Acute Myeloid Leukemia with Recurrent Cytogenetic Abnormalities
Acute Myeloid Leukemia with recurrent cytogenetic Abnormalities

-t(8;21)(q22;q22)(AML/ETO)
-inv(16) or t(16;16)
-t(15;17)
-11q23
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities
t(8;21)(q22;q22)
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)

- 5-12% of all AMLs, 1/3 of AML-M2 cases
- May present with myeloid sarcoma
- Bone marrow blasts may be less than 20%
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)

Morphology

- Bone marrow hypercellular
- Blasts with or without granules
- Auer rods frequent
- Eosinophils and basophils may be increased
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities

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**Immunophenotype**

- CD13+, CD33+, MPO+
- Often CD19+, CD56+, CD34+
- Sometimes TdT+ (dim)
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities $t(8;21)(q22;q22)$
Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)

- Responds frequently to aggressive therapy (high dose of Cytarabine)
- High complete remission rate with long term disease-free survival
Acute Myeloid leukemia with inv(16)(p13q22) or t(16;16) (p13;q22); (CBFb/MYH11)
Acute Myeloid leukemia with inv(16)(p13q22) or t(16;16)(p13;q22); (CBFb/MYH11)

Definition: AML-M4e plus chromosome abnormality (occasional cases not AML-M4e)
Acute Myeloid Leukemia with inv(16)(p13q22)

Epidemiology:
- 10-12% of AML
- Predominantly in younger patients, but can be at any age

Clinical features:
- May present with myeloid sarcoma
Acute Myeloid Leukemia with inv(16)(p13q22): Morphology and cytochemistry

Peripheral Blood: eosinophils not increased

BM: hypercellular, more than 20% blasts (may be lower than 20% in some cases)
-Most striking abnormality: eosinophils: immature granules, purple-violet in color, obscure cell morphology
-Auer rods may be seen
-3% or more blasts with MPO+ NSE+
-Neutrophils: sparse
Acute Myeloid Leukemia with inv(16)(p13q22)
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Acute Myeloid Leukemia with inv(16)(p13q22)

Immunophenotype:
- Myeloid marker: CD13, CD33, MPO
- Monocytic marker: CD14, CD4, CD11b, CD11c, CD64, CD36, lysozyme
- May show coexpression: CD2
Acute Myeloid Leukemia with inv(16)(p13q22)

Genetics:
- CBFb: heterodimer CBFα, transcription factor, binds to DNA motif like TCR enhancer
- MYH11: myosin heavy chain
- Use FISH, RT-PCR to identified submicroscopic case
Acute Myeloid Leukemia with inv(16)(p13q22)
Acute Myeloid leukemia with inv(16)(p13q22)

Fusion on q arm (leukemogenic)

5' CBFbeta MYH11 3'

Fusion on p arm

5' MYH11 CBFbeta 3'
Acute Myeloid Leukemia with
inv(16)(p13q22)

Cell origin: hematopoietic stem cells with potential
to differentiate to granulocytes and monocytes

Prognosis and predictive factors:
   Tx with Cytarabine, good response and prognosis
Acute promyelocytic leukemia
Acute promyelocytic leukemia

Definition:
- AML with t(15;17)(q22;q21);(PML/RARa)
- Variants t(v;17)
- Promyelocytes predominate: hypergranular and hypogranular types
Acute promyelocytic leukemia

Epidemiology:
- 5-8% AML
- age: mid life

Clinical features:
- typical (hypergranular) and microgranular APL: both with high risk for DIC
- microgranular APL: high WBC with numerous promyelocytes
- Basophilic cytoplasm of APL cells in patients previously treated with ATRA (relapse)
Morphology and cytochemistry

- Hypergranular APL: kidney-shaped, bilobed, dense large granules;
  “Faggot” cells: bundles of Auer rods
  MPO: (++)
- Microgranular (hypogranular): bilobed (butterfly, dumbbell) promyelocytes, MPO(++) vs (- or + in monocytes)
- BM: hypercellular, abundant cytoplasm, convoluted nuclei
Acute promyelocytic leukemia

Hypergranular

Hypogranular
Acute Promyelocytic Leukemia

Hypergranular variant

Hypogranular variant
APL hypergranular

Faggots or Sultan bodies:

EM: hexagonal arrangement of tubular structures with a specific periodicity of 250 um in contrast to 6-20 laminar periodicity of other Auer rods
Acute promyelocytic leukemia
APL hypogranular
Acute promyelocytic leukemia

**Immunophenotype:**
- CD33, homogenous, bright
- CD13, heterogeneous
- CD34(-)
- CD15(-)

Frequent CD2 and CD9 co-expression

PML Ab stain (Imunocytochemistry): nuclear multigranular vs speckled in normal promyelocytes or other blasts of AMLs
Acute promyelocytic leukemia

Features of APL with variant translocations

1) t(11;17)(q23;q21), PLZF on chr11
   Several cases reported,
   No Auer rods, regular nuclei, pseudo Pelger-Huet,
   Resistant to ATRA

2) t(5;17)(q23;q12), NPM on chr 5
   Rare, atypical APL, no Auer rods, respond to ATRA

3) t(11;17)(q13;q21), NuMA on chr 11
Acute promyelocytic leukemia

Genetics:

$t(15;17)(q22;q21)$
Acute promyelocytic leukemia

Cell of origin: Myeloid stem cell with potential to differentiate to granulocytic lineage

Prognosis: Favorable
Use of retinoids in combinatorial protocols with anthracycline-based chemotherapy for front line treatment currently results in long-term survival and potential cure in at least 60% of newly diagnosed patients.
Acute myeloid leukemia with 11q23(MLL) abnormalities
Acute myeloid leukemia with 11q23(MLL) abnormalities

Definition: AML, monocytic myelomonocytic feature (M4, M5), occasional M1, M2

Epidemiology: 5-6% of AML, more in children
Two clinical groups:
- infants
- therapy-related, topoisomerase II inhibitors
  (translocation of chromosome 11 and 4, 9, or 19)
Acute myeloid leukemia with 11q23(MLL) abnormalities

Clinical Features:

- DIC
- myeloid sarcoma (tissue infiltration: gingiva, skin)
Acute myeloid leukemia with 11q23(MLL) abnormalities

Morphology and cytochemistry:

NSE(++) , MPO(-)

(1) monoblasts:
- large
- abundant basophilic cytoplasm
- pseudopods
- round nuclei
- lacy chromatin
- 1-2 nucleoli

(2) promonocytes:
- cytoplasmic granules, vacuoles
- nuclear folds
Acute myeloid leukemia with 11q23(MLL) abnormalities
Acute myeloid leukemia with 11q23(MLL) abnormalities

Monoblasts and promonocytes

NSE
Acute myeloid leukemia with 11q23(MLL) abnormalities

Immunophenotype:

- Myeloid: CD13, CD33(+)
- Monocytic: CD14, CD4, CD11b, CD11c, CD64, CD36, Lysozyme(+)
- CD34(-)
Acute myeloid leukemia with 11q23(MLL) abnormalities

Genetics:

Human homolog of Drosophila trithorax gene, develop regulator HRX (MLL) at band 11q23 -30 different partners for 11q, most common: chromosome 9, 19 in pediatric AML, partial tandem duplication of MLL in some AML
Acute myeloid leukemia with 11q23(MLL) abnormalities

**Cell origin:** hematopoietic stem cell with multilineage potential

**Prognosis:** intermediate survival