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Leukaemia Section
Short Communication

t(9;11)(p21;q23) KMT2A/MLLT3

Jeroen Knijnenburg, H. Berna Beverloo

Department of Clinical Genetics, Erasmus Medical Center, Rotterdam, The Netherlands.
b.beverloo@erasmusmc.nl

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Huret JL. t(9;11)(p22;q23). Atlas Genet Cytogenet Oncol Haematol 1997;1(2)

Abstract

Review on t(9;11)(p21;q23), with data on clinics, and the genes involved.

Keywords
chromosome 9; chromosome 11; acute myeloid leukemia; KMT2A; MLLT3.

Clinics and pathology

Disease

Acute myeloid leukemia (AML).

Phenotype/cell stem origin

Most often found in acute monocytic and myelomonocytic leukaemias, although occasionally also seen in AML with or without maturation (WHO 2008).
M5 most often (especially M5a, M4); both found in de novo and therapy related AML with antitopoisomerase II drugs (epipodophyllotoxins, anthracyclins, actinomycin D).
Immunophenotype typically shows positivity for CD11, CD13, CD15 and CD33, but less often shows positivity for CD14, CD34 and lymphoid markers.

Epidemiology

May occur at any age, but is more common in children, being present in 5-12% of paediatric and 1-2% of adult AML, and equally common in males and females.

Clinics

Organomegaly, frequent central nervous system (CNS) involvement, especially in de novo cases; no preceding myelodysplastic phase, unlike classic therapy related AML with chromosome 5 and/or 7 involvement, short interval from initial drug therapy (may even be of 1-2 yrs). Patients may present with disseminated intravascular coagulation and may have tissue infiltration.

Cytology

Absence of trilineage dysplasia, unlike classic therapy related AML.

Prognosis

Survival is described as poor to intermediate, being superior to AML with other KMT2A translocations.

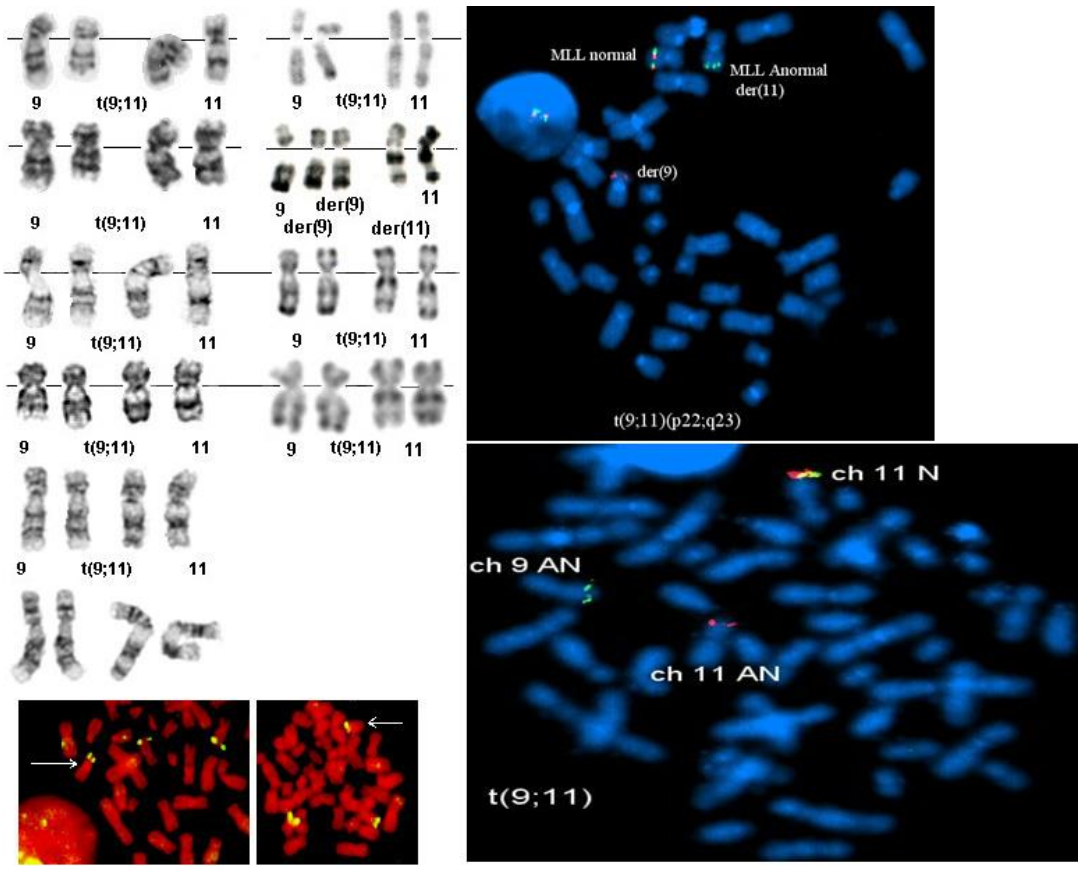
Cytogenetics

Cytogenetics morphological

May easily be overlooked. Previously described as t(9;11)(p22;q23) based on band estimation, but nowadays it is known that MLLT3 is located in 9p21.3 based on molecular positioning.

Cytogenetics molecular

FISH or RT-PCR is indicated in cases with poor chromosome morphology or in cases where the translocation is expected in cases based on morphology, immunophenotype or clinical presentation.



t(9;11)(p21;q23) G- banding (left) - Courtesy Jean-Luc Lai and Alain Vanderhaegen (top 2), Courtesy Diane H Norback, Eric B Johnson, and Sara Morrison-Delap, UW Cytogenetic Services (middle 2 and bottom 2); R-banding (right): top: - Courtesy Pascale Cornillet-Lefebvre and Stéphanie Struski, center top: t(9;11)+der(9)t(9;11) - Courtesy Christiane Chharrin; bottom 2: - Courtesy Hossein Mossafa. FISH (left) - Courtesy Pascale Cornillet-Lefebvre and Stéphanie Struski. The probe is MLL; one signal is on the normal 11, one signal on the der(11), and one signal (arrow) on the der(9); FISH (right) - Courtesy Hossein Mossafa (AN: abnormal).

Additional anomalies

None in 70% of cases, +8 in 20%, less frequently: additional trisomies of chromosome 6, 19 or 21.

Variants

Complex 3 way translocations t(9;11;Var) involving a (variable) third chromosome and insertions have been described, and showed that der(11) is the crucial on

Genes involved and proteins

MLLT3 (myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 3)

Location

9p21.3

Protein

Contains a nuclear targeting sequence; transcriptional activator; nuclear localisation.

KMT2A (myeloid/lymphoid or mixed lineage leukemia)

Location

11q23.3

Protein

Contains two DNA binding motifs (a AT hook, and Zinc fingers), a DNA methyl transferase motif, a bromodomain; transcriptional regulatory factor; nuclear localisation.

Result of the chromosomal anomaly

Hybrid gene

Description

5' KMT2A- 3' MLLT3; variable breakpoints.

Fusion protein

Description

N-term -- AT hook and DNA methyltransferase from KMT2A (1444 amino acids) fused to the 192

C-term amino acids from MLLT3 (as breakpoints are variable, this is only an exemple); 180 kDa.

Expression / Localisation
Nuclear localisation.

To be noted

You may also have a glance at 11q23 rearrangements, which gives an overview of related diseases.

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