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Case Report / Olgu Sunumu

Acute Myeloid Leukemia in a Patient with Ovarian Carcinoma

Over Karsinomu Olan Bir Hastada Akut Myeloid Lösemi

Serdal Korkmaz[1], Saadettin Kiliçkap[2], Safak Sahin[3], Mehmet Sencan[1]

Cumhuriyet University, Faculty of Medicine, Department of Internal Medicine, Division of [1]Hematology, [2]Oncology, Sivas, Turkey
[3]Gaziosmanpaşa University, Faculty of Medicine, Department of Internal Medicine, Tokat, Turkey

Abstract

The occurrence of myelodysplastic syndrome or acute myeloid leukemia has been reported after treatment with cytotoxic alkylating agent-based chemotherapy for solid tumors. We report a 50-year-old woman presented with abdominal distension, vomiting, and fatique. The abdominal tomography showed bilaterally ovarian masses and ascite. Surgery was performed and histopathology of the ovarian mass revealed moderately differentiated papillary adenocarcinoma of ovarian. The patient was treated with chemotherapy combination including paclitaxel and carboplatin for six cycles. At 4 years after chemotherapy, recurrence of the primary disease developed. She received carboplatin and paclitaxel. Two years later, complete blood count showed leukocyte count 15.700 /mm3 (15% myeloblasts), hemoglobin 8.7 g/dL, and platelet count 88.000 /mm3. Bone marrow examination and flow cytometry analysis were consistent with acute myeloid leukemia. Standard induction chemotherapy with idarubicin and cytosine arabinoside was administered with failure to achieve complete remission. At the follow-up, the patient died due to prolonged febrile neutropenia. In conclusion, patients who were treated with high dose or long term alkylating agents should particularly follow-up for secondary tumors.

Key words: Ovarian carcinoma, chemotherapy, alkylating agents, acute myeloid leukemia.

Özet

Solid tümörler için sitotoksik alkilleyici ajan içeren kemoterapi tedavisinden sonra miyelodisplastik sendrom veya akut miyeloid lösemi oluşumu bildirilmiştir. Biz karında şişlik, kusma ve yorgunluk şikayeti ile başvuran 50 yaşında kadın hasta rapor ediyoruz. Abdominal tomografide bilateral ovaryan kitle ve asit gösterildi. Cerrahi uygulandı ve ovaryan kitle histopatolojisi orta diferansiye ovaryan papiler adenokarsinom geldi. Hasta altı siklus paklitaksel ve karboplatin kombine kemoteropi tedavisi verildi. Kemoterapiden 4 yıl sonra primer hastalığı nüks etti. Hasta tekrar paklitaksel ve karboplatin tedavisi aldı. İki yıl sonra tam kan sayımında lökosit sayısı 15.700/mm3 (%15 myeloblast), hemoglobin 8,7 g/dL ve platelet sayısı 88.000/ mm3 olarak görüldü. Kemik iliği örneklemesi ve flowsitometri analizi akut myeloid lösemi ile uyumlu idi. İdarubisin ve sitozin arabinozid kombinasyonundan oluşan standart indüksiyon kemoterapi uygulaması ile tam remisyon elde edilemedi. Takibinde hasta derin febril nötropeni nedeniyle öldü. Sonuç olarak, yüksek doz veya uzun süreli alkilleyici ajanlar ile tedavi edilen hastalarda, özellikle sekonder tümörler için takip gereklidir.

Anahtar kelimeler: Over karsinomu, kemoterapi, alkilleyici ajanlar, akut myeloid lösemi

Corresponding Author / Sorumlu Yazar:

Dr. Safak Sahin
Gaziosmanpaşa University, Faculty of Medicine,
Department of Internal Medicine, Tokat, Turkey
Tel: +903562129500
E-mail: drsafaksahin@gmail.com

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Introduction

Overall survival of ovarian cancer has recently increased with effective chemotherapeutic agents including paclitaxel and carboplatin. Although the survival has improved, the long-term side effects after chemotherapy can often appear in cancer survivors[1]. Treatment-related secondary cancer is the most severe side effects in these group patients. Acute myeloid leukemia (AML) has been reported at the follow-up of patients who were treated with chemotherapy for solid tumors. Alkylating agents is the most common cause of chemotherapy-related secondary leukemia. These agents including cisplatin and carboplatin are the cornerstone of treatment of ovarian cancer both in adjuvant and in metastatic setting[2]. Herein, we reported a case of secondary AML after adjuvant platinum-based chemotherapy.

Case Report

A 50-year-old woman presented with abdominal distension, nausea, vomiting, and fatigue in January 2004. Her physical examination revealed massive ascit. The serum CA125 level at the presentation was 236 ng/dL. The abdominal tomography showed bilaterally ovarian masses and ascite. Simple total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and optimal debulking procedures were performed. The residual disease after surgical debulking was less than 2 mm. Histopathology revealed moderately differentiated serous papillary adenocarcinoma of ovarian with stage IIIC. The patient was treated with chemotherapy combination including paclitaxel and carboplatin for six cycles. The cumulative doses of carboplatin and paclitaxel were 3600 and 1800 mg, respectively. Post-treatment abdomino-pelvic computed tomography was normal. Serologic remission (normalization of CA125) was attained upon the completion of the sixth cycle of therapy. No second-look surgery was performed after the completion of the therapy. At 4 years after chemotherapy, the patient was admitted with abdominal distention and pain on the right upper quadrant. Positron emission tomography revealed 4 cm mass near the liver. The level of serum CA125 was 304 ng/dL. Surgery including tumor debulking and splenectomy was performed. Immuno-histochemistry was consistent with serous papillary adenocarcinoma. She received carboplatin (area under the curve 6 dosing) and paclitaxel 175 mg/m2/day for 6 cycles every 3 weeks. The cumulative dose was 3.000 and 1.680 mg, respectively. The patient remained without evidence of recurrence until March 2010. In routine evaluation on the date, complete blood count showed leukocyte count 15.700 /mm3 (15% myeloblasts), hemoglobin 8.7 g/dL, and platelet count 88.000 /mm3. Bone marrow examination was consistent with acute leukemia (Fig 1). A flow cytometry analysis revealed acute myeloid leukemia subtype M2. Standard induction chemotherapy with idarubicin (9 mg/m2 for 3 days every 4 weeks) and cytosine arabinoside (100 mg/m2 for 7 days every 4 weeks) was administered with failure to achieve complete remission. Secondary induction chemotherapy with high dose cytosine arabinoside was started. At the follow-up, the patient died due to prolonged febrile neutropenia.

Discussion

Platinum compounds covalently bind to the DNA pairs and thus, they inhibit DNA replication by forming DNA cross-links and strand breaks. Paclitaxel, an antimicrotubule

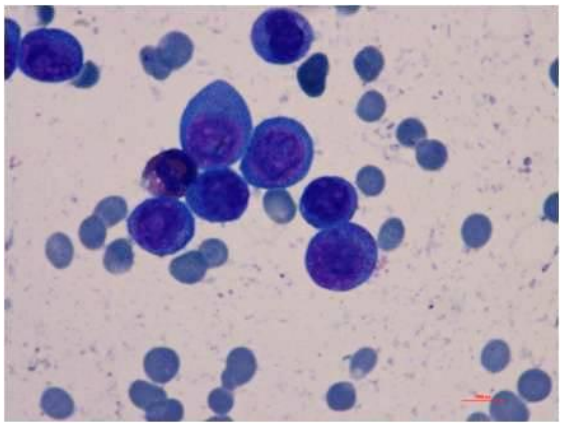

Fig. 1 Blasts of acute myeloid leukemia in bone marrow aspirate (subtype M2) (100 px)

agent used cancer treatment, has a synergistic effect if it has been combined with cisplatin or carboplatin[3]. Paclitaxel also increases the intracellularly uptake of cisplatin and inhibits the repair of cisplatin-induced DNA damage[4]. Myelosupression, nausea and vomiting, nephrotoxicity, ototoxicity and peripheral neuropathy are the most common known side effects of the combination of paclitaxel and platinum compounds. Secondary leukemia and myelodisplastic syndrome (MDS) can also be a consequence of treatment with chemotherapy including alkylating agents and topoisomeorase II inhibitors in cancer survivors. Alkylating agent–related secondary AML is often preceded with losses or deletions of chromosome 5 or 7 and tends to appear at 5 to 7 years after therapy. This type of AML occurs to be dependent on the dose[2]. Secondary leukemia after chemotherapy and radiotherapy accounts for approximately 5-10% of all AML[5]. Compared to de novo leukemia, treatment-related leukemia are resistant to chemotherapy and their prognosis are very poor. MDS or AML occurring after alkylating agents typically presents after a latency period of 5 years. These patients usually present with bicytopenia or pancytopenia. Bone marrow examination was usually characterized by myelodiysplastic changes and/or blastic infiltration[6].

Treatment-related secondary leukemia occurs usually in patients with breast cancer and Hodgkin's lymphoma because of prolonged disease-free survival after their treatments. Although the combination has been often used in patients with ovarian carcinoma, there were a few reports suggested to develop AML and MDS in these patients[2]. Travis et al., in their study, evaluated more than 28.000 women with ovarian carcinoma[7]. In this study, secondary leukemia appeared average of 4 years after the diagnosis. The development of leukemia in patients with ovarian cancer who were treated with platinum-based chemotherapy has been reported in case reports[8]. The risk factors of secondary leukemia include radiotherapy, the cumulative dose of alkylating agent, the duration of platinum-based chemotherapy, and younger patients[9]. Advanced age, however, contributes to develop AML due to additional DNA damage. Radiotherapy in addition to chemotherapy increases about 8 times the risk of secondary AML[10].

In our case, the patient was diagnosed AML (subtype M2) at 6th years after the onset of ovarian cancer. Because of recurrence of the disease she was treated for two times with combination chemotherapy containing cisplatin and paclitaxel. Thus, the patient exposed to high dose chemotherapy. But, no radiotherapy was used for our patient.

In conclusion, patients who were treated with high dose or long term alkylating agents should particularly follow-up for secondary tumors.

No conflict of interest.

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