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Del (5q), monosomy 7 and two translocations in a patient with myelodysplastic syndrome

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Abstract

Myelodysplastic syndromes are a group of hematological disorders most often affecting persons over 40 years old in which bone marrow dysfuntion is caused by both qualitative and quantitative defects of the hematopoietic cells. We present a case study of a 33 years old man, who developed hematomas and bleeding of the gums, without hepato-splenomegaly. Bone marrow showed hypocelularity with myeloid elements serie in all stages of maturation, neutrophyls with abnormalities Pelger Huet and type 2 blast. Refractory anemia with excess blast cells in transformation was diagnosed. The chromosomal analysis reported:

43, xy, -7, -15, -15, -22, +del(5q)(q22-qter), t(14q;15q), t(15q;22q).

The patient received cytarabine in low dose for twenty days, without improvement and died after a month. This findings suggest that the cytogenetic analysis is the best predictor of disease progression and that the more complex karyologic anomalies are related to unfavorable prognosis.

Key words: Chromosomal abnormalities; myelodysplastic syndrome.

Del (5q) y monosomía 7 asociada a doble traslocación en un paciente con sindrome mielodisplásico

Resumen

Los síndromes Mielodisplásicos son un grupo de desórdenes hematológicos, que afectan con mayor frecuencia personas mayores de 40 años y en los cuales ocurre una disfunción de la médula ósea que origina tantos defectos cualitativos como cuantitativos de las células hematopoyéticas. En este trabajo se presenta el caso de un paciente masculino de 33 años de edad, el cual presentó, hematomas en piel, gingivorragias, no se encontró hepato ni esplenomegalia. El aspirado de médula ósea mostró, médula hipocelular, con elementos de la serie mieloide en todas las fases de maduración, neutrófilos con anomalias tipo Pelger Huet y blastos tipo 2; se diagnosticó anemia refractaria con exceso de blastos en transformación. El análisis cromosómico reveló la siguiente fórmula cromosómica:

43, xy, -7, -15, -15, -22, +del(5q)(q22-qter), t(14q;15q), t(15q;22q).

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El paciente recibió citosar a bajas dosis x 20 días, sin mejoría de su cuadro clínico, muriendo al mes. Podemos concluir que el análisis citogenético, es el mejor indicador de progresión de la enfermedad así como también las anomalías cariotípicas complejas están relacionadas con mal pronóstico de la misma.

Palabras claves: Anomalías cromosómicas; síndromes mielodisplásicos.

Introduction

Myelodysplastic Syndrome (MDS), are hematological disorders most often affecting persons over 40 years old, in which bone marrow dysfuntion is caused by both qualitative and quantitative defects of the hematopoietic tissues. The alteration of the karyotype in the transformation of a normal cell to a neoplastic state is a widely observed phenomenon (1,2). Chromosomal abnormalities have been described associated with different types of MDS, each one of them with specific implications for prognosis (3). One of these anomalies is the loss of the distal portion from the long arm of chromosome 5 indicative of a favorable prognosis (4). Another frequent anomaly is monosomy or deletion of chromosome 7, associated to unfavorable disease prognosis (5). We presented a case of refractory anemia with excess blast and complex karyologic abnormalities that included in addition to both anomalies cited above, two chromosomal translocations. Which to our knowledge, have not been previously reported.

Case Report

A 33 year old venezuelan male developed fever, muscular weakness, cervical and joint pain. Physical examination showed: skin hematomas, bleeding gums, with absence of hepato-splenomegaly. Laboratory examinations reported; white blood cells 2.3 x 10^{9}/L, red blood cells $3.0x10^{12}$/L, hemoglobin 8.1 gm/dl, hematocrit 25.3%, platelets $0.015x10^{12}$/L, reticulocyte count 0.3%. Bone marrow aspiration showed hypocelularity with elements from myeloid serie in all stages of maturity and 10% type 2 blast. Refractory anemia with excess blast in transformation was diagnosed. Bone marrow cell were cultured as previously described (6) and GTG banding (7) was performed for identification of chromosomal abnormalities. Cytogenetic analysis of 13 metaphase revealed the following formula: 43, xy, -7, -15, -15, -22, +del(5q)(q22-qter), t(14q;15q), t(15q;22q). (Figure 1).

The patient was admitted to the hospital for treatment with continuous infusion of cytarabine for twenty days without improvement. During hospitalization the patient continued to be transfusion dependent. Bone marrow aspiration done 2 month later were consistent with acute myeloid leukemia. The patient expired a month later after his condition was complicated with perianal abscess and sepsis.

Discussion

The progression of MDS to Acute Myeloid Leukemia is frequently encountered, however not all cases of MDS evolve into AML; many patients never develop this disease (4). Others develop this condition in early or late stages of disease evolution, (5). Yunis (3) has pointed out that in patients that present the chromosomal anomaly known as del(5q), the development of AML occurs in late stages. In contrast, with the presence of monosomy or deletion of chromosome 7, the transformation appears earlier. Christadoulidou (8) first noted the association of the deletion 5q with the monosomy 7 along with other chromosomal abnormalities and its relationship with a negative prognosis of the disease. In 1993 Ohyashiki (9), reported that patients with del(5q) and monosomy 7 had a significantly shorter survival. In 1994 Parlier (10), studied 109 patient with Primary Myelodysplastic syndrome, observing that their patients with complex chromosomal abnormalities

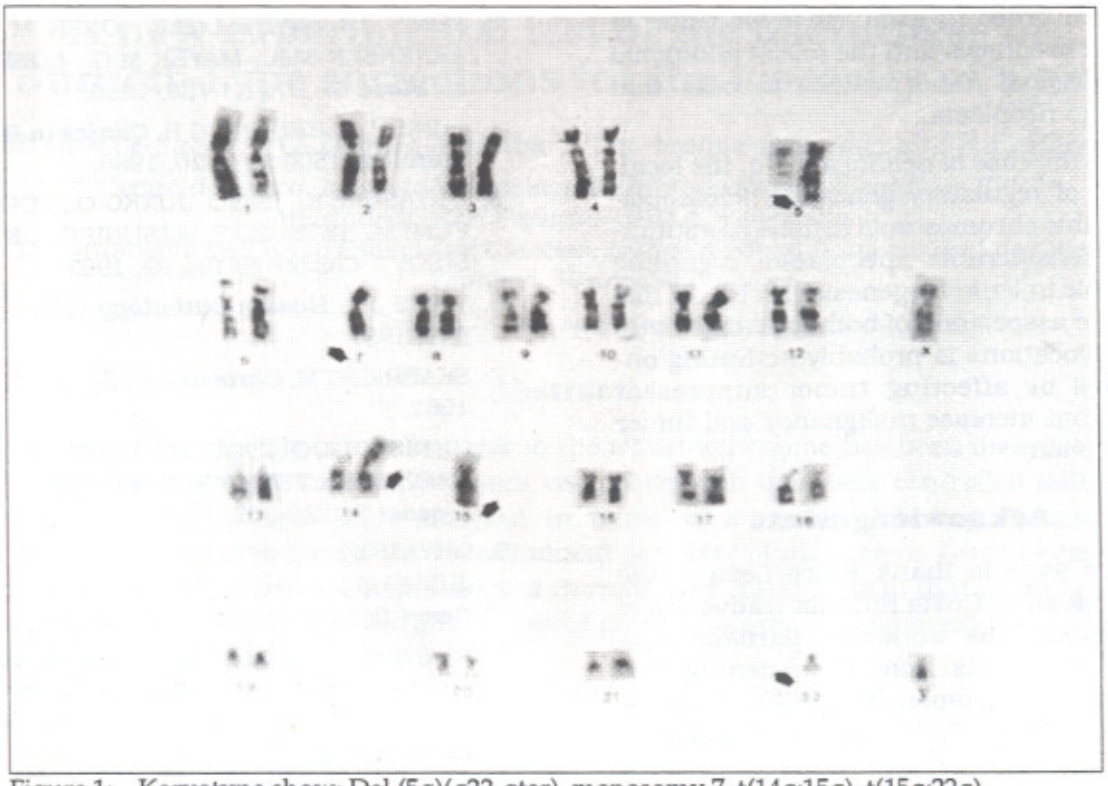

Figure 1: Karyotype show: Del (5q)(q22-qter), monosomy 7, t(14q;15q), t(15q;22q).

Tabla 1
Comparation clinicopathologic features

Rojas-Atencio	Christodoulidou
33 years old	66 years old
Pancytopenia	Pancytopenia
Muscular Weakness	-
-	Splenomegaly
Perianal abscess	-
-	Hepatomegaly
Hematomas	-
-	Atrial Fibrilation
Bleeding Gum	-
-	Chro. Obstruc. Pulm.
-	Pneumonia

had shorter survival than those with single or double defects or a normal karyotype. None of the previous case had the same anomaly reported in this paper. In our case, the association del(5q) and monosomy 7 was found associated with chromosomal translocations differing from those observed earlier and with shorter life expectancy. An important discovery was the detection of unique clinical and bone marrow findings, (Table 1). Which led us to suggest that there is no clear correlation between clinical manifestations of the disease and prognosis. Likewise, in 1978 Croce (11), pointed out that there are several neoplasias where no differences in the clinical and prognosis presentation was observed between patient with typical cytogenetics findings, compared to those patients with atypical karyotypes. This raises a serious concern about using clinical manifestations without karyologic analysis. Therefore we recommend cytogenetic studies on all patients with

MDS, in order to establish their value in disease prognosis and the role of additional chromosomal abnormalities in cells that evolve to neoplasia.

In the case of del(5q) and 7q, the localization of regulatory genes for hematopoiesis in this chromosomal regions has stimulated considerable speculation regarding their role in leukemogenesis (12,13). In this case the association of both anomalies with a translocations is probably activating oncogenes or affecting tumor suppressor genes that increase malignancy and tumor progression.

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