Spontaneous Resolution of *Pneumocystis jirovecii* Pneumonia on High-Resolution Computed Tomography in a Patient with Renal Cell Carcinoma

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Conflict of interest: None declared

**Patient:** Male, 59  
**Final Diagnosis:** *Pneumocystis jirovecii* pneumonia

**Symptoms:** Low grade fever  
**Medication:** —  
**Clinical Procedure:** Transbronchial lung biopsy  
**Specialty:** Pulmonology

**Objective:** Rare disease  
**Background:** A 59-year-old man presented to our hospital because of pyrexia (38°C) and shaking chills for 2 days. He had a history of right nephrectomy due to renal cell carcinoma and left upper lobectomy for lung metastasis in the last 1.5 years. Two months previously, he was treated with oral prednisolone (20 mg/day) plus the intravenous mTOR inhibitor, temsirolimus (25 mg/week), for brain metastasis. On radiological examination, thoracic computed tomography showed diffuse ground glass opacities spreading in bilateral middle to lower lung fields. Although transbronchial biopsy specimens and bronchoalveolar lavage fluid demonstrated the presence of accumulation of black-colored *Pneumocystis jirovecii* cysts in the lung, his chief complaints and radiological abnormalities disappeared completely with no treatment. This case demonstrates a unique clinical presentation of *Pneumocystis jirovecii* pneumonia, in that spontaneous resolution was noted on clinical and sequential radiological evaluations.

**Conclusions:** Increasing numbers of cytotoxic drugs and biological therapies have emerged, and changes in the immune status due to underlying diseases or administration of immunosuppressive drugs might affect the inflammatory process of *Pneumocystis jirovecii* pneumonia, as in the present case.

**MeSH keywords:** Multidetector Computed Tomography • *Pneumocystis jirovecii* • Remission, Spontaneous

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Background

In general, *P. jirovecii* pneumonia (PJP) occurs in patients with human immunodeficiency virus (HIV) infection, hematological malignancies, solid tumors, collagen vascular diseases, organ transplantation, and immunosuppressive therapies. Spontaneous resolution of PJP has rarely been reported [1–8]. Furthermore, no report has demonstrated complete resolution of PJP on thoracic computed tomography (CT). The present case had a unique clinical presentation in that thoracic CT provided the first evidence of complete resolution of lung involvement, along with symptom resolution, without specific treatment for PJP.

Case Report

A 59-year-old man was admitted to our respiratory department (Day 1) with chief complaints of pyrexia (38°C) and shaking chills for 2 days. He had a history of right nephrectomy for renal cell carcinoma 1.5 years earlier. One year earlier, left upper lobectomy was performed for lung metastasis. He had then been in good health up to 2 months earlier, when brain metastasis was treated sequentially with oral prednisolone (20 mg/day) plus the intravenous mTOR inhibitor, temsirolimus (25 mg/week). He had been treated for essential hypertension, type 2 diabetes mellitus, and hyperlipidemia since the previous year. On initial examination, he appeared well; vital signs and physical examination were normal except for a low-grade fever (37.6°C). His serum laboratory examinations showed a normal white blood cell count of 5900/μL (differential: neutrophils, 90%; lymphocytes, 6.0%; monocytes, 3.5%) and mild elevations of lactate dehydrogenase (412 IU/L) and C-reactive protein (1.8 mg/dL). Furthermore, marked elevations of KL-6 (10,584 U/mL) and (1→3)-β-D-glucan (491 pg/mL) (Wako Pure Chemical Industries; Tokyo, Japan) were recognized, but no anti-human immunodeficiency antibodies were detected. The chest X-ray (Figure 1A) on Day 1 showed faint infiltration in bilateral middle to lower lung fields with surgical scars in the left hilar portion. This was confirmed by thoracic computed tomography (CT) (Figure 1B), which demonstrated diffuse ground glass opacities (GGO) spreading in bilateral middle to lower lung fields. With no treatment, defervescence was noted within 24 h, accompanied by disappearance of shaking chills. Based on the tentative diagnosis of drug-induced pneumonia due to temsirolimus or interstitial pneumonia, the patient underwent transbronchial lung biopsy (TBLB) and bronchoalveolar lavage on Day 4, and he was discharged the following day. Eight days after discharge, chest X-ray (Figure 1C) and thoracic CT (Figure 1D) showed complete resolution of GGO; however, transbronchial lung biopsy specimens at the right middle lobe bronchus (B4a) and the right lower lobe bronchus (B8), and BALF obtained from right B4a, revealed accumulation of black-colored *Pneumocystis jirovecii* cysts in the lung on Grocott's methenamine silver stain, as well as a positive result for *P. jirovecii* DNA. Bronchoalveolar lavage fluid (BALF) analysis showed an increased total cell count (4.6×10³/μL), with 5% neutrophils, 22% macrophages, and 73% lymphocytes, and a CD4 to CD8 ratio of 1.04, suggesting a mild, chronic inflammatory reaction in the lung. Thus, the diagnosis was *P. jirovecii* pneumonia (PJP), showing spontaneous clinical and radiological resolution within 3 weeks of initial onset. Although the patient’s clinical condition was good, he was treated with oral trimethoprim/sulfamethoxazole for 2 weeks as an outpatient. Despite resolution of his lung involvement, he died of brain metastasis 8 months later.

Discussion

In general, PJP occurs in patients with human immunodeficiency virus (HIV) infection, hematological malignancies, solid tumors, collagen vascular diseases, organ transplantation, and immunosuppressive therapies (such as prednisolone or other cytotoxic agents). In non-HIV patients, Neumann et al. [9] reported that acute lymphoid leukemia, prolonged CD4 <200/µL, and long-term steroids are strongly associated with an increased risk for PJP, while Fillatre et al. [10] reported that, in a total of 154 patients, PJP was associated with hematological malignancies (32.5%), solid tumors (18.2%), inflammatory diseases (14.9%), solid organ transplant (12.3%), and vasculitis (9.7%). Regarding the present patient’s immune status, he had impaired cellular immunity because of steroid treatment. This immune deficiency was confirmed by the mild, chronic inflammatory reactions in the lung despite the presence of many *P. jirovecii* cysts. Of note, the present case had a unique clinical presentation in that thoracic CT provided the first evidence of complete resolution of lung involvement, along with symptom resolution, without specific treatment for PJP. The resolution of lung involvement and the paucity of lung inflammation might reflect changes in the patient’s immune status due to recurrence of renal cell cancer or steroid treatment.

With respect to pulmonary toxicity with temsirolimus, a phase II study by Yan et al. [11] showed that serious adverse effects, such as pneumonia, occurred in more than 5% of patients, and 7% of patients had interstitial lung disease. Lacovelli et al. [12] reported that pulmonary toxicity associated with mTOR inhibitors, including temsirolimus, was recognized in 10% of treated patients, and the toxicity was mild. Thus, mild to severe pulmonary toxicity of temsirolimus is seen in approximately 10% of patients, which was a reason why we performed bronchoscopy with a tentative diagnosis of drug-induced pneumonia. Despite this evidence of pulmonary toxicity associated with temsirolimus, to the best of our knowledge, there have been...
no reports of the correlation between the risk of PJP and temsirolimus treatment.

Previous reports noted that *P. jirovecii* colonization is highly prevalent in the autopsied lungs of the general population [13]. Therefore, the clinical distinction between colonization and infection among immunocompromised non-HIV patients seems to be quite difficult because of their immune fluctuation associated with chemotherapy, corticosteroids, and other immunosuppressive drugs. However, Roux et al. demonstrated that the Fungilet test® showed a high sensitivity (94.8%) and specificity (86.3%), and the positive and negative likelihood ratios were 6.9, and 0.06, respectively, for the diagnosis of PJP with a threshold set between 80 and 100 mg/μL [14]. Indeed, the present case showed a marked elevation of β-D-glucan (491 pg/mL), together with elevations of KL-6 and LDH, suggesting infection rather than colonization [15,16]. Furthermore, our patient had renal cancer and was on corticosteroid therapy, receiving more than 20 mg/day for more than 4 weeks; primary prophylaxis for PJP is highly recommended in such cases [17].

To the best of our knowledge, only 9 cases with spontaneous resolution have been reported in patients with chronic lymphocytic leukemia, [1] chronic myeloid leukemia, [2] no underlying disease, [3] acute lymphocytic leukemia, [4] acquired immune deficiency syndrome, [5] interstitial pneumonia [6], smoldering adult T cell leukemia [7], and renal transplantation and retroperitoneal fibrosis [8]. In these ten patients, including the present case (Table 1), non-specific symptoms such as fever, dry cough, and shortness of breath were noted. Regarding auscultatory findings, available data were collected from 9 patients, excluding 1 case [5]. Five patients [1–3,6,7] had fine crackles,
but the other 4 patients (cases [4,8], and the present case) had none, which means that a lack of crackles did not rule out the possibility of PJP [18]. Importantly, the time from initial onset to admission and the time required from admission to diagnosis ranged from 2 to 34 days and from 8 to beyond 60 days, respectively, which suggests an indolent clinical course, as in HIV patients [19,20]. In general, PJP in non-HIV patients occurs most often in an acute or subacute form, with profound hypoxemia, and it is poorly tolerated. Especially in PJP patients with cancer (ALL, non-Hodgkin lymphoma, severe combined immune deficiency, rhabdomyosarcoma, solid tumor on steroid treatment), posttransplant, and/or collagen vascular diseases, rapid clinical deterioration is seen within 5 days [19]. Furthermore, 7 of 10 cases (cases [2,4,6–8], and the present case), demonstrated spontaneous resolution of lung involvement at the time of diagnosis, and the other 3 cases [1,3,5] required a further 3 weeks after diagnosis. Two of 10 cases [1,5] had recurrent episodes of PJP, and 1 patient died in a second episode [1]. In this regard, although complete resolution of lung lesions was noted without specific treatment for PJP, the patient was treated with oral trimethoprim/ sulfamethoxazole, as was another case [4].

Conclusions

In the modern era, an increasing number of cytotoxic drugs and biological therapies have emerged, and changes in the immune status due to underlying diseases or administration of immunosuppressive drugs might affect the inflammatory process of PJP, as in the present case.

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Table 1. Eight cases of the PCP with spontaneous resolution.

| Age | Sex | Underlying disease | Initial symptoms | Clinical findings | DIOA | RTAD | Diagnostic methods | Prognosis | Ref. |
|-----|-----|-------------------|------------------|------------------|------|------|-------------------|----------|-----|
| 53  | M   | CML               | Shortness of breath, cyanosis, fever | Wheezes, rales   | 30   | 18   | Open lung biopsy   | Dead     | [1] |
| 53  | F   | CLL               | Fever, dyspnea, cough | Rales | 18   | 60> | Open lung biopsy   | Alive    | [2] |
| 5   | F   | none              | Cough, fever, cyanosis | Rales, rhonchi   | 34   | N.A. | Open lung biopsy   | Alive    | [3] |
| 8   | F   | ALL               | Fever, shaking chills, cough, lethargy | No rales | 3   | 18   | Open lung biopsy   | Alive    | [4] |
| 33  | M   | HIV, HTLV-1       | Chest pain, SOB, fever, weight loss | N.A. | 16   | 8>  | TBLB               | Alive    | [5] |
| 63  | M   | IIP               | Cough, SOB         | Fine cracks      | N.A. | N.A. | BAL                | Alive    | [6] |
| 58  | F   | HTLV-1            | Fever, cough, SOB  | Fine cracks      | 30   | 13   | BAL, TBLB          | Alive    | [7] |
| 31  | M   | Renal transplantation | Fever, cough     | Normal           | 14   | N.A. | BAL                | Alive    | [8] |
| 78  | F   | Retroperitoneal fibrosis | Cough             | Normal           | 14   | N.A. | BAL                | Alive    | [8] |
| 59  | M   | RCC, HT, HL NIDDM type2 | Fever, shaking chills | No rales | 2   | 11   | BAL, TBLB          | Alive     | Our case |

ABX = antibiotics; ALL = acute lymphoblastic leukemia; BAL = bronchoalveolar lavage fluid; CML = chronic myeloid leukemia; CLL = chronic lymphoid leukemia; DIOA = duration from initial onset to admission; RTAD = requiring time from admission to diagnosis; HIV = human immunodeficiency virus; HT = hypertension; HTLV-1 = Human T-lymphotropic virus Type 1; HL = hyperlipidemia; IIP = idiopathic interstitial pneumonia; N.A. = not available; NIDDM = non insulin dependent diabetes mellitus; RCC = renal cell carcinoma; SOB = short of breath; TBLB = transbronchial lung biopsy; Ref. = reference.
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