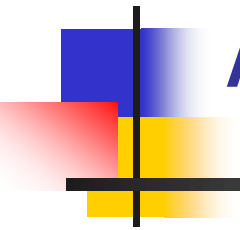
# Acute Myeloid Leukemia with Recurrent Cytogenetic Abnormalities



# 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)

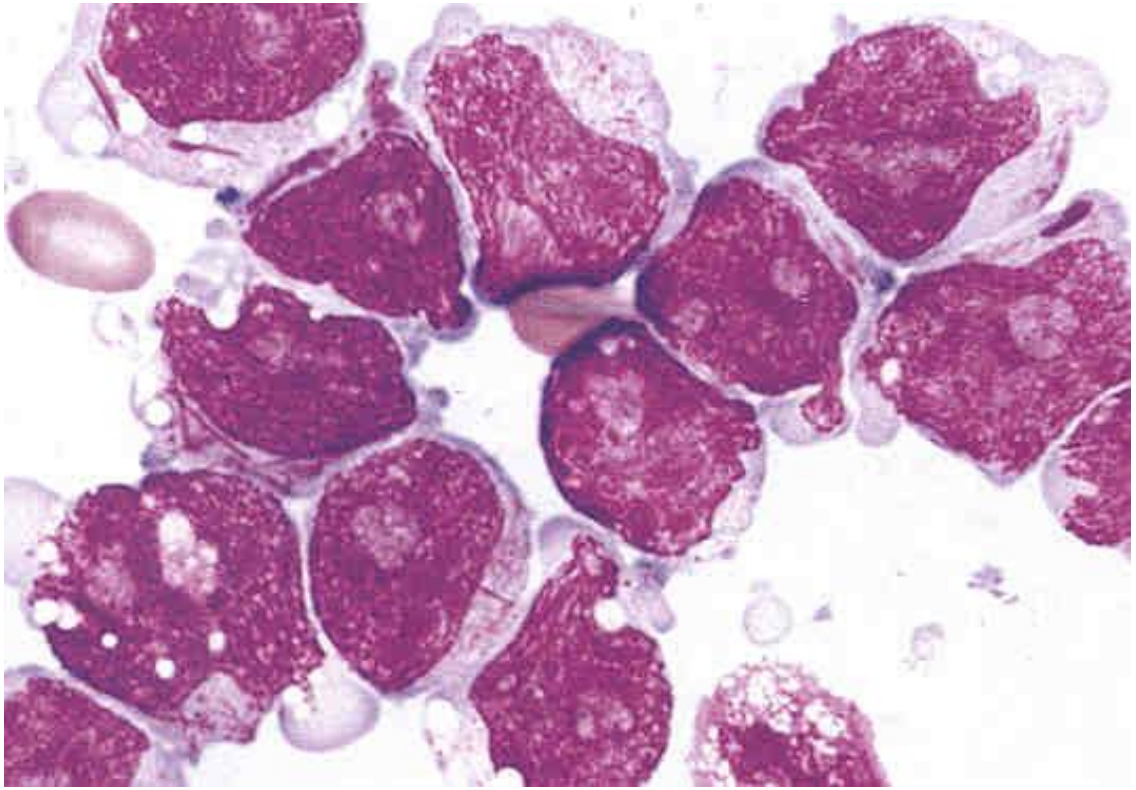
- 5-12% of all AMLs,
  1/3 of AML-M2 cases
- May present with myeloid sarcoma
- Bone marrow blasts may be less than 20%

# 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 t(8;21)(q22;q22)



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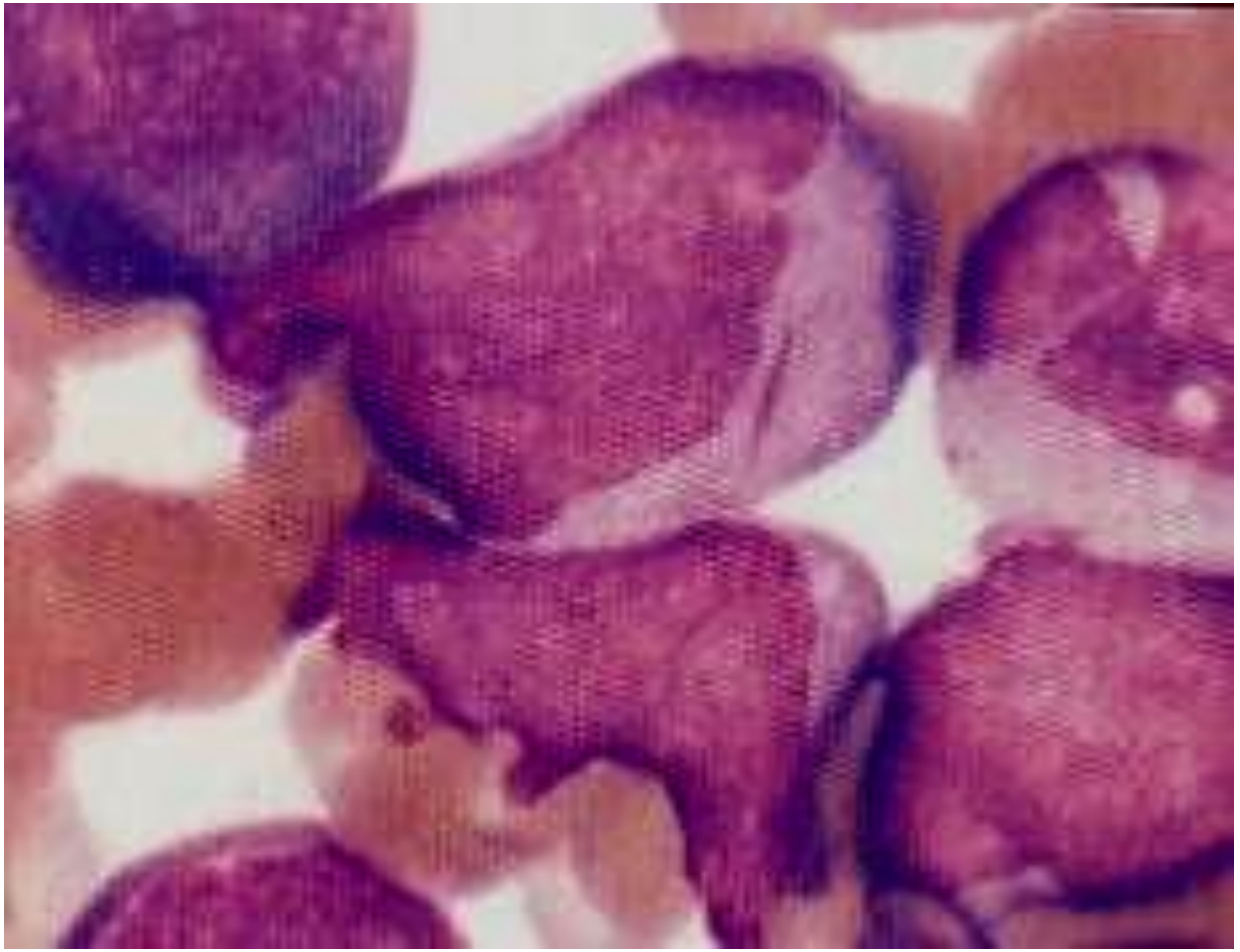
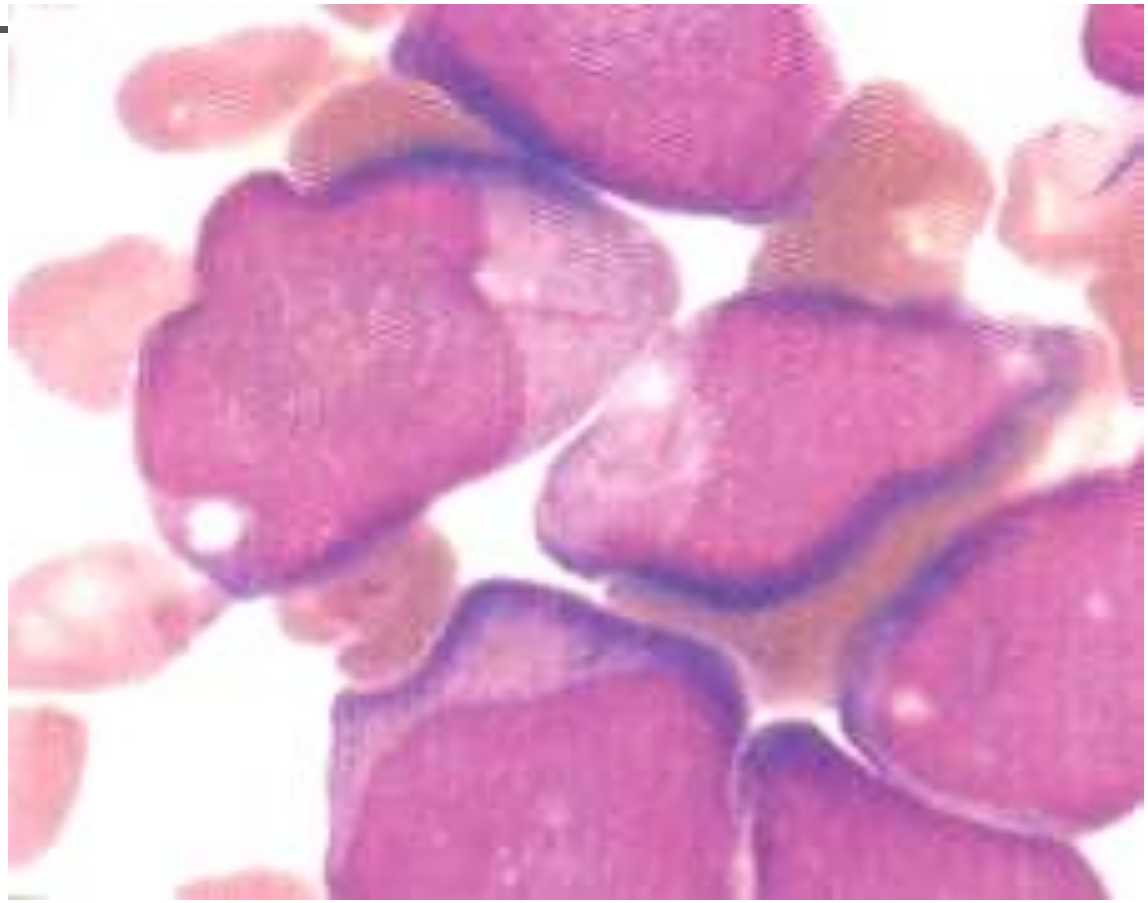


# Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)



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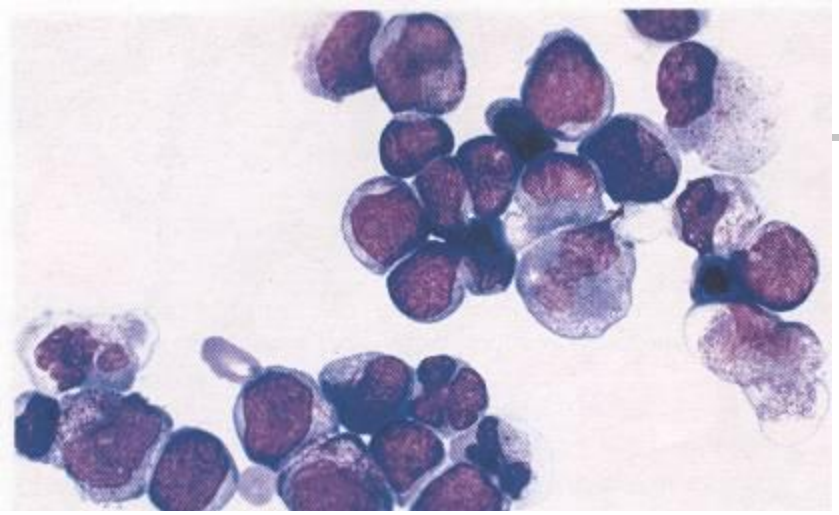
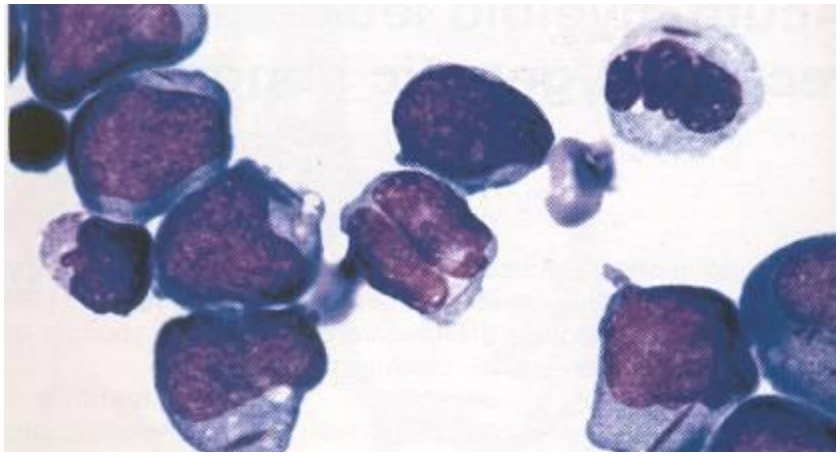
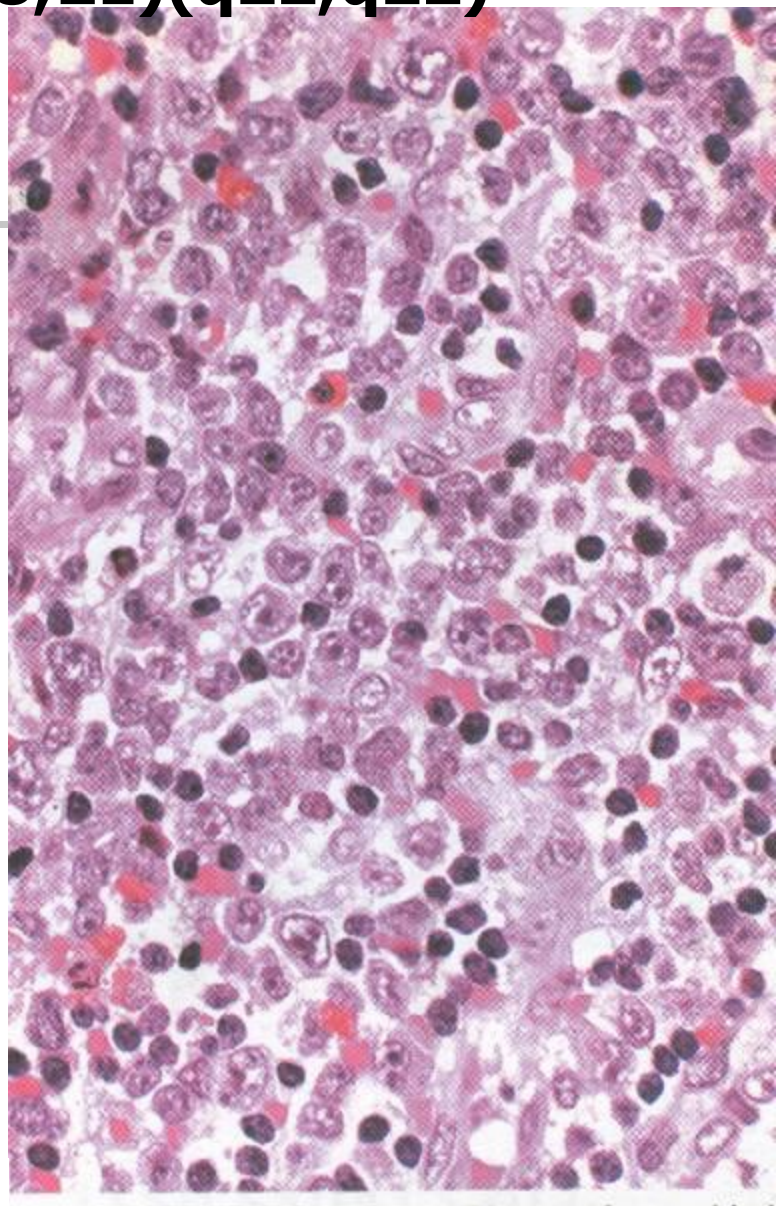




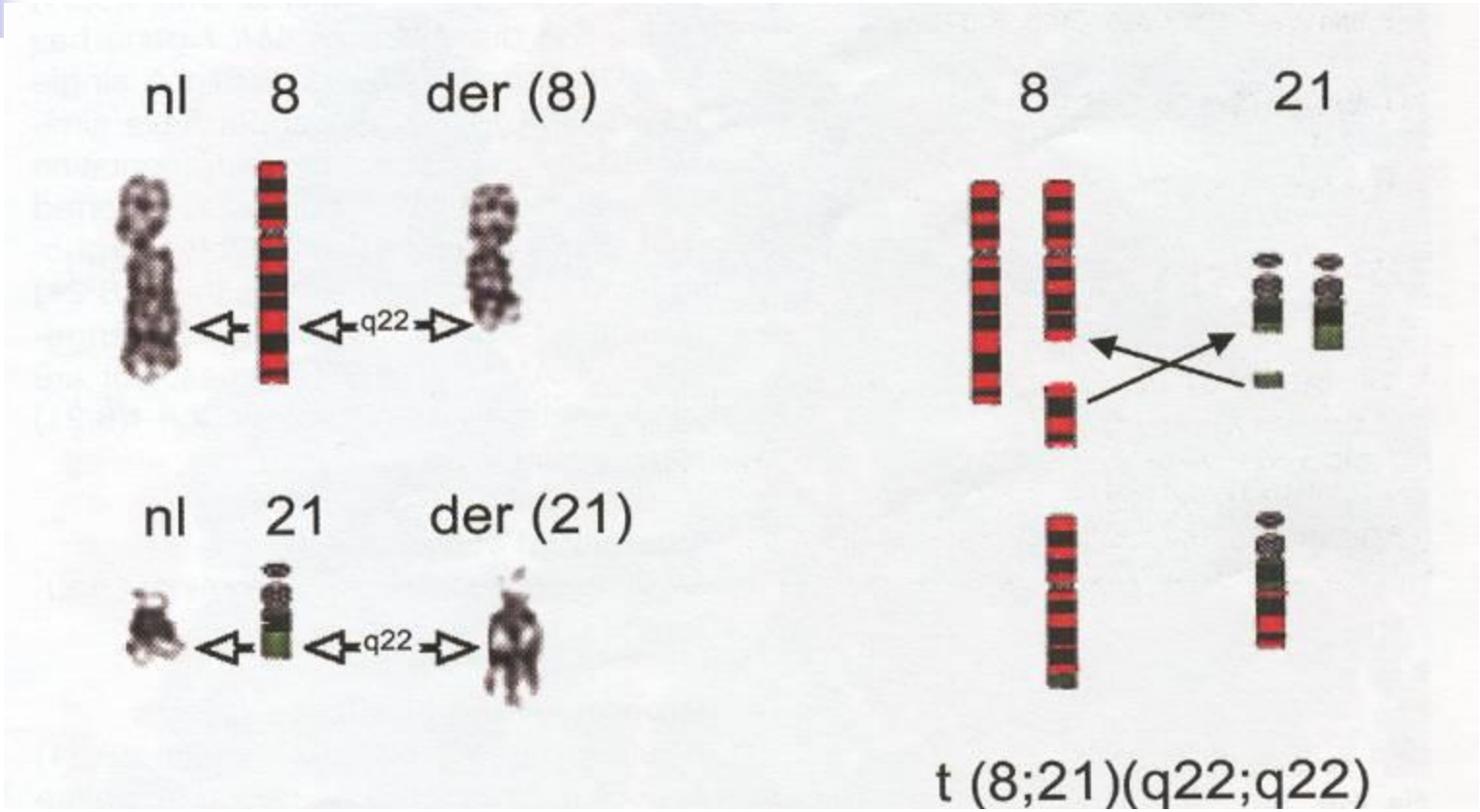


# Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)

## 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

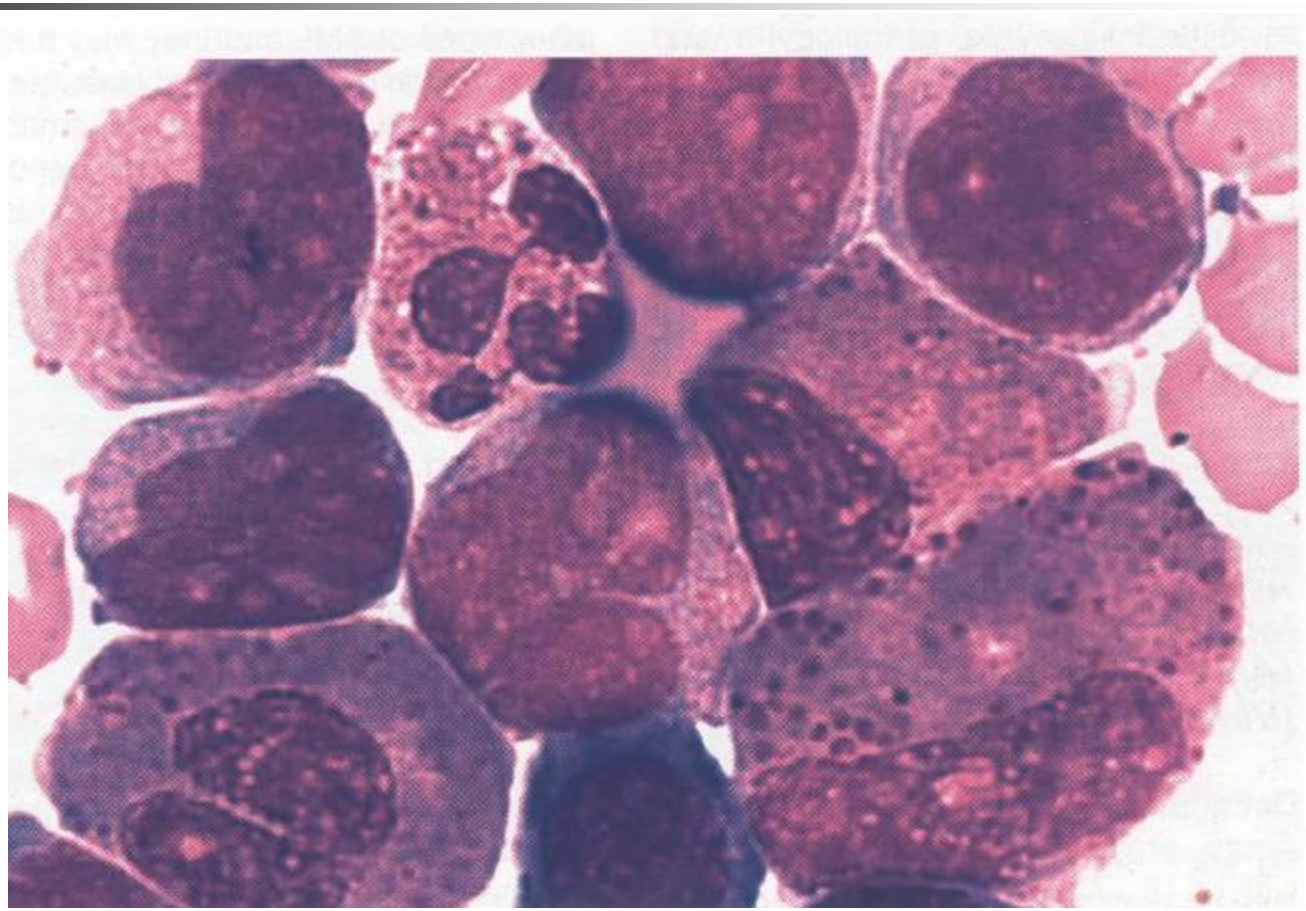
Clinical features:
-May present with myeloid sarcoma

# **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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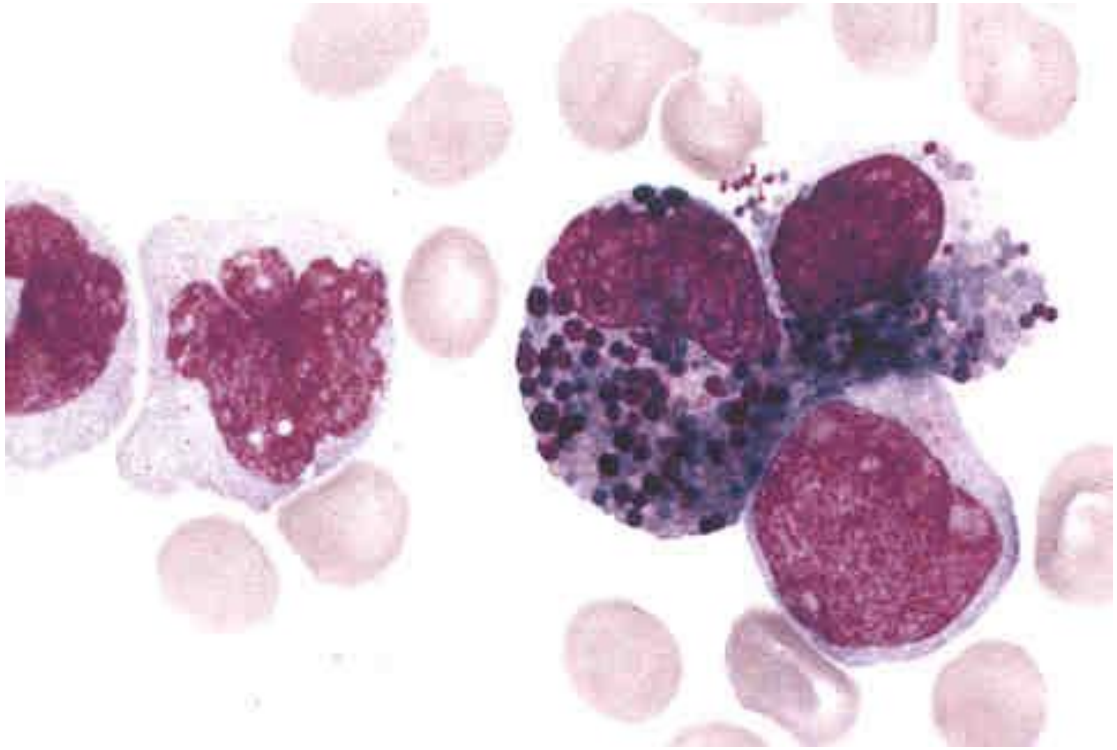


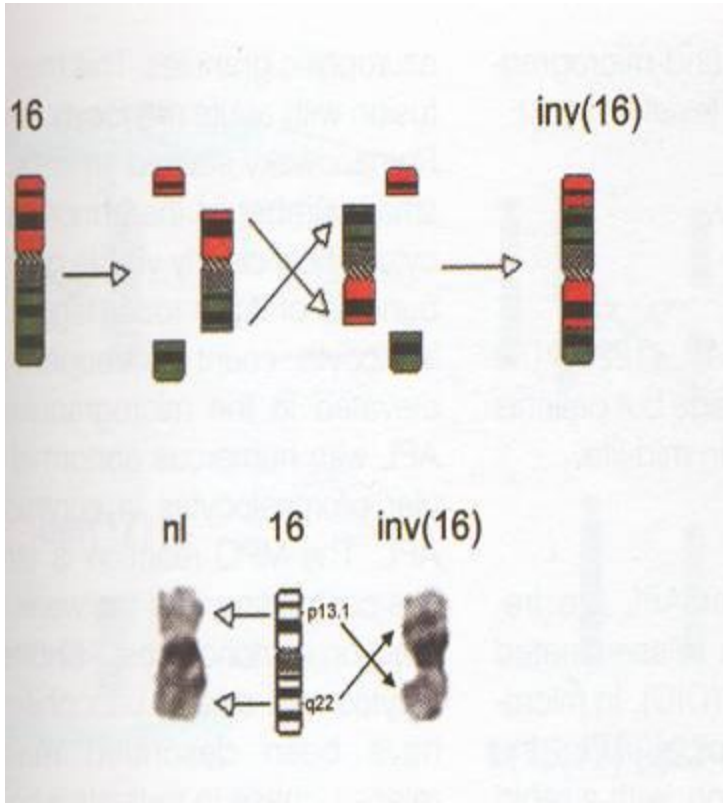
# **Acute Myeloid Leukemia with** inv(16)(p13q22)

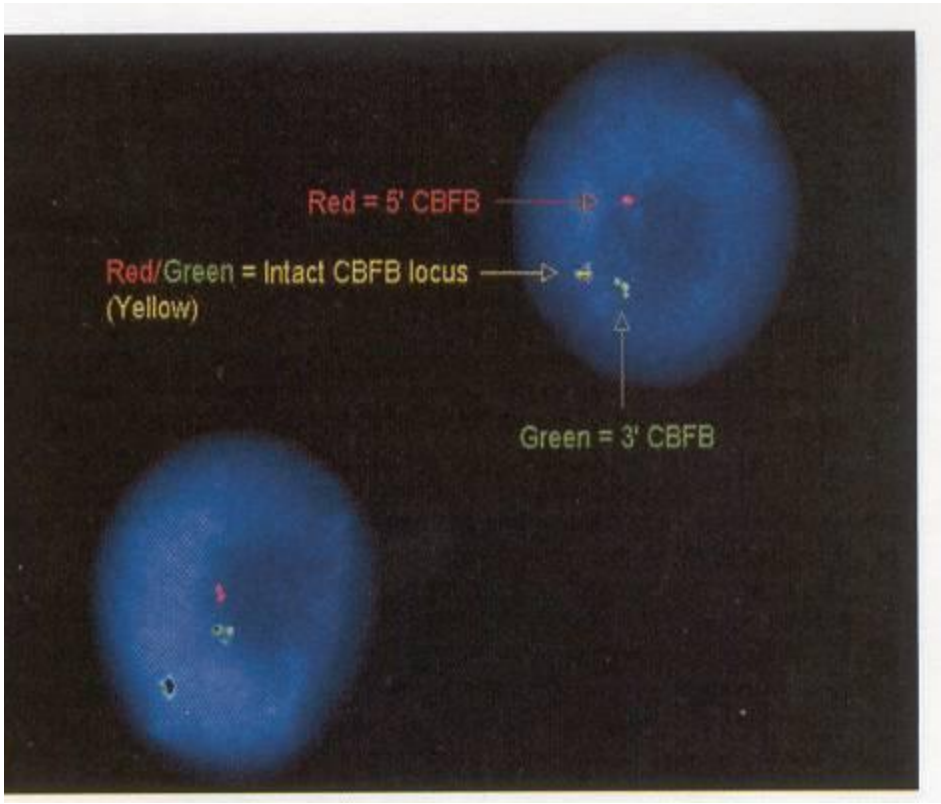
Immunophenotype:
-Myeloid marker: CD13, CD33, MPO
-Monocytic marker: CD14, CD4, CD11b, CD11c,
CD64, CD36, lysozyme
-May show coexpression: CD2

# **Acute Myeloid Leukemia with** inv(16)(p13q22)

Genetics:
-CBFb: heterodimer CBFa, transcription factor,
binds to DNA motif like TCR enhancer
-MYH11: myosin heavy chain
-Use FISH, RT-PCR to identified submicroscopic case

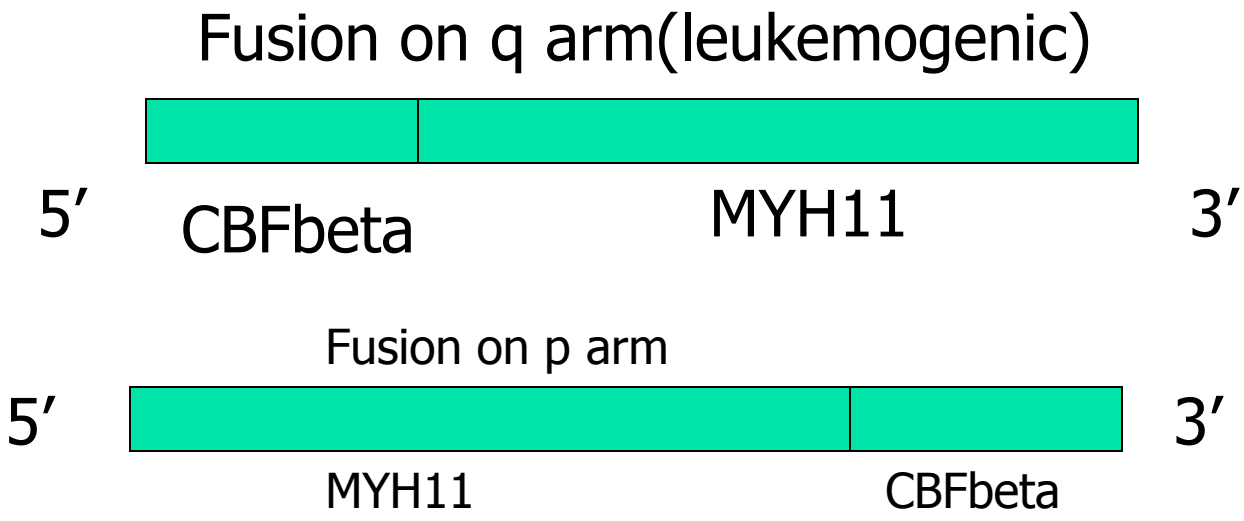
# Acute Myeloid Leukemia with inv(16)(p13q22)




FISH

# **Acute Myeloid leukemia with** inv(16)(p13q22)



# **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)

# Acute promyelocytic leukemia

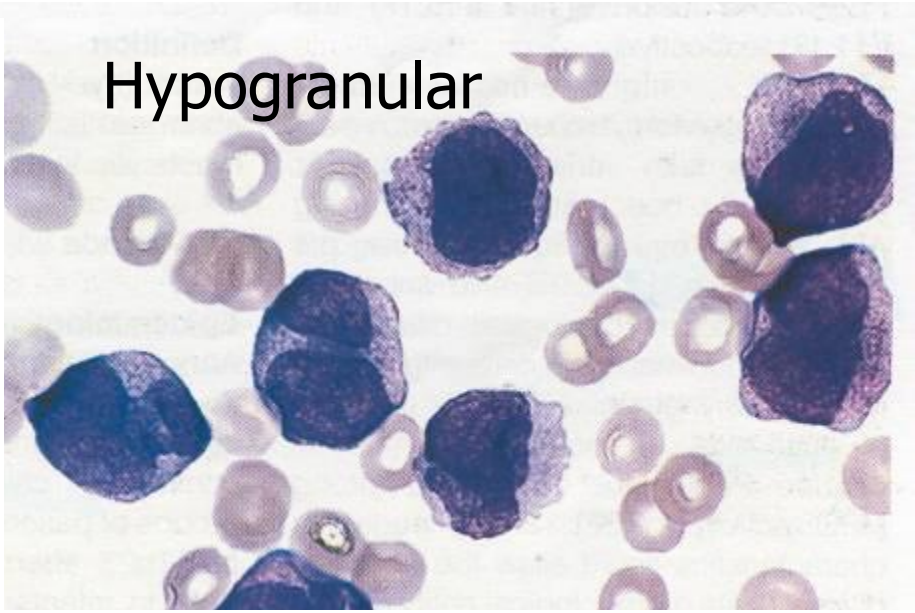
**Morphology and cytochemistry**

-Hypergranular APL: kidney-shaped, bilobed,
dense large granules;
"Faggot" cells: bundles of Auer rods
MPO: (++)

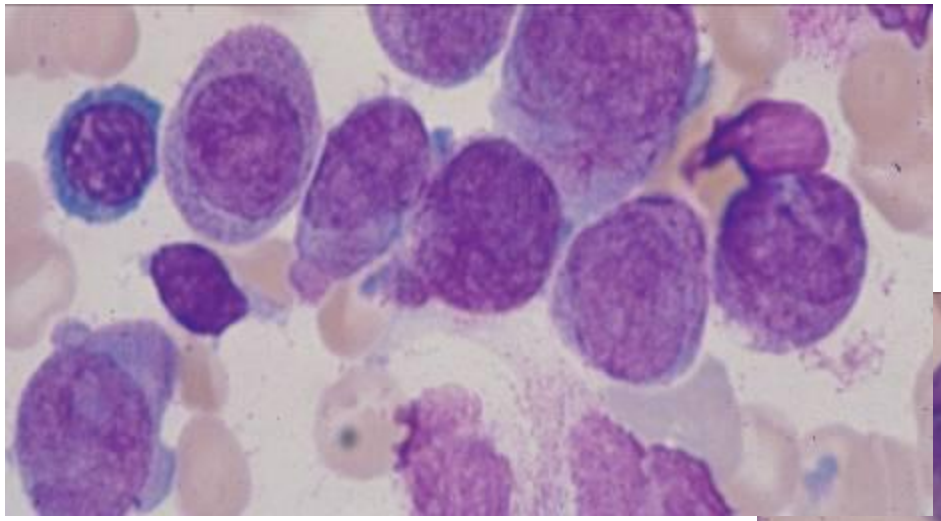
-Microgranular(hypogranular): bilobed (butterfly, dumbbell)
promyelocytes, MPO(++) vs (- or + in monocytes)

-BM: hypercellular, abundant cytoplasm, convoluted nuclei

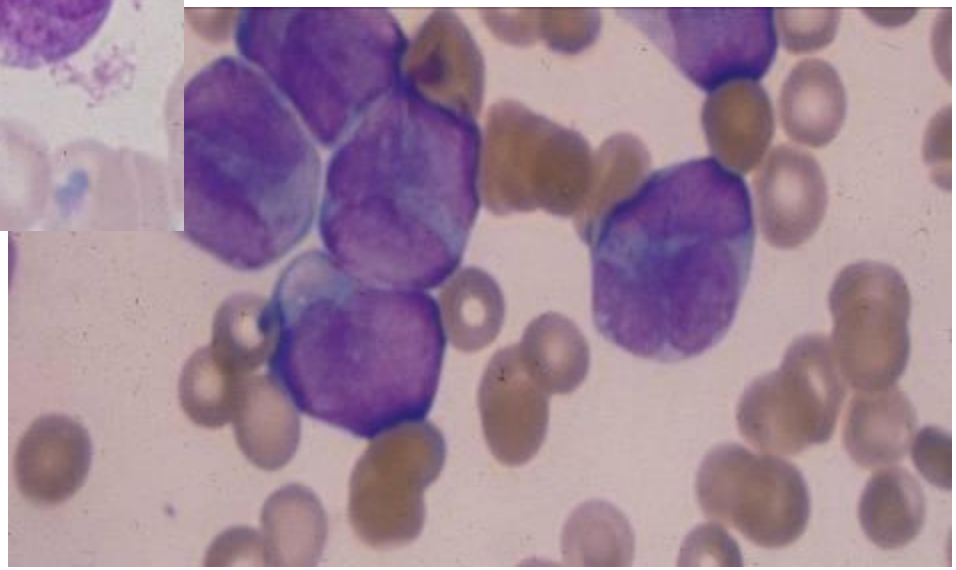
# Acute promyelocytic leukemia

# Acute Promyelocytic Leukemia

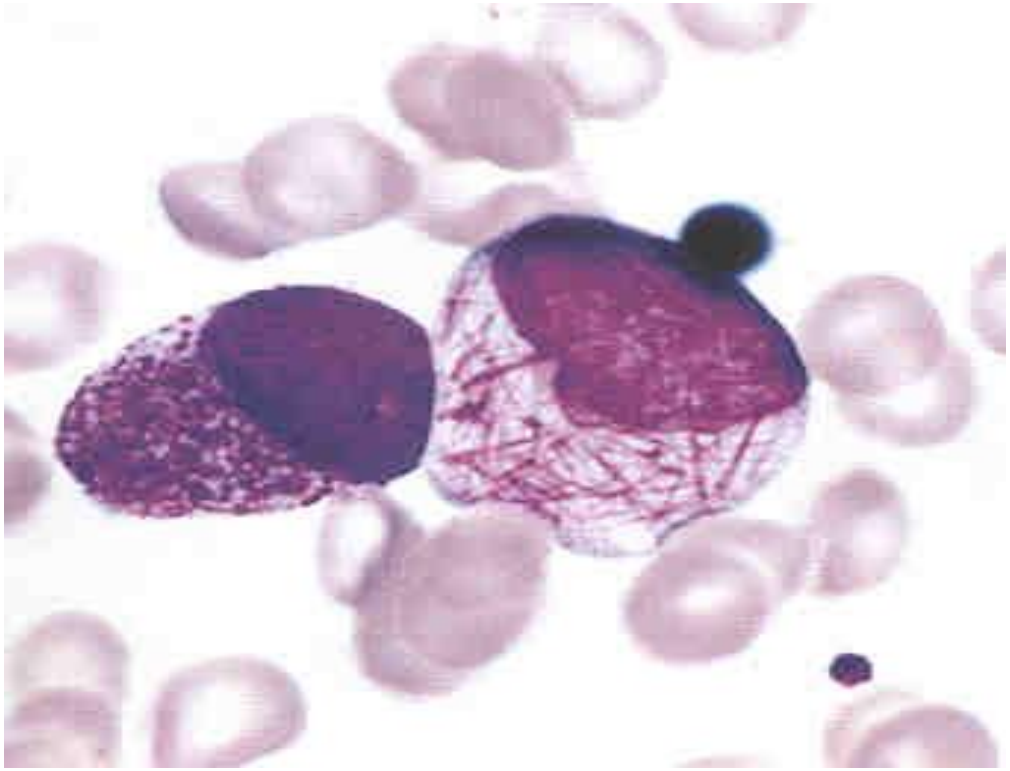


**Hypergranular variant**



**Hypogranular variant**

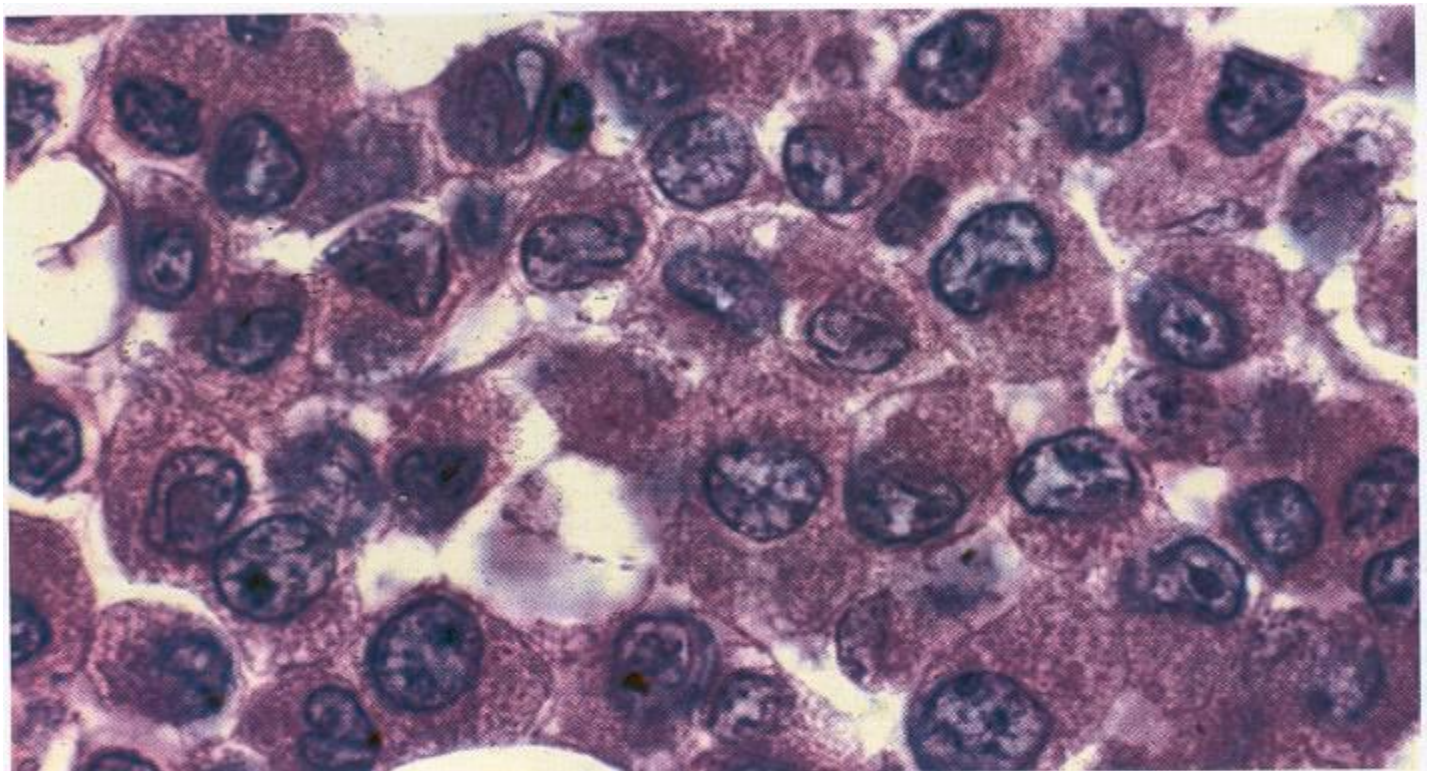
# APL hypergranular



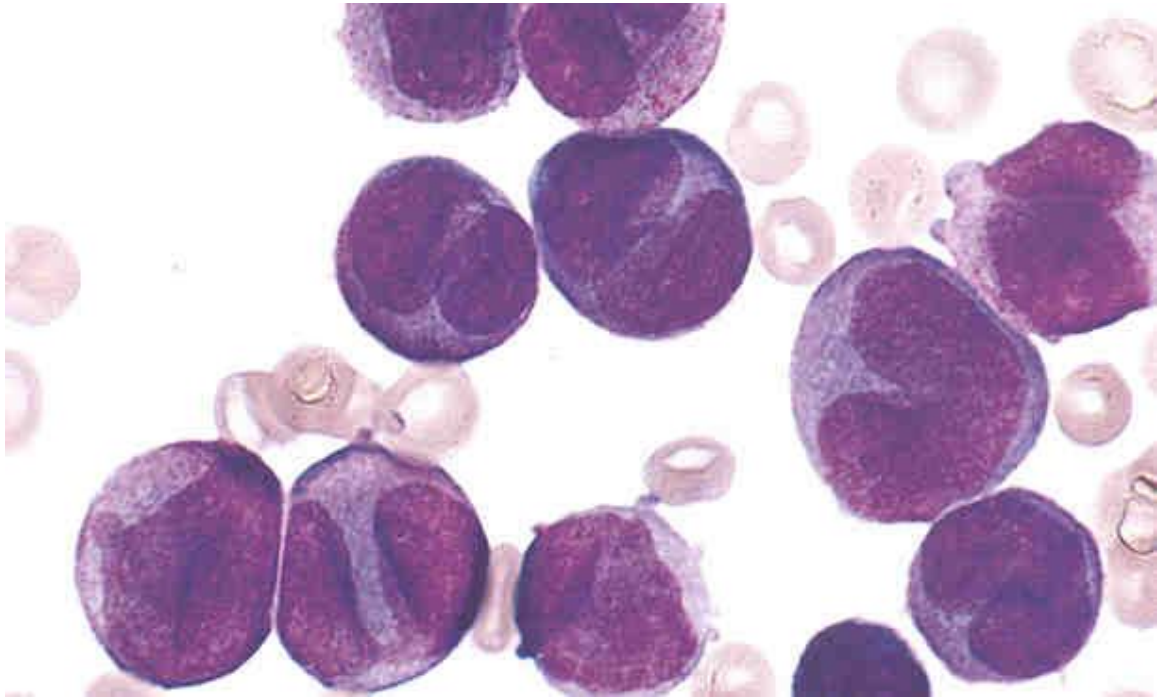
**Faggots or Sultan bodies:**

EM: hexagonal arrangement of tubular structures with a specific periodicity of 250 um in contrast to 6-20 laminar periodocity 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

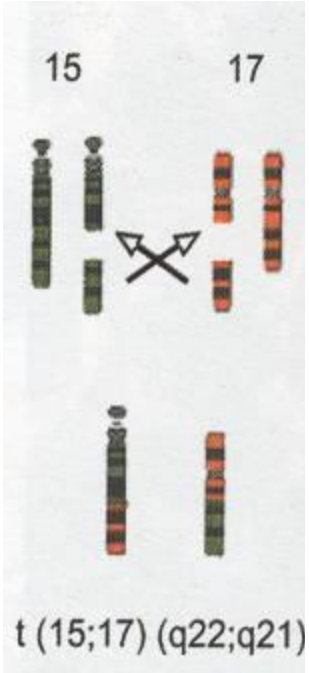
# Acute promyelocytic leukemia

**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:



# 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

## Clincal Features:

May present with
-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

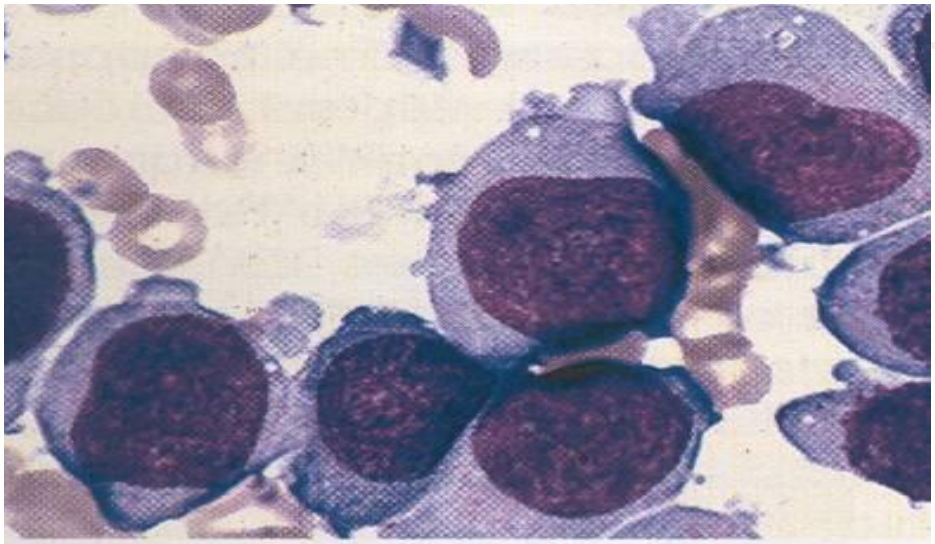
1-2 nucleoli

(2) promonocytes:

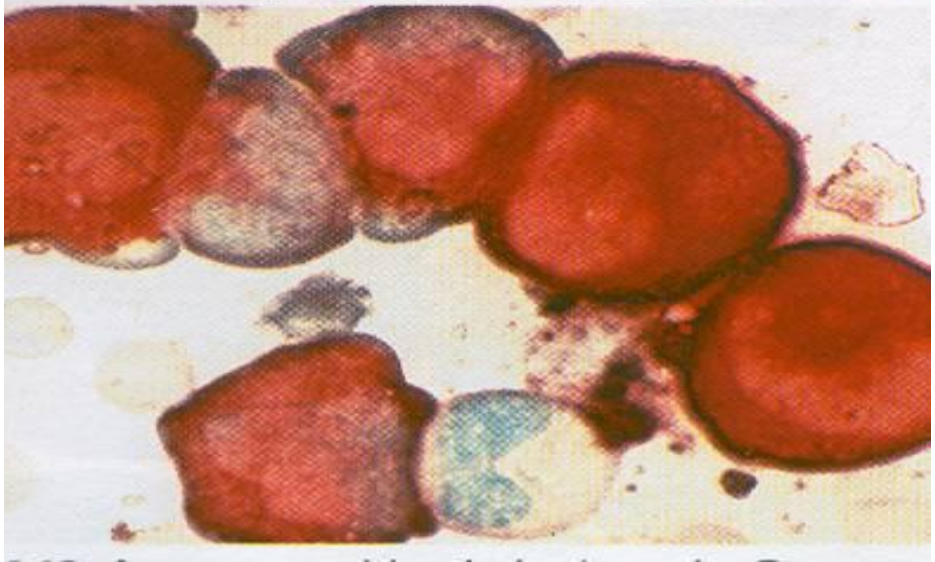
cytoplasmic granules, vacuoles

nuclear folds

# Acute myeloid leukemia with 11q23(MLL) abnormalities

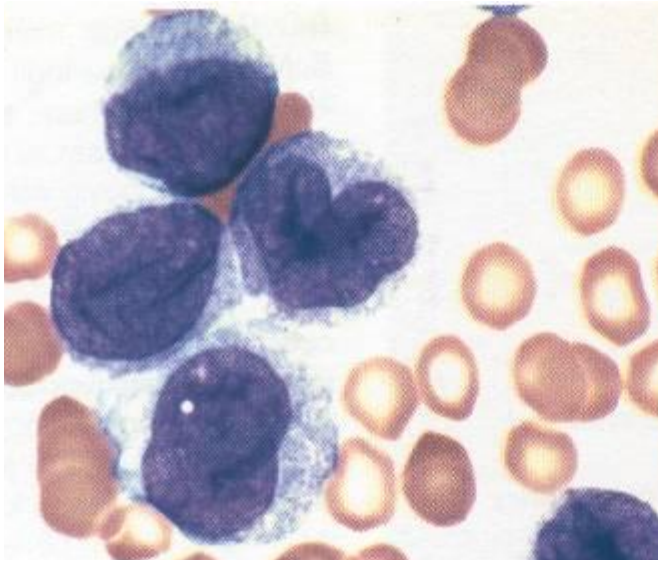


Monoblasts

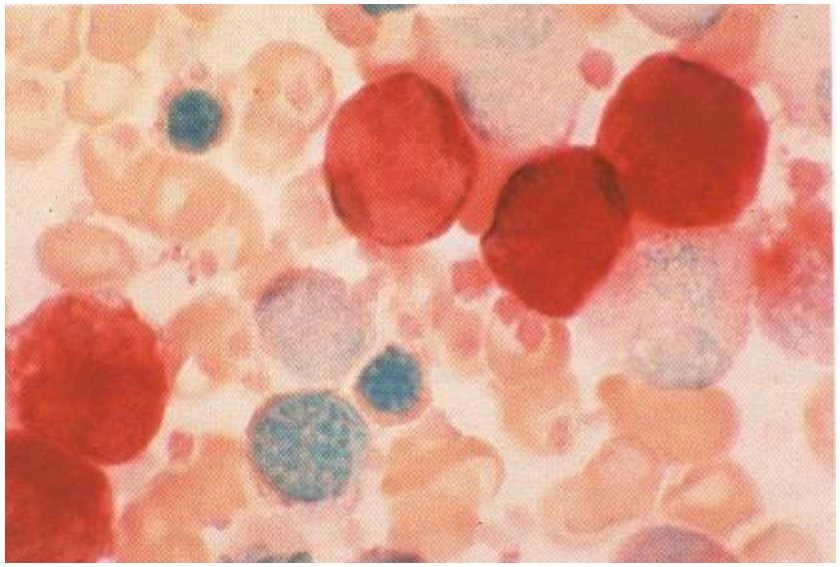


NSE

# 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