Childhood Acute Promyelocytic Leukemia: an Unusual Case of Myelodysplastic Syndrome after Successful Treatment in a Single Cancer Center in Brazil

Marcia Trindade Schramm [1,2], Teresa de Souza Fernandez[1], Roberto Capela[1], Alexandre Gustavo Apa[2], Kelly Monteso[2], Viviane Lovatel[1], Jane Dobbin[2], Maria Luiza Macedo Silva[1]

[1]Cytogenetic Department, Bone Marrow Transplantation Center (CEMO), National Cancer Institute (INCA), Rio de Janeiro, Brazil; [2]Hematology Department, National Cancer Institute (INCA), Rio de Janeiro, Brazil

INTRODUCTION

Acute promyelocytic leukemia (APL) comprises approximately 5 to 10% of childhood acute myeloid leukemia (AML) and presents distinct biological and clinical features. Its complete remission rate is greater than 90% as well as its long-term survival rate which is approximately 70-90%.

The survival rate of cancer patients has been increasing with advances in the early detection and treatment. However, cancer survivors may develop a second cancer as myelodysplastic syndrome (MDS) or AML. Although development of MDS after treatment for APL is rare, even more in children, this has been an emerging problem for APL patients in complete remission (CR).

OBJECTIVE

We described the clinical and cytogenetic features in an unusual case of child with MDS after successful treatment APL.

METHODS

We retrospectively evaluated clinical and laboratory data from fifteen APL children diagnosed at INCA, between January 2007-2017. We focused in one patient who developed MDS after successful APL treatment (approved by INCA Ethical Committee).

RESULTS

From fifteen children with APL, one relapsed nervous central system (NCS) isolated after first line treatment and was submitted to bone marrow transplantation. All patients are in CR. However, one developed MDS after treatment system (Table 1).

Table 1 – Clinical Features and Follow–up of Pediatric Patients diagnosed with APL.

Patient	Sex	Age	Treatment	Relapse/MDS	Follow-up
1	F	10	GIMEMA	-	7 yrs 5 m
2	F	12	GIMEMA	-	5 yrs 3m
3	F	17	GIMEMA	-	8 yrs 1m
4	M	14	GIMEMA	-	5 yrs 4m
5	F	2	GIMEMA	-	10 yrs 9m
6	F	13	GIMEMA	-	8 yrs 11m
7	M	3	GIMEMA	-	6 yrs 6m
8	F	11	GIMEMA	-	10 yrs 3 m
9	M	14	GIMEMA	-	3 yrs
10	M	10	GIMEMA	-	2 yrs 10m
11	M	9	GIMEMA	-	2 yrs 5m
12	M	7	GIMEMA	-	2 yrs 3m
13	M	13	GIMEMA	NCS	1 yr 11m
14	F	13	GIMEMA	-	7 yrs 4m
15	M	9	GIMEMA	MDS	3 yrs 8 m

We report a child who developed MDS after successful treatment for APL. A 9 year old boy was admitted at INCA in December 2013 with fever and bleeding. Hemogram showed hemoglobin 9.4 g/dl, white blood cells (WBC) 45x109/l and platelet 9x109/l. Fibrinogen was 83 mg/dl, INR and PTT values were 1.4 and 1.3, respectively. Bone marrow analysis showed 86% of hypergranular promyelocytes with Auer rods infiltration. FISH and RT-PCR detected *PML-RARA* fusion gene, confirming APL. In figure 1, we can see the FISH showing the *PML-RARA* fusion gene. Treatment was according to GIMEMA-AIEOP-AIDA protocol. The patient achieved morphological remission in 38 days and molecular remission was confirmed after the third consolidation course. He sustained remission until the end of the treatment, in June 2016.

After one month, pancytopenia and dysplastic features were detected. *PML-RARA* fusion gene was negative (Figure 2). G-banding and FISH analyses showed monosomy 7 (Figure 3). The diagnosis was MDS refractory anemia with excess blasts (RAEB-2). Allogeneic bone marrow transplantation was indicated and treatment with azacytidine and supportive care has been conducted.

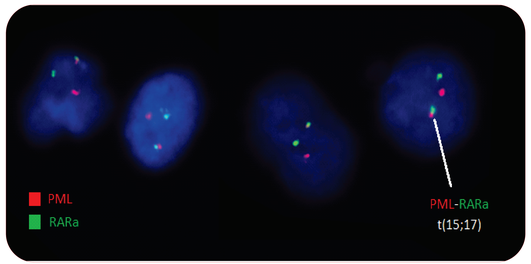

Figure 1: Fluorescence *in situ* hybridization (FISH). Interphase-FISH (I-FISH) showing *PML-RARA* fusion gene (APL). FISH analysis using the probe LSI PML spectrum orange /RARA spectrum green, single fusion (Vysis).

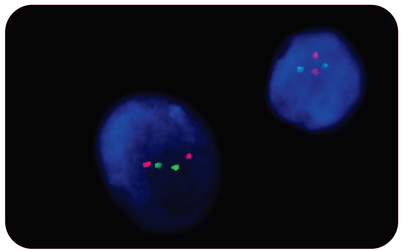

Figure 2: Interphase-FISH (I-FISH) showing *PML-RARA* fusion gene negative (after treatment). FISH analysis using the probe LSI PML spectrum orange /RARA spectrum green, single fusion (Vysis).

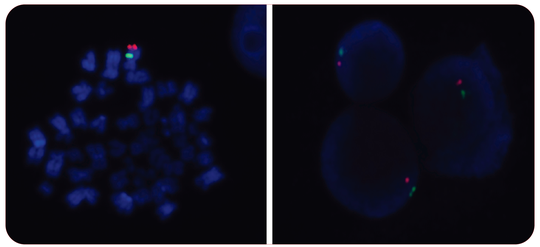

Figure 3: Metaphase and interphase nucleus FISH showing monosomy 7, using the probe D7S486 7q31 region spectrum orange/CEP 7 (D7Z1) 7p11.1-q11.1 spectrum green (Vysis).

DISCUSSION

Most patients with therapy-related-MDS or AML have bone marrow clonal chromosomal abnormalities, which often correlate with the type of preceding cytotoxic agents and latency period, defined as the time between the primary disease diagnosis and therapy-related disease onset.

To our knowledge, reviewing the literature, only a few studies reported MDS cases after using all-trans retinoic acid (ATRA) and chemotherapy for APL treatment and typically present after a latency period of 5 to 7 years.

CONCLUSIONS

With this report, we highlight the rarity of therapy-related-MDS after treatment for APL in a child and the short latency period (30 months). Also, we emphasized the importance of proper monitoring tests in all treated APL patients for early detection of therapy-related MDS and for accurate therapeutic strategies.

Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA