Pneumocystis Pneumonia in a Patient with Ovarian Cancer Receiving Olaparib Therapy: A Case Report

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Abstract:
We herein report a case of pneumocystis pneumonia (PCP) in a 77-year-old woman with ovarian cancer who was receiving olaparib therapy. After the patient’s second relapse of ovarian cancer, she was administered olaparib as maintenance therapy following successful completion of docetaxel and carboplatin therapy. On receiving olaparib, she showed symptoms of a fever and malaise. Based on laboratory and imaging findings, she was diagnosed with PCP. After treatment with corticosteroids and trimethoprim/sulfamethoxazole followed by atovaquone, the patient’s general condition improved. The lymphocytopenia observed after olaparib administration may have been associated with the development of PCP.

Key words: Pneumocystis pneumonia, ovarian cancer, olaparib, lymphocytopenia

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Introduction
Pneumocystis pneumonia (PCP) is a life-threatening opportunistic infection in immunocompromised hosts. With the improvement in anti-human immunodeficiency virus (HIV) treatments and increase in the number of patients undergoing immunosuppressive therapy, PCP has become a common complication in non-HIV-infection cases, such as cases with leukemia and solid malignancies, like lung cancer and breast cancer (1).

Recently, poly(adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitors have begun to be used as a new therapeutic approach in the management of ovarian cancer (2). Olaparib is the first PARP inhibitor to be approved for maintenance therapy in patients with platinum-sensitive, relapsed ovarian cancer. However, thus far, no PCP cases related to olaparib administration have been reported.

We herein report a case of PCP in a patient receiving olaparib subsequent to cytotoxic chemotherapy for ovarian cancer.

Case Report
A 77-year-old woman was referred to Miyazaki Prefectural Miyazaki Hospital for treatment of an abdominal tumor. She complained of a bloated stomach and epigastric pain. An ascites puncture was performed, and cytology revealed adenocarcinoma. The patient had undergone total hysterectomy, bilateral appendectomy, and partial omentectomy. Under the diagnosis of stage IV ovarian cancer, she received seven cycles of paclitaxel and carboplatin (TC) therapy as adjuvant chemotherapy.

Her ovarian cancer reoccurred 18 months after the adjuvant chemotherapy, with the splenic hilum as the recurrence site. Thus, she received six cycles of docetaxel and carboplatin (DC) therapy. Immediately after the fourth chemotherapy session, she had bacterial pneumonia, which improved with ampicillin/sulbactam therapy. Six months after the DC therapy, the ovarian cancer relapsed at the pancreatic head, para-aortic lymph nodes, liver, and splenic hilum. Thereafter, DC therapy was readministered in six cycles and
was judged to be effective, so olaparib administration was started as a maintenance therapy. Two months after the start of the olaparib therapy, the patient complained of a fever, fatigue, and appetite loss. She visited our emergency department and was admitted to the gynecology department. She was suspected as having pneumonia and was given ceftriaxone, but her symptoms did not improve. The gynecologist consulted with the department of respiratory medicine regarding her medical condition. The patient was then transferred to the department of respiratory medicine for treatment.

Her vital signs were as follows: temperature, 39.2 °C; blood pressure, 107/64 mmHg; pulse, 86 beats/min; and respiratory rate, 26 cycles/min with an O2 saturation of 96% in room air. No anomalies were observed upon auscultation. Hemogram results showed a white blood cell count of 1,350 cells/mm3 (70.0% neutrophils, 26.0% lymphocytes, 6.0% monocytes, 2.0% eosinophils, and 1.0% basophils) and C-reactive protein level of 4.34 mg/dL. The total protein (5.7 g/dL) and albumin levels (3.2 g/dL) were decreased. The Krebs von den Lungen-6 and surfactant protein D levels were elevated (551 U/mL and 138 ng/mL, respectively). The β-D-glucan levels were measured with a kinetic turbidometric assay by employing the WAKO™ Beta-Glucan Test (Wako Pure Chemical Industries, Tokyo, Japan). The serum β-D-glucan level was 8.6 pg/mL. In addition, the renal and liver function test results were normal, as well as the CA125 level (26.0 IU/L; Table).

Chest radiography revealed ground-glass opacity (GGO) of the bilateral lung fields in addition to the known bronchiectasis of the mediastinal side of the lower right lung field. Chest computed tomography (CT) also revealed bilateral GGOs (Fig. 1). Based on these findings, we suspected PCP or drug-induced pneumonia. We therefore treated the patient with systemic corticosteroid therapy with oral prednisolone at 80 mg/day and trimethoprim/sulfamethoxazole (TMP/SMX; 15 mg/kg/day).

On the second day after the patient’s transfer to our department, we performed bronchoalveolar lavage (BAL). An analysis of the BAL fluid (BALF) revealed a total cell count of 6.5×10⁴/mL (histiocytes 53%, lymphocytes 38%, neutrophils 7%, and eosinophils 2%), with no malignant cells or

| Table. Laboratory Findings on Admission. |
|---------------------------------------|
| Urinalysis                          | Biochemistry | Bacteriology        |
| Protein (−)                          | TP           | β-D-glucan 8.6 pg/mL|
| Sugar (−)                            | Alb          |                       |
| Occult Blood (−)                     | T-Bil        |                       |
| Hematology                          | AST 19 U/L   |                       |
| WBC 1,350 /mm³                       | BUN 9.4 mg/dL|                       |
| Band 4.0 %                           | Cr 0.62 mg/dL|                       |
| Seg 61.0 %                           | CRP 4.34 mg/dL| CA125 26.0 IU/L     |
| Eo 2.0 %                            | Glu 100 mg/dL|                       |
| Ba 1.0 %                            | KL-6 551 U/mL|                       |
| Mo 6.0 %                            | SP-D 138 ng/mL|                     |
| Ly 26.0 %                           | IgG 734 mg/dL|                       |
| Hb 7.5 g/dL                          |              |                       |
| Ht 21.4 %                           |              |                       |
| Pt 4.7×10⁴ /mm³                      |              |                       |

Figure 1. Chest radiograph and computed tomography images on admission. a: Chest radiography findings showing bilateral diffuse ground-glass opacity. b, c: Chest computed tomography images showing bilateral diffuse ground-glass opacities with a subpleural sparing pattern.
pathogenic organisms detected. The treatments improved the patient’s clinical condition. One week after bronchoscopy and BAL, polymerase chain reaction (PCR) of her BALF specimen was positive for *Pneumocystis jirovecii* DNA. Based on these results, she was diagnosed with PCP. We continued the administration of corticosteroids and TMP/SMX. The prednisolone dose was gradually tapered over three weeks. After seven days of administration, TMP/SMX was changed to atovaquone because of adverse events (appetite loss). The atovaquone therapy was continued for 14 days. After these treatments, the patient’s general condition and chest X-ray photography and CT findings improved (Fig. 2), and the administration of PCP prophylaxis was also initiated with atovaquone. She did not wish to receive further treatment and was not re-administered olaparib.

**Discussion**

This is the first reported case of PCP in a patient receiving olaparib therapy. In the present case, the patient’s chest radiograph presented with bilateral or diffuse GGO. In addition, high-resolution CT revealed diffuse GGO with a patchy distribution and subpleural sparing pattern. Although these imaging findings are relatively common in PCP (3), they are also found in interstitial pneumonitis, such as drug-induced lung injury. However, to our knowledge, there has been only one report of drug-induced lung injury due to olaparib. Therefore, the low pneumocystis burden (10, 11). Li et al. reported that the sensitivity of β-D glucan in non-HIV patients was relatively low compared with that in HIV-positive patients and, based on their meta-analysis, concluded that the decreased positivity rates might be explained by the lower burden of pneumocystis in non-HIV PCP individuals (6). In addition, Matsunaga et al. reported that the sensitivity and specificity for discriminating probable PCP from colonization were 76.2% and 73.3%, respectively, at a cut-off of 6.0 pg/mL (12). Therefore, the low β-D glucan level in our case does not deny the possibility of PCP and is considered to reflect the low pneumocystis burden.

Recently, PCP has emerged as a threat to non-HIV-infected, immunocompromised patients, such as those receiving chemotherapy for hematological malignancies or solid tumors, and patients receiving immunosuppressive agents for organ transplantation or connective tissue dis-

![Figure 2. Chest radiograph and computed tomography images after treatment. a: Chest radiography. b, c: Chest computed tomography. Both images show improvement in bilateral diffuse ground-glass opacities.](Image)
Figure 3. Clinical course of the patient. On initiation of olaparib administration, the number of lymphocytes began to gradually decrease.

Conclusions

This is the first reported case of PCP in a patient receiving olaparib therapy to treat ovarian cancer. Lymphocytopenia occurring after olaparib administration may be associated with the development of PCP. The incidence of lymphopenia due to olaparib is low, but careful monitoring is required.

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