To the Editor,

Synchronous multiple primary cancer (SMPC) is defined as two or more malignancies diagnosed within 6 months of each other [1]. Its incidence is low, while the simultaneous occurrence of a hematological malignancy and a solid tumor is even less common with only cases reports provided [2,3,4,5,6]. We analyzed 32 patients with a synchronous hematologic malignancy and solid tumor at The Affiliated Cancer Hospital of Zhengzhou University from June 2012 to June 2018.

Patients and disease characteristics are shown in Table 1. These 32 patients included 17 males and 15 females. The median age at diagnosis was 58.5 years (range: 30-81 years). The incidence of SMPC in our center was approximately 0.05%, while this rate was reported as 0.5% in the literature [5]. The difference in this incidence might be attributable to differences in geography, environment, race, or various diagnostic criteria or, more importantly, the experience of the clinicians or the examination methods between studies.

The median interval between the diagnoses of these 2 primary malignancy types was 0.2 months (range: 0-5.3 months). Of the 32 cases, 2 patients were lost to follow-up while the other 30 patients completed the treatment: 3 cases with complete remission (CR), 9 cases with stable disease (SD), recurrence of gastric cancer in 1 case, 1 case of lymphoma recurrence, and 16 cases of death. The median overall survival (OS) of the 32 patients was 17.7 months (range: 1.3-68 months). Among the 16 deceased patients, there were 8 patients with a median age of 60.5 years (range: 44-78 years) who survived less than 10 months, and 4 of them had reported a family history of cancer. Eight patients were diagnosed with hematologic malignancies or solid tumors of stage III or IV. Among these 8 patients, 3 patients died early after surgery, 3 patients died of pulmonary infection after radiotherapy and chemotherapy, and 2 patients died of primary disease progression.

The pathogenesis of SMPC is not completely clear. Tabor et al. [7] found that tumors of different types and different tissues might originate from identical precancerous lesions. An Argentine study group found that 32% of multiple primary cancer patients reported a family history of cancer [8]. Genetic instability may play an important role in the development of multiple primary cancers. Based on the detection of replication errors on microsatellite loci, Horii et al. [9] found that genetic defects in the mismatch repair system represent a high-risk factor for multiple primary cancer patients. We identified 8 patients whose first-degree relatives had experienced malignant tumors in our study.

No standard treatment options are available for synchronous hematological malignancies and solid tumors. The degree of malignancy of each tumor, the response of each tumor to therapy, the therapy indications, and the general condition of the patient should be considered simultaneously. For patients who were diagnosed with a solid tumor and indolent lymphoma such as mucosa-associated lymphoid tissue lymphoma or marginal zone lymphoma, chemotherapy or I-131 radiotherapy was performed first to treat the solid tumor. However, for patients who were diagnosed with an early-stage solid tumor and highly aggressive lymphoma such as diffuse large B-cell lymphoma or anaplastic large-cell lymphoma, after surgical removal of the solid tumor, chemotherapy and sequential hematopoietic stem cell transplantation were administered to treat the lymphoma and at the same time regular postoperative follow-up for the solid tumor was performed.

Keywords: Synchronous multiple primary cancer, Hematological malignancy, Solid tumor

Anahtar Sözcükler: Senkron çoklu primer kanser, Hematolojik malignite, Solid tümör

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Table 1. Clinical characteristics of 32 synchronous multiple primary cancer patients.

| No. | Sex | Age, years | Family history | Hematological malignancy | Primary site | Treatment | Interval, months | Solid tumor | Diagnosis | Primary site | Treatment | Outcome | OS, months |
|-----|-----|------------|----------------|--------------------------|--------------|----------|-----------------|------------|-----------|-------------|-----------|---------|------------|
| 1   | M   | 61         |                 | Liver cancer             | Lymph node   | ABVD×6, radiotherapy | 3               | Adenocarcinoma | Stomach   | Operation | Death      | 59        |
| 2   | M   | 57         |                 | DLBCL (stage II)         | Stomach      | CHOP×2, CHOPE×2     | 0               | Esophageal cancer | Esophageal | Radiotherapy | Death      | 28        |
| 3   | F   | 78         |                 | DLBCL (stage IV)         | Colon        | R-EPOCH×2           | 0               | Adenocarcinoma | Colon     | Operation | Death      | 3.4       |
| 4   | F   | 53         |                 | DLBCL (stage IIIA)       | Thyroid      | CHOP×3, EPOCH×3, DICE×2 | 0 | Microscopic papillary carcinoma | Thyroid | Operation | CR         | 19.3      |
| 5   | F   | 74         |                 | MZL (stage I)            | Lymph node   | Operation           | 0               | Papillary carcinoma | Thyroid | Operation + I-131 | Death      | 19.5      |
| 6   | M   | 61         |                 | MZL (stage IIIA)         | Lymph node   | R-CHOP×2, CHOP×6    | -5.3            | Microscopic papillary carcinoma | Thyroid | Operation | SD         | 26.9      |
| 7   | F   | 70         |                 | MZL (stage IS)           | Spleen       | Operation           | 0               | Squamous carcinoma | Esophageal | Operation | SD         | 52.8      |
| 8   | F   | 48         |                 | Nasal NK/T-cell lymphomas | Nose         | DDGP-L×5, radiotherapy | 0               | Lung cancer | Lung | PC×2, DN×1, DIED×2, crizotinib | Death      | 24        |
| 9   | F   | 54         |                 | NK/T-cell lymphomas (stage IVE) | Nose | Operation | 0 | Papillary carcinoma | Thyroid | Operation,radiotherapy | Lost       |           |
| 10  | M   | 30         |                 | Nasal NK/T-cell lymphomas (stage IVE) | Nose | DICE-Lx5, P-Gemox-VP16×1, radiotherapy, HSCT | 0 | Neuroendocrine neoplasm G3 | Rectum | Operation | CR         | 31.4      |
| 11  | F   | 51         |                 | MALT (stage IVE)         | Stomach      | Operation           | 0               | Adenocarcinoma | Stomach | Operation, TP×4 | Relapse    | 16        |
| 12  | F   | 73         |                 | MALT (stage IE)          | Thyroid      | FC×2                | 0               | Microscopic papillary carcinoma | Thyroid | Operation | CR         | 42        |
| 13  | M   | 67         |                 | Gastric cancer           | Stomach      | Operation           | 0               | Adenocarcinoma | Stomach | Operation, SOX×1 | Death      | 25        |
| 14  | F   | 68         |                 | AML (stage IIIA)         | Lymph node   | R-COP×4             | 5.2             | Adenocarcinoma | Lung    | Chemotherapy | Death      | 7.1       |
| 15  | M   | 43         |                 | ALK-ALCL (stage IB)      | Lymph node   | EPOCH×4, auto-HSCT, radiotherapy | 0 | Microscopic papillary carcinoma | Thyroid | Operation | Relapse    | 44        |
Table 1. Clinical characteristics of 32 synchronous multiple primary cancer patients.

| Sex | Age (years) | Site | Operation | Histology | Stage | Therapy | Outcome | Lost |
|-----|-------------|------|-----------|-----------|-------|---------|---------|------|
| M   | 46          | MCL  | Operation | Hydroxyurea and imatinib | 0.3 | Adenocarcinoma (stage III) | Stomach | Operation, mFOFOX6×4 | SD 14.5 |
| M   | 46          | CML CP | Hydroxyurea and imatinib | 0.2 | Adenocarcinoma (stage III) | Stomach | Operation | SD 1.3 |
| M   | 52          | CML CP | Hydroxyurea and imatinib | 0.1 | Adenocarcinoma (stage III) | Lung | PC×4, S-1 | SD 8.2 |
| F   | 45          | AML-M5 | HAA | -4.6 | Invasive mole (stage III) | Uterus | EMA/CO×4 | Death 6.4 |
| F   | 77          | Pancreatic cancer | AML-M2 | CAG | 1.2 | Adenocarcinoma (stage IV) | Colon | - | Death 3.8 |
| M   | 47          | AML-M2 | IA, D-Ara-c | 2.9 | Adenocarcinoma (stage IIIA) | Colon | Operation, oxaliplatin-5-FU×4 | Death 11.4 |
| M   | 56          | APL  | Arsenic trioxide and retinoic acid | 4.8 | Squamous carcinoma (stage IIIB) | Esophagus | Operation, cisplatin-5-FU×4, Radiotherapy after recurrence | Death 20.2 |

A negative interval represents a hematological malignancy that was diagnosed after the diagnosis of a solid tumor; all intervals between the 2 primary tumors were less than 6 months.

M: Male, F: female, OS: overall survival, CR: complete response, SD: stable disease, HL: Hodgkin lymphoma, DLBCL: diffuse large B-cell lymphoma, MZL: marginal zone lymphoma, MALT: mucosa-associated lymphoid tissue lymphoma, FL: follicular lymphoma, ALCL: anaplastic large-cell lymphoma, MCL: mantle cell lymphoma, RAEB-2: refractory anemia with excess blasts 2, AML: acute myeloid leukemia, ALL: acute lymphocytic leukemia, HPC: hematopoietic stem cell transplantation, ABVD: adriamycin, bleomycin, vincristine, dacarbazine, R-EPOCH: rituximab, etoposide, vincristine, pirarubicin, cyclophosphamide, prednisone, R-CHOP: rituximab, pirarubicin, cyclophosphamide, vincristine, prednisone, CHOPE: pirarubicin, cyclophosphamide, vincristine, prednisone, etoposide, DICE: dexamethasone, ifosfamide, cisplatin, etoposide, DDGP: cisplatin, dexamethasone, gemcitabine, pegaspargase, P-Gemox-VP16: gemcitabine, oxaliplatin, etoposide, doxetmethasone, asparaginase, R-COP: rituximab, cyclophosphamide, vincristine, prednisone, F: fludarabine, cyclophosphamide, EPO: erythropoietin, G-CSF: recombinant human granulocyte colony-stimulating factor, HAA: homoharringtonine, actinomycin D, methotrexate, vincristine, cyclophosphamide, 5-FU: 5-fluorouracil, oxaliplatin, folinic acid, EMA/CO: etoposide, actinomycin D, methotrexate, vincristine, cyclophosphamide, 5-FU: 5-fluorouracil, oxaliplatin, folinic acid, EMA/CO: etoposide, actinomycin D, methotrexate, vincristine, cyclophosphamide, 5-FU: 5-fluorouracil.
Successful Outcome of a Case of Acute Myeloid Leukemia with t(8;21)/AML-ETO Following Langerhans Cell Histiocytosis

Langerhans Hücreli Histiositozunu Takiben Gelişen t(8;21) Akut Myeloid Lösemi Olgusunun Başarılı Tedavisi

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To the Editor,

The occurrence of Langerhans cell histiocytosis (LCH) and acute myeloid leukemia (AML) in the same case has been reported occasionally. We report a new case of AML with t(8;21)/AML-ETO in an adolescent after LCH. To our knowledge, this is the first description of AML with t(8;21)/AML-ETO after LCH diagnosis and therapy.

A 15-year-old boy was diagnosed with LCH in October 2010. He presented with a 1-year history of a skull mass. After 9 cycles of ifosfamide, vincristine, etoposide, and prednisone, the skull mass disappeared. Two years later, the patient presented to the Hematology Department of Beijing Friendship Hospital with progression of his disease in the form of lumber fracture. The mutation BRAF V600E was negative. After relapse of LCH, he received 6 cycles of etoposide and prednisone and 1 cycle of etoposide, prednisone, cyclophosphamide, and vincristine. On 12 March 2013, he received an autologous hematopoietic stem cell transplant. When he came to the clinic with complaints of dizziness on 20 November 2017, a routine blood examination was performed with the following results: white blood cell count, 6.3x10^9/L; hemoglobin, 60 g/L; and platelet count, 12x10^9/L. Bone marrow biopsy showed 69% myeloblasts, and Auer rods were found. The immunophenotype profile of the blast cells was CD34 (+), CD13 (+), CD33 (+), CD117 (+), CD38 (+), CD15 (+). Cytogenetic analysis revealed 46, XY, t(8;21)(q22;q22)[20]. The AML-ETO and WT1 genes were positive. The patient responded well to induction chemotherapy. Standard DA chemotherapy (daunorubicin and cytarabine) was given and the boy achieved complete response (CR) after one cycle. After an additional cycle of DA consolidation chemotherapy, he received an HLA-identical sibling allogeneic hematopoietic stem cell transplant (HSCT). He received a conditioning protocol composed of busulphan and cyclophosphamide, and he was given fluconazole and acyclovir as infection prophylaxis and cyclosporine and mycophenolate mofetil as graft-versus-host disease prophylaxis. Up to 30 March 2019, the patient was in a state of persistent CR for 16 months after the diagnosis of the AML, and the AML-ETO and WT1 genes were negative.