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# PNEUMOCYSTIS PNEUMONIA DURING POSTOPERATIVE ADJUVANT CHEMOTHERAPY FOR EARLY BREAST CANCER: A CASE REPORT

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**ABSTRACT**
We describe a case of pneumocystis pneumonia in a 47-year-old Taiwanese woman who received postoperative adjuvant chemotherapy for early breast cancer. She was successfully treated with oral trimethroprim-sulfamethoxazole (TMP/SMX). To the best of our knowledge, this is the first report of definite diagnosis of Pneumocystis pneumonia during adjuvant chemotherapy for early breast cancer and recovered by adequate therapy.

## INTRODUCTION

*Pneumocystis* pneumonia (PCP) is caused by Pneumocystis jirovecii [1]. It is recognized as a fungal organism based on phylogenetic analysis of Pneumocystis 16S-like rRNA [2]. PCP is one of the leading causes of opportunistic infection in patients with acquired immunodeficiency syndrome (AIDS) [3]. But it can also occur in patients with cancer receiving chemotherapy, particularly in those with hematologic malignancies such as leukemia or lymphoma and is less common in patients with solid tumors [4]. Here, we describe the case of *Pneumocystis* pneumonia during adjuvant chemotherapy for early breast cancer. She was successfully treated with medical management.

## CASE REPORT

A 47-year-old woman was admitted because of fever and shortness of breath.

The patient, who was an office worker, had a history of invasive ductal carcinoma of the right breast, stage T1cN0M0, grade 2 of 3, estrogen-receptor–positive and HER2-negative. She underwent a mastectomy for right breast cancer four months before admission. She had received the fifth cycle of adjuvant chemotherapy with fluorouacil, 400 mg/m$^2$, doxorubicin, 40 mg/m$^2$, and cyclophosphamide, 400 mg/m$^2$, (FAC regimen) 19 days before admission. She had been well until four days earlier, when she began to have fever and dyspnea. She had no other symptom, except for mild headache, which she attributed to fever. She did not have cough, orthopnea, edematous legs, night sweats, weight fluctuations, pain of any kind, nausea, vomiting, urinary problem, rashes or joint problems.

She had no known allergies. She did not smoke cigarettes, drink alcohol or use illicit drugs. There was no

travel history during the previous three months. There was no family history of cancer or autoimmune diseases. On examination, her body temperature was 38.6°C. The pulse was 100 beats per minute and regular, the blood pressure 122/68 mmHg, the respiratory rate 22 breaths per minute and labored, and the oxygen saturation 97 percent while the patient was breathing ambient air. The physical examination revealed faint crackles in both lungs and the remainder of the examination was normal. The lab study showed leukopenia (WBC: 3300/uL, segment: 57%, lymphocyte: 19%) and mildly elevated C-reactive protein (CRP: 2.56 mg/dL, reference range: < 0.5mg/dL). The tests of platelet count, serum creatinine and alanine aminotransferase were normal. Chest radiography showed ground-glass appearance in bilateral upper lung field (Figure 1). On hospital day 1, levofloxacin 750mg a day was prescribed intravenously.

During the first three hospital days, the fever and dyspnea persisted. On the third day of admission, computed tomography (CT) of the chest was obtained which revealed widespread patchy ground-glass opacities in the bilateral lobes (Figure 2). Analyses of specimens obtained from sputum culture showed no growth of pathogen, nasal mucosa were negative for antigens of influenza A and B, a urine specimen was negative for Legionella pneumonphila antigen, and blood culture and sputum culture for bacteria yielded negative results. She was treated with oral trimethroprim-sulfamethoxazole (TMP/SMX), intravenous hydrocortisone (100mg twice a day) and oseltamivir in consideration of the possibility of PCP and influenza infection. Levofloxacin was discontinued. One day later, fever subsided and dyspnea improved.

On the sixth hospital day, bronchoscopy was performed. The airways appeared normal. The white-cell count of the lavage fluid was 185 cells per cubic millimeter, with 57% lymphocytes, 1% neutrophils, and 42% monocytes. Examination of bronchoalveolar lavage (BAL) fluid was positive for DNA of Pneumocystis jirovecii and was negative for antigen and DNA of Cytomegalovirus (CMV). Chest radiography on the eighth day of admission showed resolution of bilateral lung infiltration (figure 3). She was discharged without symptoms ten days after admission.

**Figure1. A frontal chest radiography shows ground-glass appearance in bilateral upper lung field.**

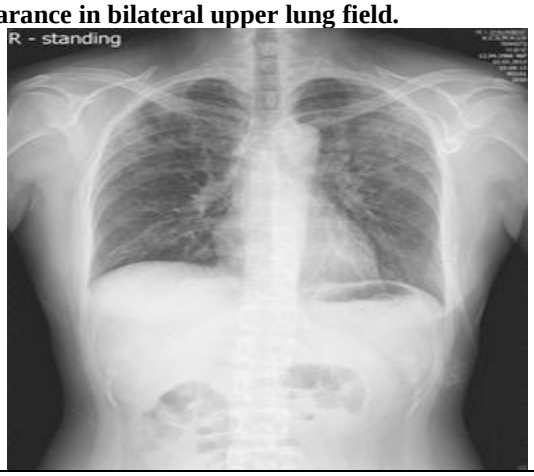


**Figure 2. Computed tomography (CT) of her chest shows widespread patchy ground-glass opacities in the bilateral lobes.**

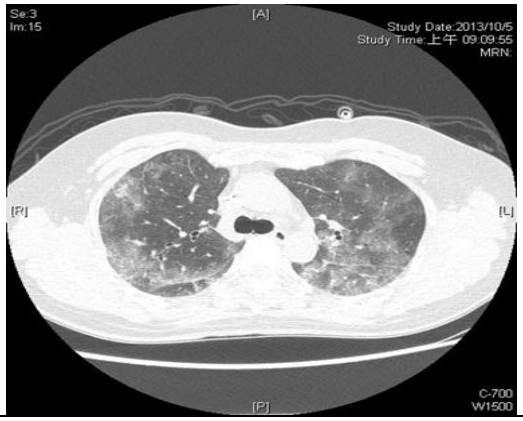


**Figure 3. Chest radiography on the eighth day of admission showed resolution of bilateral lung infiltration.**

## DISCUSSION AND CONCLUSION

Diagnosis of PCP requires identification of Pneumocystis jirovecii in respiratory specimens such as induced sputum specimen or BAL fluid. Because Pneumocystis jirovecii cannot be cultured, microscopy with staining is a method to confirm the pathogen. Gram-Weigert, Wright-Giemsa, and modified Papanicolaou stains are used to find trophic forms of Pneumocystis jirovecii. Calcofluor white, Gomori methenamine silver and toluidine blue can be used to identify the cell wall of the cyst. Both trophic forms and cysts can be seen with direct fluorescent antibody staining. Microscopic staining of sputum induction using hypertonic saline has a diagnostic yield of 50 to 90 percent in HIV-infected patients. The diagnostic yield is over 90 percent in HIV-positive patients by staining of BAL fluid [5]. However, the diagnostic yield is thought to be lower in those non-HIV-infected patients due to less organism burden as comparing with HIV-infected patients [6]. Polymerase chain reaction (PCR) assays is useful in non-HIV-infected patients because of its high sensitivity [7]. Accordingly, we used PCR assays to detect DNA of Pneumocystis jirovecii rather than using microscopic staining first.

Cyclophosphamide, a nitrogen mustard alkylating agent, adds an alkyl group to DNA and interferes with DNA replication by forming DNA crosslinks. It is one of the most potent immunosuppressive therapies available for the treatment of breast cances, lymphomas, leukemias, and multiple myeloma. It can be administered either orally or intravenously. It is also used to treat certain autoimmune diseases such lupus nephritis [8,9] and antineutrophil cytoplasmic autoantibody-positive vasculitis [10]. One study stated that 121 cases of PCP were identified in 76,156 SLE patients treated with cyclophosphamide (0.16%) [11]. Six cases of PCP in 23 granulomatosis with polyangiitis (Wegener's) patients treated with cyclophosphamide and corticosteroids was reported (24%) [12]. We can conclude that cyclophosphamide is a risk factor of PCP.

Glucocorticoid use is a significant risk factor for PCP in patients without HIV infection as well. A retrospective analysis revealed that the median dose of prednisone equivalent in non HIV-infected patients developing PCP was 30 mg/day and the median duration of glucocorticoid therapy before the development of PCP was 12 weeks [13]. It is unknown whether intermittent use of dexamethasone for antiemesis is a risk factor of developing PCP.

Occurence of PCP in patients with breast cancer under chemotherapy are rare. Most of them developed PCP with high-dose chemotherapy for metastasis [14-17]. Only three reports have described PCP occurring in breast cancer patients receiving postoperative adjuvant chemotherapy [18-20]. However, no evidence of definite diagnosis such as DNR assay is mentioned by these reports. One report states that serum lymphocyte counts appear to be lowest around fifth cycle in non-HIV-infected patients during treatment with dose-dense chemotherapy with doxorubicin and cyclophosphamide (AC) followed by paclitaxel (T) [19]. This patient had received fifth cycle of chemotherapy with FAC regimen 19 days before presentation. Moreover, leukopenia and lymphopenia were only noted after fifth cycle of chemotherapy rather than previous cycles.

In contrast to the typically indolent presentation of PCP in HIV-infected patients, the presentation is usually severe in non-HIV infected patients [21]. The mortality rate among non-HIV infected patients is 30 to 60 percent [22]. In conclusion, clinicians have to keep in mind that PCP can be induced by postoperative adjuvant chemotherapy with cyclophosphamide regimen in breast cancer patients, and early diagnosis and treatment are crucial.

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