Clinical Characteristics and Treatment Outcomes of Therapy-related Acute Lymphoblastic Leukemia: A Single-institution Experience

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Background: Therapy-related leukemia is defined as leukemia arising because of the mutagenic effect of chemotherapy or radiotherapy. Therapy-related myeloid neoplasm (t-MNs), which account for 10-20% of all cases of myeloid neoplasms, are classified as a distinguishable diagnosis and their prognosis is known to be poorer than that of de novo myeloid neoplasms. On the other hand, therapy-related acute lymphoblastic leukemia (t-ALL) is not an established category in the WHO classification yet for its rarity, but a few reports about t-ALL demonstrated inferior outcomes. In this study, we report the clinical characteristics and outcomes of patients diagnosed with t-ALL in our institution.

Materials and Method: We retrospectively reviewed 171 patients who were diagnosed with acute lymphoblastic leukemia (ALL) in Severance Hospital, Yonsei University, from January 2012 to March 2021. Therapy-related ALL was defined as ALL patients who had history of receiving chemotherapy or radiotherapy for previously diagnosed other malignancies, which accounted to a total of 9 patients (5.8%). For those patients, clinical characteristics, laboratory findings and treatment outcomes were analyzed.

Results: All 9 patients showed B-cell ALL, and 4 had Philadelphia chromosome. The type of prior malignancy was breast cancer (2), stomach cancer (2), osteosarcoma (2), hepatocellular carcinoma, ovarian cancer, rectal cancer, thyroid cancer, and acute promyelocytic leukemia. The median duration from the diagnosis of prior malignancy to t-ALL diagnosis was 6.4 years (1.5-26.8). Anthracyclines were the most frequently exposed chemotherapeutics (85.7%), followed by alkylating agents (71.4%). There was no MLL(11q23) abnormalities, which was frequent in t-MN, in 4 patients with available NGS data. TP53 mutation was found in 2 of 4 patients. All patients received induction therapy, and HyperCVAD with/without TKI was the most common regimen (77.8%). Eight patients (88.9%) achieved a CR, and 1 was primary refractory. Five patients (55.6%), including 2 receiving allogeneic hematopoietic stem cell transplant (HSCT), are still alive. The median overall survival was 12.7 months and the median progression free survival was not reached.

Conclusion: Patients with t-ALL made up about 5% of total patients with ALL. As similar to t-MN, t-ALL seems to be a distinct entity with higher genomic instability and poorer outcome. Proper treatment strategy for t-ALL is unclear, but more aggressive treatments including upfront allogeneic HSCT may be beneficial. Further studies with larger scale are needed to conclude.

Keywords: Therapy-related ALL, Cytogenetic abnormalities, MLL, TP53