Conventional and Molecular Cytogenetic Study in Pediatric Patients with Myelodysplastic Syndrome treated with Allogeneic Hematopoietic Stem Cell Transplantation

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INTRODUCTION

Myelodysplastic syndrome (MDS) is a group of clonal disorders of hematopoietic stem cells. It is characterized by ineffective hematopoiesis, presence of dysplasias in bone marrow and peripheral blood cytopenias (Figure 1). Approximately 10-40% of MDS patients evolve to acute myeloid leukemia (AML). Pediatric MDS is an uncommon disorder, accounting for less than 5% of hematopoietic malignancies. In children, MDS appears with distinct clinical and laboratory characteristics when compared with adults, which may reflect special biological issues of MDS during childhood. Due to its variety, its pathogenesis has not been adequately studied. The allogeneic hematopoietic stem cell transplantation (HSCT) has been indicated as the main treatment for pediatric patients with MDS. However, as the transplant is a procedure of high toxicity, morbidity and mortality, the selection and timing of indication for this treatment are considered a difficult task due to the heterogeneity of the disease. Cytogenetic has been identified as an important marker for diagnosis and prognosis in MDS. Because of the rarity of MDS in childhood, few cytogenetic studies were performed in this group of patients treated with bone marrow transplantation.

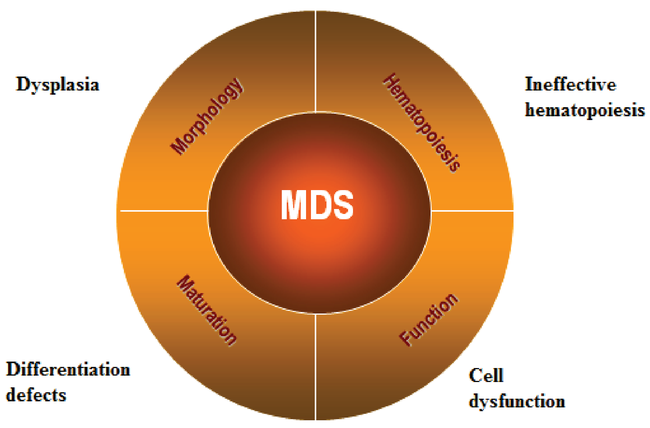

Figure 1: MDS characteristics.

OBJECTIVES

The aim of this study was to analyze the chromosomal pattern through conventional and molecular cytogenetic in pediatric patients with primary MDS treated with allogeneic HSCT in order to verify the frequency of abnormal karyotypes, the main chromosomal abnormalities and the role of the cytogenetic in the indication and in the relapse of the disease.

MATERIAL AND METHODS

A retrospective and prospective study was conducted between 1991 and 2017 in pediatric patients with primary MDS treated with allogeneic HSCT. All the 52 patients studied were from the Bone Marrow Transplantation Center (CEMO), National Cancer Institute (INCA). Cytogenetic analysis was performed before and during the follow up after allogeneic HSCT (Figure 2). This project was approved by the Research Ethics Committee - INCA (CEP nº 62/2010). The workflow of this study is in Figure 3.

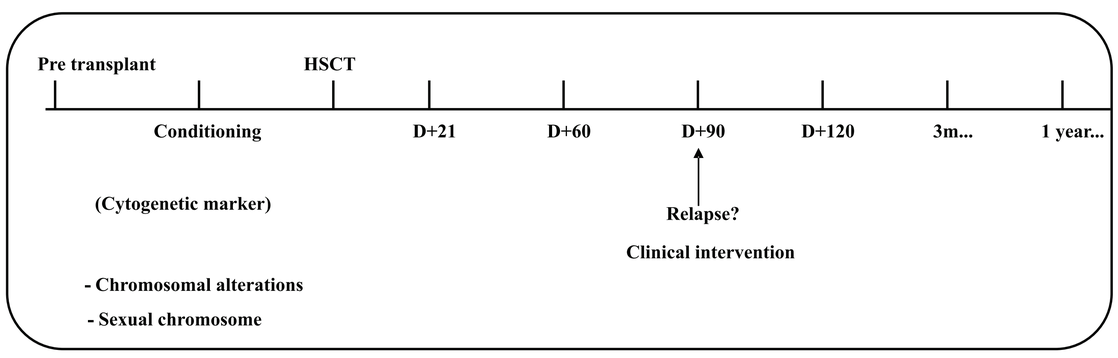

Figure 2: Cytogenetic analysis in pediatric patients with MDS treated with allogeneic HSCT.

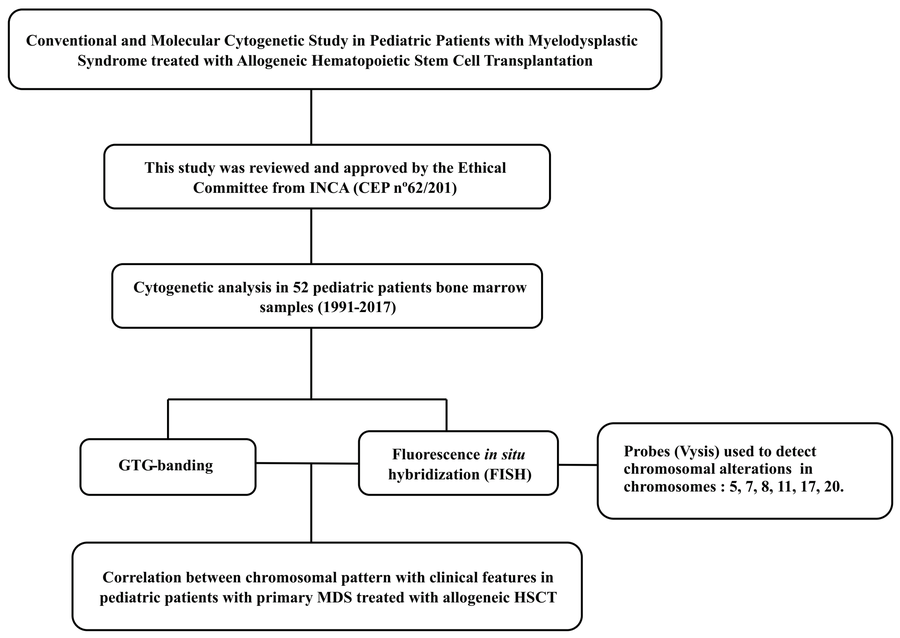

Figure 3: Workflow of this study.

RESULTS

Abnormal karyotypes were detected in 67% (35/52) in pediatric patients with MDS (Figure 4). The main chromosomal alterations found in this study were: del(7q)/-7, del(11)(q23) and complex karyotypes (Figure 5). These chromosomal alterations were associated with relapse of the disease.

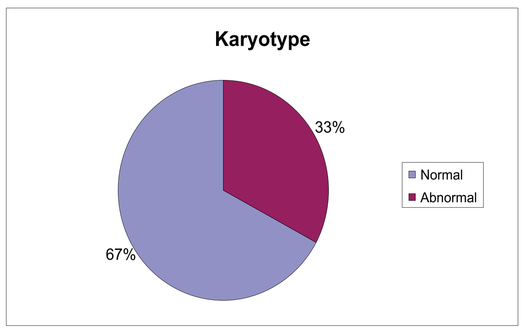

Figure 4: Frequency of cases with normal and abnormal karyotypes.

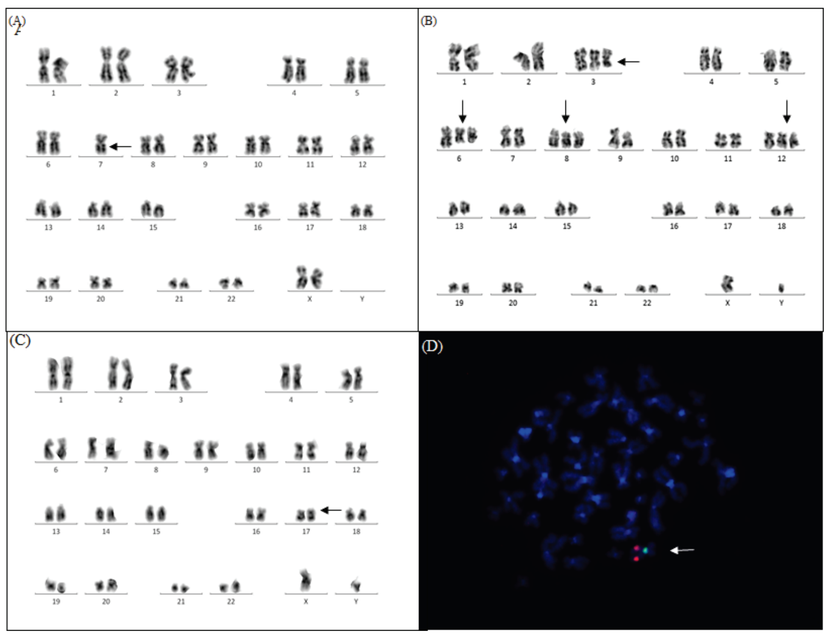

Figure 5: GTG banding analysis. (A) Monosomy of chromosome 7. (B) Complex karyotype. (C) Deletion of the short arm of chromosome 17. (D) FISH: Chromosome 7 probe (LSI D7S486 spectrum orange / CEP 7 spectrum green, Vysis, Inc. Downers Grove, USA). The green probe segment marks the centromeric region of chromosome 7 and the red color, the region 7q31. In metaphase, we also observed the marking on only one chromosome, confirming the monosomy of 7 (arrow).

CONCLUSIONS

Our results suggest that pediatric patients with primary MDS must be indicated to allogeneic HSCT in early stage of disease, when the presence of chromosome abnormalities plays an important role in the indication, in the selection and in monitoring the response of this treatment.

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