

Juvenile Chronic Myelogenous Leukemia (JCML)

Identity

Note the proper terminology of this disorder is controversial; many authors, including the European Working Group on MDS in Childhood favor the term JMML; another working group suggests using the term JMML syndrome with a qualifier with or without [monosomy 7](#) or 7q-

Other names Juvenile myelomonocytic leukemia (JMML)
Juvenile myelomonocytic leukemia syndrome (JMML syndrome)

Clinics and Pathology

Disease JCML is a chronic myeloproliferative disorder that typically affects young children: more than 95% of cases are diagnosed before age 4

Phenotype / cell stem evidence exists for leukemic involvement of CD34-positive stem cells and monocyte-macrophage, erythroid, and B-lymphoid lineages in origin cases with cytogenetic abnormalities

Epidemiolog annual incidence is estimated to be roughly 4/million; median age 1-4 y
yrs; sex ratio: 1.4M/1F

Clinics splenomegaly, lymphadenopathy, and skin rash are common; typical peripheral blood findings include leukocytosis (usually less than $100 \times 10^9/L$), monocytosis, and thrombocytosis with variable degree of left shift; myeloblasts average about 5% of total nucleated cells; elevation of fetal hemoglobin (hbF) very common; absence of the Philadelphia chromosome in all cases

proposed clinical criteria from the International Juvenile Myelomonocytic Leukemia Working Group includes: 1. white blood cell count $> 13 \times 10^9/L$ (corrected for nucleated red blood cells)
2. absolute monocyte count $> 1 \times 10^9/L$ (corrected)
3. presence of immature myeloid precursors (myelocytes, promyelocytes, and myeloblasts) in the peripheral blood
4. bone marrow aspirate revealing $< 30\%$ blasts
5. no Ph chromosome on cytogenetic assessment

about 15% of cases are associated with [neurofibromatosis type 1](#) ([NF-1](#) mutation)

Pathology blood: leukocytosis, monocytosis, left shift in myeloid maturation, circulating nucleated red blood cells

bone marrow: hypercellular marrow with mildly increased M:E ratio (typically 5:1), dispersed erythroid elements, and decreased numbers of megakaryocytes; dysplasia is usually not prominent

Treatment intensive chemotherapy and all trans retinoic have not been shown to induce durable remissions; complete remissions have been achieved with stem cell transplantation

Prognosis the disease is uniformly fatal when treated with conventional chemotherapy; among those who undergo bone marrow transplantations, the majority ultimately relapse, with an overall survival

rate of 25%

Cytogenetics

Cytogenetics other than the frequent association with monosomy 7, no consistent Morphological cytogenetic abnormalities have been identified; whether the infantile monosomy 7 syndrome is distinct from JCML is controversial

Genes involved and Proteins

Note mechanisms of Oncogenesis:
JCML patients show spontaneous growth of granulocyte-macrophage colony forming units (CFU-GM) from peripheral blood, which appears to be the result of hypersensitivity to GM-CSF, [IL-3](#), or [SCF](#); cases associated with NF-1 are likely to be the result of constitutive activation of the [Ras](#) pathway as a result of decreased GTPase activity although there is also evidence of a GAP independent function; up to 30% of cases show mutations in [K-ras](#) and [N-ras](#); the importance of the RAS pathway has been confirmed in mouse models with targeted disrupted of Nf-1; recently data suggest that [TNF \$\alpha\$](#) produced by neoplastic cells may prevent expansion of hematopoietic progenitors

Bibliography

Loss of NF1 results in activation of the Ras signaling pathway and leads to aberrant growth in haematopoietic cells.

Bollag G, Clapp DW, Shih S, Adler F, Zhang YY, Thompson P, Lange BJ, Freedman MH, McCormick F, Jacks T, Shannon K.

Nat Genet 1996; 12: 144-148.

Medline [96154185](#)

Juvenile Chronic Myelogenous Leukemia.

Hess JL, Zutter MM, Castleberry RP, Emanuel PD.

Am J Clin Path 1996; 105: 238-248.

Medline [96187727](#)

Nf1 deficiency causes Ras-mediated granulocyte/macrophage colony stimulating factor hypersensitivity and chronic myeloid leukaemia.

Largaespada DA, Brannan CI, Jenkins NA, Copeland NG.

Nature Genetics 1996; 12: 137-143.

Medline [96154184](#)

Juvenile myelomonocytic leukemia: analyses of treatment results in the EORTC Children's Leukemia Cooperative Group (CLCG).

Lutz P, Zix-Kieffer I, Souillet G, Bertrand Y, Dhooge C, Rubie C, Mazingue F, Marguerite F, Machinud-Lacroix F, Riolland X, Plouvier E, Behar C, Vilmer E, Philippe N, Otten J.

Bone Marrow Transplantation 1996; 18: 1111-1116.

Medline [97126465](#)

Loss of heterozygosity of NF1 gene in juvenile chronic myelogenous leukemia with neurofibromatosis type 1.

Kai S, Sumita H, Fujioka K, Takahashi H, Hanzawa N, Funabiki T, Ikuta K, Sasaki H. Int J Hematol 1998; 68: 53-60.

Medline [98378790](#)

Nf1 regulates hematopoietic progenitor cell growth and ras signaling in response to multiple cytokines.

Zhang YY, Vik TA, Ryder JW, Srour EF, Jacks T, Shannon K, Clapp DW.
J Exp Med 1998; 187: 1893-1902.

Medline [98270918](#)

Myelodysplastic syndrome, juvenile myelomonocytic leukemia, and acute myeloid leukemia associated with complete or partial monosomy 7.

Hasle H., Arico M, Basso G, Biondi A, Rajnoldi AC, Creutzig U, Fenu S, Fonatsch C, Haas OA, Harbott J, Kardos G, Kerndrup G, Mann G, Niemeyer CM, Ptoszkova H, Ritter J, Slater R, Stary J, Stollmann-Gibbels B, Testi AM, van Wering ER, Zimmerman M.

Leukemia 1999; 13: 376-385.

Medline [99184532](#)

Alternative donor bone marrow transplantation for children with juvenile myelomonocytic leukemia.

Bunin N, Saunders F, Leahey A, Doyle J, Calderwood S, Freedman MH.
J Ped Hematol Oncol 1999; 21: 461-463.

Medline [20065717](#)

Nf1 and GM-CSF interact in myeloid leukemogenesis.

Birnbaum RA, O'Marcaigh A, Wardak Z, Zhang YY, Dranoff G, Jacks T, Clapp DW, Shannon KM.

Molecular Cell 2000; 5: 189-195.

Medline [20142671](#)

Evidence that juvenile myelomonocytic leukemia can arise from a pluripotential stem cell.

Cooper LJ, Shannon KM, Loken MR, Weaver M, Stephens K, Sievers EL.
Blood 2000; 96: 2310-2313.

Medline [20435367](#)

Myelodysplastic syndromes in children. A critical review of the clinical manifestations and management.

Novitzky N.

Am J Hematol 2000; 63: 212-222.

Medline [20170720](#)

Contributor(s)

Written 12-2000 Jay L. Hess

Citation

This paper should be referenced as such :

Hess JL . Juvenile Chronic Myelogenous Leukemia (JCML). Atlas Genet Cytogenet Oncol Haematol. December 2000 .

URL : <http://www.infobiogen.fr/services/chromcancer/Anomalies/JCMLID1099.html>

© Atlas of Genetics and Cytogenetics in Oncology and Haematology

