Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section

Mini Review

Acute megakaryoblastic leukemia (AMegL) M7 acute non lymphocytic leukemia (M7-ANLL)

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Published in Atlas Database: November 2003

Online updated version : http://AtlasGeneticsOncology.org/Anomalies/M7ANLLID1100.html
DOI: 10.4267/2042/38052

Identity

Alias: AML-M7

Note: Sometimes presenting as "acute myelofibrosis"

Clinics and pathology

Phenotype/cell stem origin

This leukemia is thought to derive from the transformation of a multipotent myeloid progenitor cell. In the adult patient multilineage dysplasia is a common finding and in some cases a minority of myeloid blast cells is present.
The blast cells show one or more megakaryocytic markers (i.e. Factor VIII, CD61, CD41, or CD42), they test negative when using the anti-myeloperoxidase monoclonal antibody and never show coordinated expression of lymphoid markers, though isolated CD2 or CD7 positivity can be found on some occasions. The CD34, CD13 and CD33 markers are positive in a substantial fraction of cases, as is the case with the CD36/thrombospondin receptor.
The myeloperoxidase stain is negative by light microscopy, but ultrastructural peroxidase activity with a specific peri-nuclear staining pattern can be detected at the electron microscopy level.

Epidemiology

The disease is rare and, due to difficulty in diagnosis, its exact incidence is not known. Reasonably, it may account for approximately 1-2% of all de novo acute myeloid leukemias (AML) in the adult population, but the incidence in the
pediatric age group is higher, partly due to an association with Down syndrome.

Clinics

The presentation is usually acute, though AMegL may develop after myelodysplastic syndrome or chronic myelogenous leukemia (CML).
In some cases acute myelofibrosis is the presentation picture.
AMegL should be distinguished from AML with megakaryoblastic involvement showing a minority of megakaryoblasts.
In children there is an association with Down syndrome.

Cytology

The blast cell morphology varies from case to case. In some patients the blasts are undifferentiated and the diagnosis requires immunophenotyping or electron microscopy studies.
Dysmegakaryocytopoiesis is rather frequent. Other patients may show bleb-forming blasts, but this feature is not specific for megakaryoblasts. Micromegakaryocytes can be frequently seen.

Pathology

The bone biopsy almost invariably shows fibrosis, which can be extensive in up to 75% of the cases.
Spleen enlargement is frequently seen in children, less frequently in adults.

Treatment

Myeloablative treatment followed, whenever possible, by allogeneic or autologous bone marrow transplant is the treatment of choice.

Prognosis

In general, the prognosis is severe. 30-to-50 % of the adult patients achieve a complete morphologic

remission, but the majority relapse within a few months. Median duration of CR and survival in a study was 10.6 months and 10.4 months, respectively. Some children may fare better, with a 50% 3-year event free survival in AML-M7 post Down Syndrome or with the t(1;22) (see below). Prognosis is dismal in children with other cytogenetic abnormalities.

Cytogenetics

Cytogenetics morphological

a) Adults

There is no cytogenetic anomaly that is specific for AML-M7. The karyotype is abnormal in the vast majority of cases with complex aberrations (i.e. 3 or more clonal aberrations) occurring more frequently than in other AMLs. -5/5q- and/or -7/7q+ are found, as a rule, in virtually all cases with complex karyotype, which globally account for 70-80% of abnormal cases.
3q21 or q26 aberrations are found in 20-30% of the cases; the t(9;22) is another recurrent chromosome aberrations in de novo AML-M7.
Trisomy 19 and 21 may occur in de novo as well as in secondary AML-M7. They are the most frequently occurring chromosome gains and they may be associated with any of the cytogenetic group listed above.

b) Children

The t(1;22)(p13;q13) is specifically associated with children AML-M7, being found in approximately half of the cases. The remaining patients may show +21 (irrespective of the association with Down syndrome), +19, +8. The karyotype may be normal in approximately 10% of the cases.

Cytogenetics molecular

Partial trisomy 19, involving the q13 band, can be shown to occur at a 20-30% incidence by comparative genomic hybridization.
The t(1;22)(p13;q13) fuses the OTT (RBM15) gene on 1p13 to the MAL (MLK1) gene on chromosome 22, leading to the OTT-MAL fusion gene on the derivative 22.

Genes involved and proteins

OTT (one twenty-two) or RBM15 (Rna-binding motif protein 15)

Location

1p13

MAL (Megakaryocytic acute leukemia) or MLK1 (megakaryoblastic leukemia-1)

Location

22q13

Result of the chromosomal anomaly

Hybrid gene

Note

The fusion gene OTT-MAL is on the der(22) chromosome and contains almost all of the sequences of each gene.

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This article should be referenced as such:

Cuneo A, Cavazzini F, Castoldi GL. Acute megakaryoblastic leukemia (AMegL), M7 acute non lymphocytic leukemia (M7-ANLL). Atlas Genet Cytogenet Oncol Haematol. 2004; 8(1):32-34.