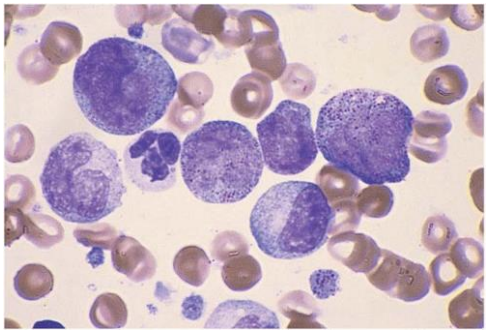
Cancer Association of South Africa (CANSA)

Fact Sheet on Acute Myelomonocytic Leukaemia

Introduction

Leukaemia is a cancer of the white blood cells. All blood cells are produced in the bone marrow, the spongy substance at the core of some of the bones in the body.



[Picture Credit: Acute Myelomonocytic Leukaemia Bone Marrow Aspirate]

Acute Myelomonocytic Leukaemia (AMML)

Acute Myelomonocytic Leukemia (AMML) is a form of Acute Myeloid Leukaemia that involves a proliferation of both neutrophil and monocyte precursors with 20% or more myeloblasts in the bone marrow.

Li, W., Cooley, L.D. & August, K. 2018.

"Juvenile myelomonocytic leukemia (JMML) is a rare aggressive childhood leukemia characterized by an excess proliferation of cells of granulocytic and monocytic lineages. The WHO classifies JMML with the myelodysplastic/myeloproliferative neoplasms. Myelodysplasia in JMML is usually minimal to mild. Auer rods have never been reported in JMML. We present a 2-year-old boy with splenomegaly, leukocytosis, thrombocytopenia, anemia, and excess myeloblasts with easily seen Auer rods, and marked dysgranulopoiesis and dyserythropoiesis. Conventional cytogenetic analysis showed a sole abnormality of t(3;5)(q25;q35). Microarray analysis showed a terminal 21 Mb region of copy-neutral loss of heterozygosity on 19q. Disease-related somatic NRAS mutation was detected. This case represents an unusual JMML with Auer rods and marked myelodysplasia. These unusual histopathologic features may be related to the t(3;5)(q25;q35). A t(3;5) with variable breakpoints has been reported in a small proportion of acute myeloid leukemias and myelodysplastic syndromes. To our knowledge, this is the first JMML case reported with this translocation."

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Xie, W., Hu, S., Xu, J., Chen, Z., Medeiros, L.J. & Tang, G. 2019.
"t(8;16)(p11.2;p13.3)/KAT6A-CREBBP is a rare recurrent cytogenetic abnormality associated with acute myeloid leukemia (AML). We report 15 cases with t(8;16)(p11.2;p13.3). All patients were adult and had AML: 13 women and 2 men, with a median age of 50 years. Ten patients had a history of malignancy and received cytotoxic therapies before therapy-related AML (t-AML), and five patients had de novo AML. All cases of AML showed monoblastic (n = 12) or myelomonocytic (n = 3) differentiation. Hemophagocytosis was observed in seven patients. All patients had t(8;16) in the stemline: seven had t(8;16) as the sole abnormality, two had one additional abnormality, and six had a complex karyotype. KAT6A/CREBBP rearrangement was confirmed by fluorescence in situ hybridization in 13 patients who had material available for analysis. All patients received induction chemotherapy, and 11 achieved complete remission after first induction. At the time of last follow-up, nine patients (eight t-AML and one de novo AML) died and six were alive, with a median overall survival of 18.2 months. The patients with de novo AML and/or patients with non-complex karyotype showed an "undefined" overall survival. We conclude that t(8;16)(p11.2;p13.3) commonly exhibits monoblastic or myelomonocytic differentiation and commonly arises in patients with a history of cancer treated with cytotoxic therapies. Patients with de novo AML with t(8;16) or t-AML with t(8;16) without adverse prognostic factors (e.g., complex karyotype) have a good outcome."

Incidence of Acute Myelomonocytic Leukaemia (AMML)
In providing the incidence figures of Leukaemia in South Africa, the outdated National Cancer Registry (2016) does not make provision for the reporting of the different types of Leukaemia – it also does not differentiate between acute and chronic Leukaemia - neither does it provide for different statistics for cases of adult and childhood Leukaemia - except in the 'Frequency of Histologically Diagnosed Cancer in South Africa' Section of the Registry .

According to the National Cancer Registry (2016) the following number of Leukaemia cases was histologically diagnosed in South Africa during 2016:

Group - Males 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	264	1:801	0,68%
Asian males	10	1:659	1,02%
Black males	135	1:1 233	1,03%
Coloured males	17	1:1 105	0,33%
White males	102	1:354	0,48%

Group - Females 2016	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	227	1:1 107	0,54%
Asian females	9	1:798	0,72%
Black females	117	1:1 846	0,59%
Coloured females	21	1:844	0,41%
White females	80	1:465	0,49%

The frequency of histologically diagnosed cases of Leukaemia in South Africa for 2016 was as follows (National Cancer Registry, 2016):

Group - Males 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	156	15	28	20	46	34	53	12
Asian males	1	0	1	1	1	3	2	0
Black males	45	11	22	10	18	15	13	1
Coloured males	1	1	2	3	4	2	4	0
White males	8	3	3	6	23	14	34	11

Group - Females 2016	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	38	26	17	26	31	37	37	15
Asian females	2	0	0	1	2	3	1	0
Black females	31	22	11	12	16	13	10	2
Coloured females	1	3	1	3	2	3	8	0
White females	4	1	5	10	11	18	18	13

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Signs and Symptoms of Acute Myelomonocytic Leukaemia

Signs and symptoms include:

- Looking very pale
- Fever
- Regular infections
- Bone pain
- Lethargy and fatigue
- Shortness of breath
- Easy bruising
- Having fever and sweating
- Unusual bleeding, such as frequent nosebleeds and bleeding from the gums

Diagnosis of Acute Myelomonocytic Leukaemia

The following tests may be done to assist in making a diagnosis of Acute Myelomonocytic Leukaemia:

Taking of complete medical history

- Physical examination
- Bone Marrow Biopsy
- Bone Marrow Aspiration
- Peripheral Blood Smear
- Complete Blood Count (CBC)
- Blood chemistry
- Blood coagulation test
- Flow cytometry
- Cerebrospinal fluid examination
- Immunohistochemistry
- Cytogenetics
- Fluorescent *in situ* hybridisation (FISH)

- Polymerase Chain Reaction (PCR)

Risk Factors for Acute Myeolomonocytic Leukaemia (AMML)

Factors that may increase one's risk for acute myelogenous leukaemia include:

- Increasing age
- Being male
- Previous cancer treatment
- Exposure to radiation
- Exposure to certain chemicals, such as benzene
- Smoking
- People who have had another blood disorder, such as myelodysplasia, polycythaemia vera or thrombocythaemia
- Certain genetic disorders, such as Down syndrome
- Many people with AMML have no known risk factors

Treatment of Most Cases of Acute Myelomonocytic Leukaemia (AMML)

Treatment of most cases of acute myeloid leukaemia (AMML) is usually divided into 2 chemotherapy phases and may include:

- Remission induction (often just called *induction*) – getting rid of as many leukaemia cells as possible
- Consolidation (post-remission therapy) - treatment is given to try to destroy any remaining leukaemia cells and help prevent a relapse

Treatment usually needs to start as quickly as possible after the diagnosis because AML can progress very quickly.

One or more of the following four types of standard treatments may be used:

- Chemotherapy
- Radiation therapy
- Stem cell transplant
- Other drug therapy

New types of treatment being tested in clinical trials:

- Targeted therapy

Patients may consider taking part in a clinical trial.
Follow-up tests may be needed. Patients should consult their treating physician in this regard.

Helbig, G., Chromik, K., Woźniczka, K., Kopińska, A.J., Boral, K., Dworaczek, M., Koclęga, A., Armatys, A., Panz-Klapuch, M. & Markiewicz, M. 2019.

"The administration of azacitidine (AZA) was found to be more effective than conventional care regimen (CCR) in patients with higher-risk myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML) with lower blast count. We designed a study to determine efficacy and safety of AZA therapy in "real life" patients with MDS, CMML and AML. The study included 83 patients (65% male) with a median age at diagnosis of 68 years. 43 patients were diagnosed with higher-risk MDS, 30 had AML and 10-CMML.

Median AZA dose was comparable between treated groups. AZA dose reduction was required for 44% of MDS, 17% of AML and 25% of CMML patients. Complete remission (CR) was achieved in 14% of MDS, 7% of AML and 10% of CMML patients. Overall response rate was following: 27% for MDS, 20% for AML and 20% for CMML. Estimated OS at 12 months was 75% for MDS, 60% for AML and 75% for CMML. Median follow-up for MDS/AML/CMML from AZA initiation to last follow-up was 9.0, 9.4 and 9.4 months, respectively. The most common toxicity of AZA therapy was myelosuppression and infections. AZA treatment was effective in a limited number of patients with acceptable safety profile."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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https://www.mayoclinic.org/diseases-conditions/acute-myelogenous-leukemia/basics/symptoms/con-20043431
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