

Spotlight on Health

Acute Myeloid Leukemia: Laboratory Testing Can Guide Treatment

Acute myeloid leukemia (AML) is a cancer of the blood and bone marrow. Initial symptoms are typically nonspecific. However, the disease progresses very quickly, and prompt diagnosis improves outcomes. In addition, identification of the subtype of AML guides treatment options.

This newsletter will discuss AML, typical symptoms, and how the laboratory can help to make a diagnosis that guides treatment.

AML

AML is also called acute non-lymphocytic leukemia, or acute myelogenous leukemia. Normally, precursor cells in the bone marrow (called myeloid precursor or stem cells) develop into blood cells. In AML, the myeloid cells develop into abnormal leukemic cells. Leukemic cells can multiply very quickly, build up in the bone marrow and blood, and prevent the development of normal blood cells.^{1,2}

Who Gets AML?

Anyone can get AML. The disease is slightly more common in men than women, and affects all ethnicities.³ AML is more common in older individuals, with a median age of 68 years at diagnosis. Approximately 60% of cases occur in persons 65 years and older.³ However, some types are more common in children.¹ Overall, AML accounts for about 1% of all cancers and about 80% of leukemia in adults.^{1,3} Known risk factors for leukemia are⁴

- Exposure to high levels of radiation
- Repeated exposure to certain chemicals (for example, benzene)
- Chemotherapy
- Down syndrome
- A strong family history of leukemia

Signs and Symptoms

AML can be difficult to diagnose at an early stage. People with AML may complain of flu-like symptoms, feeling “run-down,” or just not feeling well. Symptoms that should trigger suspicion of AML include⁴

- Bleeding from the gums or nose
- Bone pain
- Fever, chills, or night sweats
- Frequent infections
- Increased bruising
- Shortness of breath
- Swollen tonsils
- Pale skin
- Pinhead-size red spots on the skin
- Tiredness, fatigue, or weakness
- Unexplained weight loss



Factors Associated With a Better AML Prognosis^{1,2}

- Younger age (60 years old or younger)
- Remission with initial treatment
- Translocation between chromosomes 8 and 21 or 15 and 17, or translocation or inversion of chromosome 16
- Changes in the *NPM1* gene and/or changes in both copies of the *CEBPA* gene

Factors Associated With a Poorer AML Prognosis^{1,2}

- Advanced age
- White blood cell count >100,000/ μ L at diagnosis
- Prior blood disorder or treatment for cancer
- Systemic blood infection at the time of diagnosis or central nervous system involvement
- Various chromosomal abnormalities
- Mutations of the *FLT3*, *TP53*, *RUNX1*, or *ASXL1* genes
- Leukemic cells that are positive for CD34 or MDR1

Diagnosis

The World Health Organization (WHO) defines AML by the presence of 20% or more blasts in peripheral blood or bone marrow.² Initial evaluation should include a complete blood count (CBC), tests of liver and kidney function, and serum uric acid and lactate dehydrogenase (which have prognostic relevance).² A bone marrow biopsy and analysis are used to determine the type of AML and evaluate molecular markers (eg, mutations in *FLT3*, *NPM1*, *CEBPA*, *KIT*, and other genes) that are important for risk assessment, establishing a prognosis, and guiding treatment.²

The current WHO classification of AML defines 6 types (with each type having a number of subtypes) and takes into account molecular genetic information.⁵ The inclusion of genetic factors, in addition to clinical and cytogenetic factors, aids in determining the prognosis (see Sidebar on previous page) and guiding treatment.^{1,2,5}

Management and Prognosis

Chemotherapy is the most common treatment for leukemia; progress is monitored by laboratory testing. The goals of initial treatment are bone marrow blast cells <5%, a normal CBC, and no signs/symptoms of disease.² Subsequent chemotherapy (consolidation therapy) eliminates remaining leukemic cells in the bone marrow. A patient is considered to be in remission when no leukemic cells can be identified by sensitive tests such as flow cytometry or PCR.² These tests monitor minimal residual disease (MRD)—the small number of leukemic cells that can persist during or after treatment, which are major indicators of potential relapse.²

A subtype of AML, acute promyelocytic leukemia (APL), is characterized by coagulopathy and bleeding diathesis. Diagnosis is confirmed by a distinct cytological morphology in combination with molecular or cytogenetic testing.² Standard chemotherapy can worsen the disease; instead APL is treated with differentiation agents that promote the development of blasts into normal white blood cells.⁶

In addition, a number of novel therapies are available for individuals with certain genetic or cytogenetic changes of leukemic cells. For example, targeted therapies are available for patients with *FLT3* internal tandem duplication mutations,² and monoclonal antibody therapy is available for those with CD33-positive leukemic cells.¹

The overall 5-year survival rate for patients with AML is approximately 27%.³ However, clinical and disease factors play important roles in determining outcomes (see Sidebar on previous page). Age is one of the most important prognostic factors. In general, the prognosis is poor in the elderly, and younger patients are more likely to achieve remission.¹⁻³

How the Laboratory Can Help

In addition to the Comprehensive Hematopathology Report (test code 17734[X]), which can be used to identify AML, Quest Diagnostics offers genetic and cytogenetic testing to determine AML type and subtype and identify leukemic cell markers. Determination of gene variants and specific cell markers can provide prognostic information and assist in guiding treatment. For example, the LeukoVantage®, Acute Myeloid Leukemia (AML) (test code 36787) uses next-generation sequencing (NGS) technology to subclassify and assess prognosis in patients with newly diagnosed AML. Quest also offers tests to monitor MRD during and after treatment by detecting AML-associated cytogenetic and molecular abnormalities.

References

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