal antibody therapy) for autoimmune diseases, those with solid-organ or hematological malignancies receiving hematopoietic stem cell transplantation, and those who have undergone bone marrow or solid-organ transplantation.²

In the current case, we reported an HIV-negative patient with advanced prostatic cancer, diagnosed as having PJP. Some

**Figure 2.** New lung lesions (arrow) in CT images obtained on 27 March 2020. A, anterior; P, posterior. CT, computed tomography.

**Figure 3.** The patient developed a skin rash on his back (left) and leg (right) after beginning clindamycin therapy.
data suggest that malignancy itself can increase the likelihood of PJP.\textsuperscript{5} Previous studies have revealed that the use of corticosteroids in chemotherapy regimens is a major risk factor for developing PJP.\textsuperscript{6} Duarte et al also reported two PJP cases in patients with metastatic prostatic cancer receiving long-term dexamethasone.\textsuperscript{7} Therefore, the risk of PJP increased with the use of dexamethasone in our patient’s treatment for prostatic cancer. Furthermore, decreased CD4\textsuperscript{+} T cell numbers, especially to <200 cells/\mu L, is the most significant risk factor for developing PJP.\textsuperscript{7} Our patient also had a decreased CD4\textsuperscript{+} T cell count, although the count was >200 cells/\mu L (417 cells/\mu L). Another risk factor for PJP is previous or simultaneous cytomegalovirus (CMV) infection. This virus suppresses helper T cell and antigen-presenting cell function, thereby altering the host immune response.\textsuperscript{8} Our patient was CMV-negative according to NGS testing; however, the successful detection of EBV and \textit{Candida albicans} in the BALF revealed immunodeficiency.

PJP in non-HIV patients is characterized by more rapid onset and faster progression of symptoms, which are also more serious, than those in HIV-infected individuals.\textsuperscript{2,8} Patients with non-HIV PJP have more severe hypoxemia than that in those with HIV-PJP. Some reports showed that respiratory failure ensued within 5 to 7 days of symptom onset in non-HIV PJP, thereby requiring a higher oxygen flow and more frequent invasive mechanical ventilation than those in HIV-PJP patients.\textsuperscript{2,9} The time from symptom onset to seeking medical consultation was 21 days for patients with HIV and 5 days for those without HIV, in one study.\textsuperscript{10} In the current case, the time from symptom onset to seeking medical consultation was 8 days. The longer time in our report than that in previous reports may have resulted from the outbreak of coronavirus disease 2019 (COVID-19) in China.

In accordance with a previous study,\textsuperscript{11} we also found that the serum level of LDH was elevated in our patient. This can be explained by the adhesion of \textit{P. jirovecii} to the surface alveolar epithelium of type I alveolar cells, which could cause lung injury and further cause the release of LDH.\textsuperscript{3} CT is the most reliable imaging technique for the diagnosis of PJP and monitoring the effects of therapy. PJP shows a variety of presentations with CT, among which, extensive GGO is the main feature.\textsuperscript{12} The distribution of GGO is usually symmetrical, and GGO appear predominantly in the perihilar region and the apices, with peripheral sparing.\textsuperscript{12} The typical clinical manifestations and imaging features can provide clues for the diagnosis of PJP. It should be noted in particular that COVID-19 infection was considered a differential diagnosis in this patient, and the history of a lack of contact with COVID-19 patients helped rule out this diagnosis. Historically, a diagnosis of PJP relied on the visualization of cysts or trophic forms in respiratory material; however, cysts and trophic forms are low in numbers in non-HIV-infected patients owing to the lower fungal load.\textsuperscript{13} Based on this finding, some doctors use polymerase chain reaction (PCR) testing or LDH measurement plus 1,3-\beta-D-glucan evaluation to improve the diagnostic rate of PJP.\textsuperscript{14-17} The most attractive technique may be NGS because of the higher sensitivity.\textsuperscript{18} In our case, the elevated 1,3-\beta-D-glucan concentration and the NGS results confirmed the diagnosis of PJP.

Treatment for PJP should be initiated when symptomatology and diagnostic evidence conclude that \textit{P. jirovecii} is the likely causative pathogen.\textsuperscript{3} TMP-SMX is used as a first-line treatment for PJP. The recommended strength for treatment in both adults and children is 15 to 25 mg/kg/d (based on the TMP component), orally or intravenously (IV), divided into 3 to 4 doses per day, for 21 days.\textsuperscript{3,4,19} Echinocandins,
and caspofungin in particular, can be used as salvage therapy.\textsuperscript{20,21} In our case, TMP-SMX plus caspofungin was used for the \textit{Candida albicans} infection as well as for the \textit{P. jirovecii} infection. Corticosteroids were also used to increase the success of treatment. In contrast to the treatment in our case, Fujikura et al considered that corticosteroids did not affect mortality in non-HIV patients and that there was no beneficial effect in patients with severe hypoxemia (PaO\textsubscript{2} < 70 mmHg), after analyzing seven observational studies.\textsuperscript{22} Other PJP treatment options are dapsone plus TMP, clindamycin plus primaquine, and atovaquone and pentamidine.\textsuperscript{13} It should be emphasized that prolonged therapy is required, and TMP-SMX must be used earlier, as prophylaxis, in high-risk groups. However, when to start and how long to continue TMP-SMX for prophylaxis in non-HIV patients requires more study. Additionally, determining why our patient experienced a relapse is yet to be revealed.

In conclusion, PJP is a rare but fatal disease in immunodeficient patients. Early diagnosis and effective treatment can reduce the mortality rate.

The reporting of this study conforms to the CARE guidelines.\textsuperscript{23}

**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Authors’ contributions**

Chen Tiantian analyzed the patient’s data and was a major contributor to writing the manuscript. Jin Xiaoyan designed the study. Yan Jin, Zhang Jing, Feng Jing, and Jin Xiaoyan revised the article. All authors read and approved the final manuscript.

**Ethics statement**

This study protocol was not approved by an ethics review committee because this was a retrospective study, and treatment of this patient was approved by the patient. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Declaration of conflicting interest**

The authors declare that there is no conflict of interest.

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