REVISTA BRASILEIRA
DE HEMATOLOGIA
E HEMOTERAPIA

Relato de Caso / Case Report

Isolated trisomy 11 in *de novo* acute myeloid leukemia

Trissomia 11 isolada em leucemia mielóide aguda de novo

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*The real mechanism involved in trisomies and leukemogenesis remains unknown and more information about this connection is essential, but unfortunately the clinical outcome and hematological profile of patients with isolated trisomy 11 and AML have not been well characterized. Considering the limited data on the specific disease entity, the current report describes two cases of de novo acute monocytic leukemia (AMoL) and isolated +11, in which this event was further characterized. Rev. bras. hematol. hemoter. 2008;**30**(3):253-255.*

***Palavras-chave**:Trisomy 11; acute myeloid leukemia; chromosomes.*

Introduction

Chromosomal trisomies are characterized by an additional copy of genomic material. Isolated trisomies (+8,+11,+13,+21) comprise 90% of all trisomies[1] and 7% of adult de novo acute myeloid leukemia (AML).[2] Little is known about the clinical and hematological characteristics of de novo acute monoblastic leukemia (AMoL) patients with isolated trisomy 11, but immunophenotypic studies have shown that trisomy 11 and AML are associated with an early myeloid precursor,[3] probably as a result of a pluripotent stem cell disorder being discovered in primary as well as in secondary myelodysplastic syndromes (MDS)/AML. Sierra and coworkers[3] proposed that de novo AML with trisomy 11 can be considered a specific entity associated with poor outcomes and characterized by morphology of blasts cells with myelodysplastic characteristics. Concerning cytogenetic results, isolated trisomy 11 is the third most common isolated trisomy in de novo AML, reported in 5.7% of AML patients with normal karyotypes, 37.5% of cases with trisomy 11 and other cytogenetic abnormalities and 79% of cases with trisomy as the sole karyotypic abnormality.[4] In AML or MDS isolated trisomy 11 occurs in less than 3% of all cases[4-7] often with no full description of clinical and hematological features.[8]

Besides +11, abnormalities involving chromosome 11, translocations, interstitial deletions and duplications are reported in various hematologic disorders, especially MLL Partial Tandem Duplication (MLL - PTD), which confers, both in childhood and adult AML, a worse prognosis and shortened overall and event free survival.[9] Molecular studies of AML with trisomy 11 have revealed a high incidence of partial tandem duplication of the *MLL* gene[11] but it is still uncertain how MLL gene duplication and trisomy 11 arise and how they are related during leukemogenesis. The aim of this report is to describe, with clinical and laboratory data, two cases of isolated trisomy 11 and de novo AMoL, to provide more information about this event.

Case history and results

Case 1

A 59 year-old female patient was admitted to hospital in February 2000 due to fever, fatigue and weight loss. Routine blood analysis showed anemia (hemoglobin 5.2g/dL), white blood cell count (WBC) of 0.31 x10^9/L with 82% of blast cells and 12.6 x10^9/L platelets. Bone marrow aspiration presented 92% of monoblasts and immunophenotyping showed: positive CD11c, CD13, CD14, CD15, CD33, CD38, CD45, CD65 and HLA-DR. Bone marrow karyotype showed 47,XX,+11[5]/46,XX.[12] The diagnosis of AMoL (poorly differentiated) by WHO[13] or AML M5a according to the FAB[14] classification was established. The patient was scheduled to a Dauno +

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AraC (3+7) regimen but complete remission was achieved only after a second induction with AraC, VP16 and Mitoxantrone. Consolidation was achieved with the last regimen at the same doses. Intensification was not considered due to the frail aspect (low Karnofsky index) of the patient, but a maintenance regimen with Ara-C for 15 months was administered. Seventeen months out of therapy the patient relapsed and died due to sepsis.

Case 2

A 54 year-old female patient was admitted to the hospital because of abdominal pain, sickness, watery diarrhea and skin infections in February 2001. She presented hepatomegaly (8cm). Blood analysis showed anemia (hemoglobin 6.7g/dL), WBC was 3.99x 10^9/L with 87% of blasts and 1.09 x10^9/L platelets. Bone marrow aspiration showed 88% of monoblasts and immunophenotyping showed positive CD4, CD11c, CD13, CD15 and CD33. Bone marrow karyotype revealed 47,XX,+11/46,XX.[12] The diagnosis of AMoL, poorly differentiated by WHO[13] or AML M5a FAB[14] was made. The patient developed respiratory insufficiency and died before the start of chemotherapy.

Discussion

Patients with trisomy 11 and AML are associated with short first complete remission and poor response to subsequent chemotherapeutic regimens.[6,15] Due to the variable clinical course and prognosis, they may be included in the intermediate cytogenetics risk group for success of induction and overall survival[16] or in the unfavorable risk group.[17] It is currently unknown whether isolated trisomy 11 constitutes an independent prognostic factor. This numerical chromosome change is not correlated with any specific WHO subgroup of MDS/AML, despite, in previous studies, trisomy 11 has been associated with older age, M2 and M1 FAB subtypes, high platelet count, low incidence (13-15%) of patients with WBC counts (> 50x10^9/L) and short long term disease free survival,[4] it has been suggested that +11 is especially associated with myelomonocytic proliferation.[6]

The patients here presented AMoL FAB M5, white blood cell count > 20.000x10^9/L, platelet count >10×10^9/L and were more than 50 years old. Acute monoblastic leukemias (M5a and M5b) are considered aggressive diseases due to their association with hyperleukocytosis, extra medullar and gingival or cutaneous infiltration.[6] These cases represented 1.3% (2/154) of all the AMLs admitted to the Department of Hematology – Unifesp from 1995 to 2005. In studies, the incidence ranges from 0.9% to 0.76% as the sole abnormality.[3,4]

Approximately 90% of adults with sole +11 and AML and 11% of adult patients with *de novo* AML and normal cytogenetics carry a molecular rearrangement of the *MLL* gene (mixed lineage leukemia or myeloid/lymphoid leukemia).[7] This rearrangement occurs in the early phase of the disease and is not a genetic event induced by chemotherapy.[18] Caligiuri and colleagues[7] did not find additional mutated *MLL* genes in AML with trisomy 11 and proposed that the extra copy of chromosome 11 containing the wild type allele provides a selective growth or survival advantage over normal cells.[19] This is provocative and warrants further molecular investigations of AML with trisomy 11 and the *MLL* gene, as this may give useful information on the genetic mechanisms leading to the formation of trisomies during leukemogenesis.

Resumo

*O mecanismo envolvido em trissomias e leucemogênese permanece não esclarecido e mais dados sobre esta relação são fundamentais, mas infelizmente os resultados clínicos e o perfil hematológico dos pacientes com trissomia 11 isolada e LMA ainda não foram bem caracterizados. Considerando o limitado número de informações, este relato descreve dois casos de leucemia monocítica de novo e trissomia 11 onde este evento foi caracterizado. Rev. bras. hematol. hemoter. 2008;**30**(3):253-255.*

Palavras-chave: *Trissomia 11; leucemia mielóide aguda; cromossomos.*

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Avaliação: Editor e dois revisores externos
Conflito de interesse: não declarado

Recebido: 06/11/2007
Aceito: 21/02/2008