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CASE STUDY

# FUNGAL COMPLICATIONS IN A PATIENT UNDERGOING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Tables: 1

Figures: 1

References: 11

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**Summary**

Hematologic oncology patients are particularly susceptible to infections due to immunosuppression caused by both the cancer itself and the treatment used. This patient group often experiences infectious complications of bacterial, viral, and fungal etiology. One of the pathogens responsible for pneumonia, especially in individuals with profound immunosuppression, is *Pneumocystis jirovecii* (PCJ), a fungus that produces cysts detectable in bronchial washings or sputum. This infection most commonly affects patients with HIV; however, it can also occur in individuals with hematologic diseases treated with the VTD regimen (bortezomib, thalidomide, and dexamethasone), who achieved partial response (PR) and subsequently underwent autologous hematopoietic cell transplantation (auto-HCT) as consolidation therapy. The transplantation was uneventful; however, during post-chemotherapy bone marrow aplasia, the patient developed febrile neutropenia. Empiric broad-spectrum antibiotic therapy was initiated. Blood cultures were negative, but a sputum sample revealed PCJ cysts. Despite initial respiratory colonization status, therapeutic doses of trimethoprim-sulfamethoxazole (TMP-SMX) were administered due to persistent cough and high risk of severe complications. Early detection of cysts and therapeutic TMP-SMX administration prevented full-blown *PCJ* pneumonia , underscoring prophylaxis effectiveness in severely immunocompromised patients.

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**Keywords:** TMP-SMX prophylaxis, *Pneumocystis jirovecii* pneumonia, autologous hematopoietic stem cell transplantation, multiple myeloma, immunosuppression

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## Introduction

*Pneumocystis jirovecii* (PCJ) is an opportunistic fungal pathogen responsible for pneumonia, primarily affecting immunocompromised patients, and often leading to a severe clinical course. High-risk groups include individuals with HIV infection, hematologic malignancies, and those receiving immunosuppressive therapies, such as chemotherapy or hematopoietic stem cell transplantation (HSCT) [1,2]. Among hematologic patients, those who have undergone HSCT—particularly allogeneic HSCT—face an elevated risk of PCJ pneumonia due to the profound immune suppression associated with induction therapy, graft-versus-host disease (GVHD), and prolonged neutropenia [3,4].

Recent studies indicate that PCJ pneumonia is more prevalent in allogeneic HSCT recipients than in those receiving autologous HSCT, although both groups remain at risk, particularly in the absence of prophylaxis [5]. Early symptoms of PCJ infection, including fever, cough, and dyspnea, are nonspecific, which can delay diagnosis. The pathogen predominantly colonizes the alveolar epithelium, forming cystic structures detectable in sputum samples or bronchoalveolar lavage (BAL) fluid [6]. If untreated, PCJ pneumonia can progress, leading to diffuse alveolar damage (DAD) and, in severe cases, acute respiratory distress syndrome (ARDS), which carries a high mortality risk [7].

The diagnostic challenges associated with PCJ pneumonia have historically made early detection difficult. However, real-time PCR (rt-PCR) assays have demonstrated high sensitivity and specificity, surpassing traditional microscopy-based methods [8,9]. Imaging techniques, particularly high-resolution CT scans showing ground-glass opacities, also contribute to early diagnosis [10]. In suspected cases, early detection and prompt initiation of appropriate treatment are crucial to improving clinical outcomes [11].

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The aim of this study was to trace the course of PCJ infection in a hematologic oncology patient and analyze the therapeutic interventions implemented to minimize the risk of health complications.

**Case description**

A 41-year-old male without significant comorbidities, diagnosed with IgG kappa multiple myeloma, stage I (Durie-Salmon classification, ISS), underwent induction therapy (VTD regimen: bortezomib, thalidomide, dexamethasone), achieving partial response (PR). He then underwent auto-HCT as consolidation therapy.

After excluding active disease and multidrug-resistant pathogens, intravenous melphalan (200 mg/m²) was administered, followed three days later by stem cell transplantation. The procedure proceeded uneventfully. Granulocyte Colony-Stimulating Factor (G-CSF) prophylaxis was initiated from day +3 to +17 post-transplant. During bone marrow aplasia, the patient required three platelet transfusions (five units each). On day +5, the patient was diagnosed with neutropenic fever (38.3°C), without other signs of infection. The patient showed no signs of septic shock. Procalcitonin (PCT) was 0.341 ng/ml (normal: <0.5 ng/ml).

Due to the rapid increase in C-reactive protein (CRP) levels (from 124.24 mg/L to 261.68 mg/L; normal: <8 mg/L) (Figure 1) and persistent fever >38°C, the patient was started on empiric intravenous antibiotic therapy with meropenem (1 g) and amikacin (1 g/4 ml), later adding vancomycin (1g IV). Antibiotic therapy was continued for 13 days.

In the following days, the patient's condition improved, and the fever resolved. CRP levels showed a downward trend, decreasing from 261.68 mg/L to 61.66 mg/L (Figure 1).

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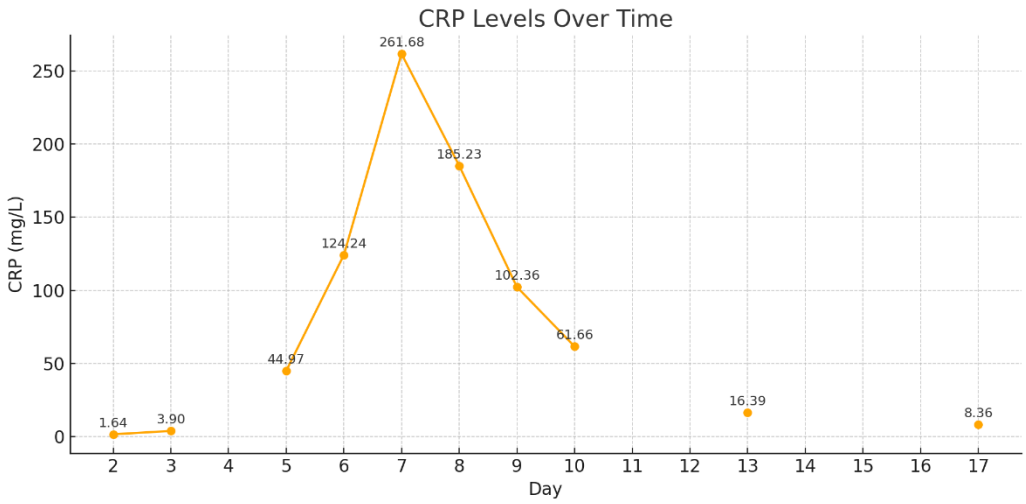


**Figure 1.** Changes in serum C-reactive protein levels in the patient during hospitalization

Notes: The transplant procedure is marked as day (0).

Control blood cultures and sputum cultures were ordered. No bacteremia/fungemia was detected; however, PCJ cysts were identified in the sputum. A carrier state was identified in the patient, and prophylactic treatment of TMP-SMX was initiated in a dosage of 960 mg, 1 tablet twice a day, two days a week due to persistent cough and high risk of complications. The fever resolved, and chest X-rays showed no abnormalities. A high-resolution CT was not performed.

As a result of previous broad-spectrum antibiotic therapy and the use of TMP-SMX, the patient stopped experiencing fever, with no clinical signs of respiratory system involvement. Three chest X-rays were performed during treatment, all of which showed no pathological changes. At discharge, follow-up tests of lower respiratory tract samples for PCJ showed negative results. In the following days of hospitalization, the patient did not develop any respiratory tract infection symptoms.

After 24 days of hospitalization when hematopoiesis had recovered (Table 1), the patient was discharged in good condition with a recommendation to continue prophylactic TMP-SMX (960 mg, 1 tablet twice a day, two days a week).

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**Table 1.** Hematologic parameters during aplasia and after recovery

| Morphological parameters | Bone marrow aplasia (10^3/mm$^3$) | Hemopoiesis regeneration (10^3/mm$^3$) |
|---|---|---|
| **WBCPE** | 0.1 | 4.2 |
| **PLTPE** | 44 | 32 |
| **LYMPEN** | 0.02 | 0.66 |
| **MONPEN** | 0.01 | 1.70 |
| **NEUPEN** | 0.01 | 1.71 |

Notes: Labels and measurement units have been standardized (e.g. WBC [10^3/mm^3]).

The patient was also informed that in the event of life-threatening symptoms, such as shortness of breath or fainting, he should immediately go to the nearest emergency department and have blood tests (including CRP) and other necessary diagnostics performed. The patient adhered to the prescribed prophylaxis and did not experience respiratory infections during subsequent follow-up visits.

## Case analysis

Multiple myeloma (MM) is a hematologic malignancy characterized by monoclonal plasma cell proliferation, leading to immunosuppression and a higher risk of opportunistic infections, including PCJ pneumonia. The combination of high-dose chemotherapy and hematopoietic stem cell transplantation (HSCT) further exacerbates immune suppression, making these patients particularly vulnerable to severe infections [1,2].

Febrile neutropenia (FN) is one of the most common complications following HSCT, necessitating empirical broad-spectrum antibiotic therapy as a standard management approach. However, given the high incidence of secondary fungal infections, additional prophylactic strategies are crucial [3]. PCJ is a rare but serious fungal pathogen in this

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population, and its incidence remains particularly high in patients undergoing allogeneic HSCT compared to autologous HSCT [4].

Prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) remains the gold standard for preventing PCJ pneumonia in HSCT and hematology patients. Recent studies have demonstrated that intermittent, low-dose TMP-SMX regimens provide effective prophylaxis while reducing toxicity compared to daily high-dose regimens [5]. The case presented in this study supports these findings, as intermittent TMP-SMX prophylaxis successfully prevented PCJ progression without notable adverse effects.

Advancements in PCJ pneumonia diagnostics have significantly improved early detection rates. Real-time PCR (rt-PCR) has replaced traditional staining techniques as the preferred diagnostic tool, offering superior sensitivity and specificity; however, microscopical detection is still diagnostically bonding [6,7]. Additionally, high-resolution CT scans have emerged as a critical component in PCJ pneumonia diagnosis, often revealing characteristic ground-glass opacities even before microbiological confirmation [8,9].

A recent meta-analysis on PCJ prophylaxis in HSCT patients confirmed that TMP-SMX reduces PCJ pneumonia incidence by over 80% compared to non-prophylaxed patients [10]. Alternative agents, including atovaquone and inhaled pentamidine, are considered in TMP-SMX-intolerant individuals, though their efficacy remains inferior [11].

Despite being uncommon in autologous HSCT patients, PCJ pneumonia continues to pose a significant risk.

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## Conclusions

Early diagnosis and implementation of appropriate treatment helped prevent severe fungal infections, such as PCJ pneumonia. The use of prophylactic TMP-SMX therapy was

effective in reducing the risk of developing full-blown infection, emphasizing the importance of this medication in the prevention of fungal infections in patients with deep immunosuppression. In high-risk patients, it is always essential to rule out fungal infections, as early diagnosis significantly reduces the risk of complications.

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