THERAPY-RELATED MYELOID LEUKEMIA

Marta Manubens Oliveras, Degree in Genetics.
Universitat Autònoma de Barcelona, 08193 Bellaterra, Catalonia, Spain
manubens.marta@gmail.com

INTRODUCTION

Secondary leukemia or therapy-related leukemia (t-AML) is a well recognized clinical syndrome that occurs as a late complication after cytotoxic therapy, which is believed to be the cause of subsequent mutations. The most common one is acute myeloid leukemia, on which this work will be focussed, as well as
the effect of the topoisomerase inhibitor-based therapy, and therapy-related acute myeloid leukemia mutations.

MATERIAL AND METHODS

As a basis for the development of this work, many information sources such as paper, reviews, books, on-line official web pages and on-line catalogue were consulted.

OBJECTIVES

The aim of this work is to make a review of the effects of chemotherapy on the occurrence of leukemia, focusing on topoisomerase inhibitors, and acute myeloid leukemia.

t- AML

Myeloid therapy-related leukemia (t-AML) is a clinical syndrome well known that appears as a late complication after the cytotoxic therapy[6]. The term "therapy-related" of the leukemia is descriptive and it is based in the exposition time of cytotoxic agents of a patient.

INCIDENCE

Fig. 2: Age distribution at diagnosis of 161 patients with secondary acute myeloid lekemia.

The risk of developing a second malignancy has been estimated in the range of 8 % to 12 % at 20 years after diagnosis of the first cancer and the incidence increases with age.

It should be emphasized that the proportion of secondary acute leukemia is increasing; this is associaated with a widespread use of chemotherapy and radiotherapy, which increased the survival of patients with cancer and aging .

The latency time after treatment until the disease is longer with alkylating agents , and shorter with topoisomerase II.

The average age of the t- AML patients is 69 years.

SUBTYPES

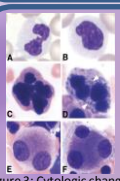

Figure 3: Cytologic changes in therapy related leukemia

Characteristics of the therapy-related leukemia and development depends on the exposition to specific agents, the cumulative dose and the intensity of the therapy.

In the classic form of the treatment with **alkylating** agents:

-Bone marrow resemble the primary tumours of MDS.

-Partial or total loss of chromosomes 5 and/or 7 have been reported in more than 90% of the cases.

-This form of t-MDS /T-LMA is developed usually in 5-7 years' time after the chemotherapy and gives a bad prognosis.

Treatment with **topoisomerase II inhibitors:**

- Displacements that imply chromosomal bands 11q23 or 21q22 can imply gene MLL that might suffer balanced translocations to the chromosomal band 11q23. , or the genes LPM / RARA in the acute promyelocitic therapy-related leukemia.

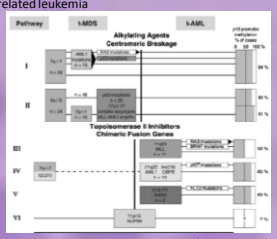

Figure 4. Genetic pathways identified in 140 cases of t-MDS and t-AML by Pedersen-Bjergaard *et al.*

CONCLUSIONS:

During this work I have seen that secondary leukemias are something that happens and will happen. So I think it would be good to try to reduce as far as possible this risk and to maximize treatment outcomes

I also think it would be essential that patients with therapy-related leukemia take a test in order to determine cytogenetic mutations that are causing this tumor, and receive treatment according to these mutations.

However animal studies should be made to check the different ways and try new therapies against this tumor.

In conclusion, it is necessary to gain more knowledge of secondary leukemia, and identify the optimal therapy administration.

PROGNOSIS

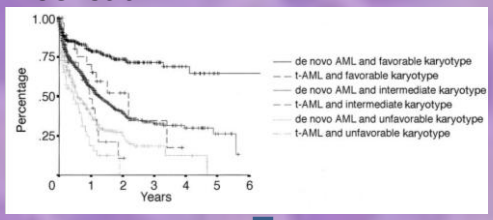

Fig. 1: Prognosis of t- AML9.
Godley, LA. *et Al. 2002*

As far as survival of patients suffering from t-AML is concerned, it is proven that depending on the kariotype presented the prognose varies. With balanced aberrations in chromosomes 5 and 7, the survival is higher.

However, in t-AML cases it is shown that cases presenting a non-favorale cytogenetics are more common.

Factors influencing the outcome in t - AML

The t- AML is generally a fatal disease. Some potential factors may explain the poor outcome of patients with therapy:

The persistence of the primary malignancy causes morbidity and mortality independent from the failure of the bone marrow caused by leukemia

Damage to the organs and the vascular supply of the previous treatment may compromise the ability of these patients to receive intensive remission induction chemotherapy or bone marrow transplantation .

The high frequency of unfavorable cytogenetic aberrations arising during or after chemoradiotherapy appears to lead to the rapid emergence of resistance to chemotherapy in t - AML Stem Cells.

Karyotype	No. of pts		Median survival (months)		p
	t-AML (n = 121)	de novo AML (n = 1511)	t-AML	de novo AML	
Favorable	29	306	27	Not reached	0.02
Intermediate	34	903	12	16	0.19
Unfavorable	58	302	6	7	0.006

Table 1: Survival according to karyotype group for patients with t-AML or de novo AML treated by the German AML Cooperative Group (AMLCG)

TREATMENT

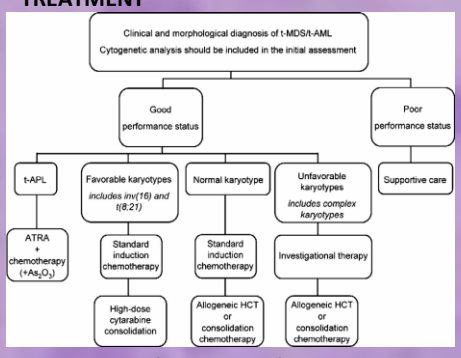

Figure 5: Desicion tree for the management of t-AML

References:

1. Kern W, Haferlach T, Schnittger S, Hiddemann W, Schoch C. Prognosis in Therapy-related acute myeloid leukemia and impact of karyotype. *J Clin Oncol*. 2004;22(12):2510-1
2. Larson R a. Is secondary leukemia an independent poor prognostic factor in acute myeloid leukemia? *Best Pract Res Clin Haematol*. 2007;20(1):29-37.
3. Leone G, Mele L, Pulsoni A, Equitani F, Pagano L. The incidence of secondary leukemias. Haematologica. 1999 Oct;84(10):937-45.
4. Lucy A. Godley, M.D., Ph.D. and Richard A. Larson, M.D.Therapy-related Myeloid Leukemia. Seminars in Oncology (Impact Factor: 4.33). 09/2008; 35(4):418-29.