THERAPY - RELATED ACUTE MYELOID LEUKEMIA (t - AML) FOLLOWING CHEMOTHERAPY FOR NON - HODGKIN'S LYMPHOMA

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ABSTRACT

The patient, a 22-year-old female, was diagnosed with diffuse large B-cell lymphoma (an aggressive non-Hodgkin's lymphoma). The patient had completed 6 cycles of R-CHOP (from March 2018 to July 2018). After that, the patient was re-examined regularly monthly (manifested with moderate and hypochromic anemia, bone marrow aspiration was negative for malignancy). In November 2019, the complete blood cell (CBC) findings were as follows: White blood cell (WBC) count 81 x10^9/liter, neutrophils 7%, lymphocytes 22%, monocytes 2%, blasts 69%; red blood cell count 2.6 x 10^6 /ml, hemoglobin 7.8 g/dl, platelet count 192.000. Bone marrow (BM) aspiration: acute myeloid leukemia (AML5?) (81% blasts in BM); blast cells were positive for PAS, myeloperoxidase (MPO) and sudan black negative. The bone marrow biopsy: myeloid malignant proliferation. Cluster of Differentiation (CD): positive for CD13, CD33, CD64, HLA-DR, CD (±): CD117, CD14, CD 16, CD34; negative for: CD11b, CD35, CD71, CD15, CD19, CD20, CD7, CD3, CD38; monoblasts composed 90% of bone marrow cells.

Key words: *Non-Hodgkin's Lymphoma, t-AML.*

I. INTRODUCTION

According to The World Health Organization (WHO) classification, AML is classified into different subtypes. t - MDS/AML is a complication of primary malignancies including solid tumors and/or hematological and/or non - hematological neoplasms (systemic lupus erythematosus,...) after exposure to chemotherapeutic agents and/or radiotherapy and/or immunosuppressive drugs. T - AML accounts for approximately 10% - 20% of total AML cases (4). Those diseases can be: Hodgkin Lymphoma (HL), non - Hodgkin Lymphoma (NHL), acute lymphoblastic leukemia, sarcoma, ovarian and testicular cancer, autologous hematopoietic cell transplant [1,2].

Diffuse large B - cell lymphoma is an aggressive NHL, which represents approximately 25 - 30% of all lymphomas and is the most common subtype worldwide. The R - CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prenisolone) has been shown to result in improved survival [3].

T - AML following NHL was relatively less frequently reported than t - ALL and t - MPAL (Mixed Phenotype Acute Leukemia) following NHL was much more rarely reported [3].

The specific morphological and cytogenetic features of t - MDS/t - AML are related to the type

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of prior cytotoxic therapy that the patient received for his/her primary medical condition [2]. T - MDS/t - AML following chemotherapy with alkylating agent (AA) is characterized by loss of part or all of chromosomes 5 and/or 7 (centromeric breakage); this form of t - MDS/t - AML typically occurs within 5 - 7 years after chemotherapy and/or radiotherapy have been given, and confers a poor prognosis for patients. T - MDS/t - AML following chemotherapy with topoisomerase II inhibitor (TI) is characterized by translocations involving chromosome bands 11q23 or 21q22, inv (16); t(15,17). They occur with a shorter latency, often within 2 - 3 years of the first cytotoxic therapy. Although they also have a poor prognosis overall, they are more responsive to initial induction chemotherapy. In contrast to AA - associated t -AML, these leukemias are rarely preceded by t - MDS [2].

We reported a case with t-AML following chemotherapy for NHL 18 months since the first cytotoxic therapy.

II. CASE REPORT

Name: Doan Thi Tra M., a 22 - year - old female.

Address: Thua Thien Hue province.

Admitted at Hue Central Hospital in November, 2019 because of elevated white blood cells.

Family history: Normal.

Personal history: Non-Hodgkin Lymphoma treated with R-CHOP (March, 2018-July, 2018), the patient was re-examined regularly every month.

Physical examination: Pulse: 75 beats/min, BP: 110/60 mmHg, Tem: 37^0C.

No fever, no edema. Pale. No hemorrhage. Liver, spleen, lymph nodes not palpable.

Blood test:

RBC: 2,6 x 10^6 /ml, Hb: 7.8g/dl. PLT count: 192,000.

WBC total: 81 x10^9/liter, Blast: 69 %, Neu: 7%, Mono: 2%, Lym: 22%

Ure: 5,4 mmol/L; Cre: 51 µmol/L, LDH: 256 U/L. ALT: 25 U/L, AST: 18 U/L

Abdominal untrasound: Normal.

Peripheral blood smear: Acute Myeloid Leukemia?

Bone marrow aspiration showed hypercellularity with 81% monoblasts.

Bone marrow biopsy: Malignant proliferation of leukocyte (> 60%).

Cluster of Differentiation (CD): Positive for: CD13, CD33, CD64, HLA - DR.

+ Negative for: CD11b, CD35, CD71, CD15, CD19, CD20, CD7, CD3, CD38.

III. DICUSSION

Acute myeloid leukemia (AML) is defined as ≥ 20% myeloblasts in the marrow at diagnosis. Based on the immune phenotype (CD), it is easy to identify acute monocytic leukemia (AML5). It is important to distinguish t - AML with stage IV lymphoma invading bone marrow. At the time of diagnosis of NHL, bone marrow has not shown malignancy, results of biopsy of lymph node and immunohistochemistry showed that non - Hodgkin lymphoma was large, diffuse; however, at the present, malignant cells in the bone marrow was the monoblast (if the lymphoma invaded the bone marrow, the malignant cells in the bone marrow must be malignant lymphocytes). The patient was treated with Doxorubicin (TI) and Cyclophosphamide (AA) which altered DNA, chromosomes causing t - AML.

Jone Bennett reported 35 cases with t - MDS/t - AML (3,5%) in NHL patients treated with I^{131} Tositumomab (5). In the German Hodgkin's Lymphoma Study Group trials between 1993 and 2009, t - AML/t - MDS was diagnosed in 106/11952 patients who treated for Hodgkin lymphoma (0,9%); median time from HL treatment to t - MDS/t - AML was 31 months, overall survival with a median of 7.2 months; the results of cytogenetic and/or molecular genetic evaluations were available for 61 of 106 patients (abnormalities in chromosome 5 and/or chromosome 7 were found in 8/61 patients, MPAL

rearrangement was detected in 19/61 patients) (3). Delwail et al. analyzed 462 patients treated with ABVD and 373 with MOPP, followed by high - dose irradiation, between 1972 and 1998; 13 patients developed a therapy-related leukemia: 11 t - AML and 2 t - ALL, both with a 11q23 translocation [4]. clinical characteristics of some reported cases are shown in Table 1.

Table 1: Comparison of clinical characteristics of some reported cases

Characteristics	**Xubo Gong [3]**	**Jingfang S. [5]**	**Dan Yang [6]**	**Our report**
Age	56	42	56	22
Gender	Male	Male	Male	Female
Lymphoma	Diffuse large B cell lymphoma	Extranodal NK/T-cell lymphoma	Peripheral T-cell lymphoma	Diffuse large B cell lymphoma
Treatment	R-CHOP	CHOP	CHOP, CVAP	R-CHOP
Time period between first cytotoxic therapy and t-AML diagnosis	33 months	48 months	14 months	18 months
Clinical symptoms	Fever, weight loss, abdominal pain.	Pale and pharyngeal hyperemia	Axillary lymphadeno-pathy	Pale and lymphadeno-pathy
Hemoglobin	6,7 g/dl	6,8 g/dl	9,6 g/dl	7,8 g/dl
Platelet count	137,000	26,000	106,000	192,000
WBC	6,7 $x10^9$/liter (75% Blast)	1,5 $x10^9$/liter (30% Monoblast)	24 $x10^9$/ liter (53% Myeloblast)	81 $x10^9$/liter (69% Blast)
Bone marrow	85.5% Blast	49% Monoblast	87 Blast	81% Blast
CD	(+): CD13, cMPO, CD15, CD19, cCD79a, CD117, CyCD22, CD 34, HLA-DR → MPAL	CD 34, CD117, HLA-DR, CD38, CD33, CD13→ AML5	CD34, CD33, CD13, CD7,CD56 → AML2	CD13, CD33, CD64, HLA-DR → AML5
Chromosome abnormalities	46, XY, del (7) (q22), t(6;9) (p23;q34)	CBFB-MYH11		
Treatment	heterologous hematopoietic stem cell transplantation	Daunorubicin Arabinoside	Daunorubicin Cytarabine	Daunorubicin Cytarabine

Our case was the most similar to the case of Jingfang S. in regard to clinical features, cell morphology and CD and our diagnosis was t-AML (AML5) following chemotherapy for Non-Hodgkin's Lymphoma.

IV. CONCLUSION

We reported a case of t-AML/t-MDS after chemotherapy for NHL. T-AML/t-MDS occurs more and more often and its prognosis is very poor for patients (3). The correct use of dosage of chemical agents is important (1). Currently, allogeneic hematopoietic stem cell transplantation is the most effective treatment for t-AML/t-MDS (1), (6), (3).

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