PRIMEVIEW

ACUTE MYELOID LEUKAEMIA

nature REVIEWS DISEASE PRIMERS

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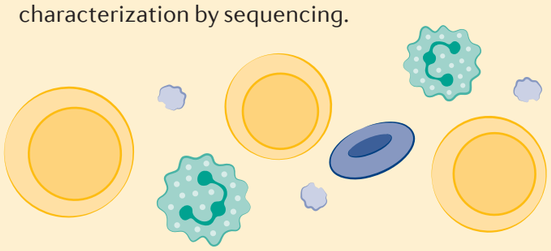
Acute myeloid leukaemia (AML) is a malignant disorder of haematopoietic stem cells (HSCs) or progenitor cells, leading to an expansion of immature myeloid precursors (myeloblasts) at the expense of their terminally differentiated counterparts, such as red blood cells, platelets and white blood cells.

DIAGNOSIS

AML has a rapid onset and can progress to terminal stages within weeks or months if left untreated. The clinical presentation of AML at diagnosis varies from an incidental finding on a routine blood test through to a life-threatening illness. Typical features reflect bone marrow failure and include fatigue and shortness of breath due to anaemia, recurrent infections due to neutropaenia and an increased tendency to bruise due to thrombocytopaenia. AML is diagnosed on the basis of full blood cell counts, the accumulation of myeloblasts in the bone marrow and blood, immunophenotyping by flow cytometry, cytogenetic profiling by karyotying and/or fluorescence *in situ* hybridization and molecular characterization by sequencing.



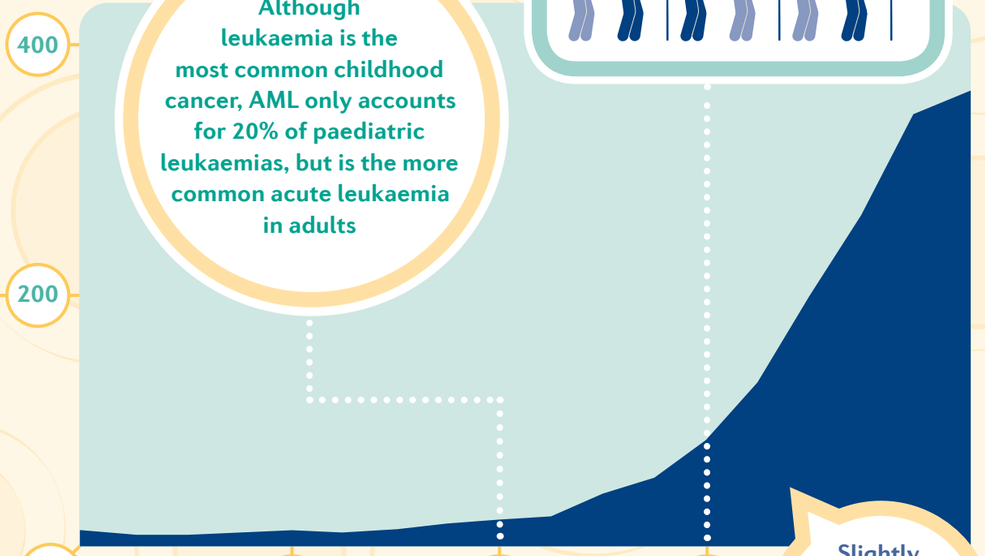
The risk of developing AML is moderately increased by exposure to DNA-damaging agents, including ionizing radiation (usually radiotherapy) and cytotoxic chemotherapy, genetic predisposition and certain inherited disorders (such as Down syndrome). However, the vast majority of patients do not have any of these predisposing risk factors.

EPIDEMIOLOGY

White people may have a better survival rate when treated than other ethnic groups, as do people with a higher socioeconomic status

Although leukaemia is the most common childhood cancer, AML only accounts for 20% of paediatric leukaemias, but is the more common acute leukaemia in adults

The median age of diagnosis is approximately 70 years, with a rise in the age-related incidence rates from around 40 to 50 years of age and a steep increase from 60 to 64 years of age



Slightly more men develop AML than women

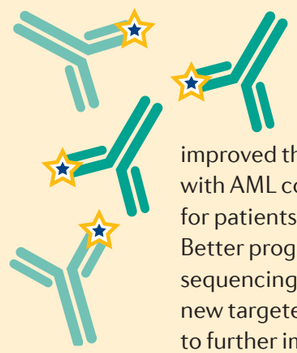
MECHANISMS

The abnormalities in cell proliferation, survival and differentiation of AML cells are underpinned by various genetic and epigenetic changes. Approximately 50% of all AMLs have gross structural chromosomal changes, including balanced translocations and chromosomal gains or losses. Far fewer coding sequence mutations are found in AML cells than in most solid tumours. These mutations are predominantly found in genes encoding proteins that are involved in gene transcription, cell signalling and epigenetic modifications.

MANAGEMENT

Patients with AML require considerable supportive care (treatment that is focused on symptoms and complications, not remission) to manage infections (anti-fungals and antibiotics) and bleeding risk (platelet transfusions). Leukostasis — an occlusion of blood vessels due to an aggregation of excess myeloblasts — is a life-threatening complication and should be diagnosed and treated promptly with chemotherapy and sometimes leukapheresis. Induction and consolidation therapy is aimed at complete remission and the elimination of minimal residual disease (MRD). The choice of treatment depends on the general well-being of the patient. Although induction therapy results in remission in most patients, the relapse rate is still high and depends on age, the cytogenetic and molecular profile of the leukaemia and the amount of MRD. Taking these risk factors into account, allogeneic HSC transplantation (HSCT) can be considered. Although HSCT is the most effective post-remission treatment to prevent relapse, treatment-related morbidity and mortality limit its use.

OUTLOOK



Advances in treatments have improved the survival of patients with AML considerably — especially for patients <60 years of age. Better prognostic markers based on sequencing and MRD analysis and new targeted therapies might lead to further improvements. Drugs currently under investigation target pathways that are activated owing to mutations or consist of conjugated antibodies carrying a cytotoxic agent.

Designed by Laura Marshall

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