Thirty-Two Case Reports of Synchronous Hematological Malignancy and Solid Tumor

Eş Zamanlı Hematolojik Malignite ve Solid Tümörü Olan Otuz İki Olgunun Analizi

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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			Interval, months	Solid tumor			Outcome	OS, months
				Diagnosis	Primary site	Treatment		Diagnosis	Primary site	Treatment		
1	M	61	Liver cancer	HL (stage IVS)	Lymph node	ABVD×6, radiotherapy	3	Adenocarcinoma (stage I)	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 (stage I)	Colon	Operation	Death	3.4
4	F	53		DLBCL (stage IIIA)	Thyroid	CHOP×3, EPOCH×3, DICE×2	0	Microscopic papillary carcinoma (stage I)	Thyroid	Operation	CR	19.3
5	F	74		MZL (stage I)	Lymph node	Operation	0	Papillary carcinoma (stage IVA)	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 (stage I)	Thyroid	Operation	SD	26.9
7	F	70		MZL (stage IS)	Spleen	Operation	0	Squamous carcinoma (stage IB)	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 (stage I)	Thyroid	Operation,radiotherapy	Lost	
10	M	30		Nasal NK/T-cell lymphomas (stage IVE)	Nose	DICE-L×5, P-Gemox-VP16×1, radiotherapy, HSCT	0	Neuroendocrine neoplasm G3 (stage I)	Rectum	Operation	CR	31.4
11	F	51		MALT (stage IVE)	Stomach	Operation	0	Adenocarcinoma (stage IV)	Stomach	Operation, TP×4	Relapse	16
12	F	73		MALT (stage IE)	Thyroid	FC×2	0	Microscopic papillary carcinoma (stage I)	Thyroid	Operation	CR	42
13	M	67	Gastric cancer	MALT (stage IE)	Stomach	Operation	0	Adenocarcinoma (stage IIIB)	Stomach	Operation, SOX×1	Death	25
14	F	68	AML	FL (stage IIIA)	Lymph node	R-COP×4	5.2	Adenocarcinoma (stage IV)	Lung	Chemotherapy	Death	7.1
15	M	43		ALK-ALCL (stage IB)	Lymph node	EPOCH×4, auto-HSCT, radiotherapy	0	Microscopic papillary carcinoma (stage I)	Thyroid	Operation	Relapse	44

16	M	46		MCL	Lymph node	Operation	0	Papillary carcinoma (stage I)	Thyroid	Operation	Lost	
17	M	57		B-NHL	Submandibular gland	Operation	-4	Squamous carcinoma (stage IIIA)	Esophageal	Operation, TP×3	SD	68
18	M	44	Liver cancer	B-NHL	Stomach	Operation	0	Liver cancer (stage IIIB)	Liver	Operation	Death	2
19	M	65	-	CLL		Monitoring	-3.6	Adenocarcinoma (stage IIIB)	Stomach	Operation, DP×4	SD	46
20	M	60	-	Plasmacytoma		Operation	1.2	Adenocarcinoma (stage I)	Stomach	Operation	SD	54
21	F	65	Lung cancer	MDS-RA		Stanozolol, EPO	0.4	Adenocarcinoma (stage II)	Breast	Operation, FEC×6	SD	14.2
22	M	55	Colon cancer	MDS RAEB-2		Decitabine + CAG	0.3	Squamous carcinoma (stage IIIB)	Esophageal	-	Death	3.4
23	F	67	-	MDS-RCMD		G-CSF, EPO	0.3	Squamous carcinoma (stage IIIA)	Esophageal	Operation, TP×3	SD	8.4
24	M	66	-	MDS-RCMD		EPO, danazol	4.2	Adenocarcinoma (stage IV)	Prostate	Endocrinotherapy	Death	6.2
25	M	76	Esophageal cancer	CML CP		Hydroxyurea and imatinib	0.3	Adenocarcinoma (stage IIB)	Stomach	Operation, mFOLFOX6×4	SD	14.5
26	F	46	-	CML CP		Hydroxyurea and imatinib	0.2	Adenocarcinoma (stage IIIB)	Stomach	Operation	Death	1.3
27	M	52	-	CML CP		Hydroxyurea and imatinib	0.1	Adenocarcinoma (stage IIIB)	Lung	PC×4, S-1	SD	8.2
28	F	81	-	CML CP		Hydroxyurea	0.2	Squamous carcinoma	Scalp	Operation	Death	13.6
29	F	45	-	AML-M5		HAA	-4.6	Invasive mole (stage III)	Uterus	EMA/CO×4	Death	6.4
30	F	77	Pancreatic cancer	AML-M2		CAG	1.2	Adenocarcinoma (stage IV)	Colon	-	Death	3.8
31	M	47		AML-M2		IA, D-Ara-c	2.9	Adenocarcinoma (stage IIIA)	Colon	Operation, oxaliplatin-5-FU×4	Death	11.4
32	M	56	-	APL		Arsenic trioxide and retinoic acid	4.8	Squamous carcinoma (stage IIIB)	Esophageal	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, B-NHL: B-cell non-Hodgkin lymphoma, CLL: chronic lymphocytic leukemia, MDS: myelodysplastic syndrome, RA: refractory anemia, RCMD: refractory cytopenia with multilineage dysplasia, RAEB-2: refractory anemia with excess blasts 2, CML CP: chronic myeloid leukemia in the chronic phase, AML: acute myeloid leukemia, APL: acute promyelocytic leukemia, auto-HSCT: autologous 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, dexamethasone, asparaginase, R-COP: rituximab, cyclophosphamide, vincristine, prednisone; FC: fludarabine, cyclophosphamide; EPO: erythropoietin; G-CSF: recombinant human granulocyte colony-stimulating factor; HAA: homoharringtonine, aclacinomycin, cytarabine, CAG: cytarabine, aclacinomycin, G-CSF; IA: idarubicin, cytarabine, ID-Ara-c: intermediate-dose cytarabine, PC: pemetrexed, carboplatin, DN: docetaxel, nedaplatin, DIED: vinorelbine, ifosfamide, epirubicin, dexamethasone, TP: taxol, oxaliplatin; S-1: tegafur-gimeracil-oteracil potassium capsule, SOX: oxaliplatin, S-1; DP: cisplatin, docetaxel, FEC: fluorouracil, epirubicin, cyclophosphamide, mFOLFOX6: fluorouracil, oxaliplatin, folic acid calcium, EMA/CO: etoposide, actinomycin D, methotrexate, vincristine, cyclophosphamide, 5-FU: 5-fluorouracil.

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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 (+), HLA-DR (++), MPO(+). 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.