Spotlight on hematology

Acute leukemia in the doctor's practice

MQZH 2017-02

Introduction

Acute leukemias are malignant degenerations of the hematopoeic stemm cells (hematopoesis). They are principally divided into lymphatic and myelotic forms. The pathological picture is characterized by proliferation and accumulation of the degenerated cells in the bone marrow and peripheral blood. Untreated, acute leukemia leads to a patient's death within weeks to a few months.
A diagnosis, and thus making adequate therapy available to the patient, must therefore be made as soon as possible.
Our blood picture is derived from a 56-year-old patient with acute myeloid leukemia, FAB M4, AML with mutated NPM1 in accordance with WHO 2016

About the diagnostics of acute leukemias

The first suspicion is raised because of abnormal hemogram results. The cellular morphology (appearance) in the blood smear often provides the first indication whether this is more of a lymphatic or myeloid type. However, acute leukemias are actually a much more heterogeneous group of diseases. Additional blood and bone marrow tests therefore follow. Today, in addition to common cytochemical stains, these mainly include cytochemical and molecular genetic methods, and the determination of cell surface antigens by immunophenotyping.

Note: Many patients with acute leukemia present with pancytopenia in the peripheral blood while the blasts are visible only in the bone marrow.

Today, the treatment of acute leukemia is adapted according to subtypes and risk, to the extent possible; the treatment approach in patients who are younger than 70 years old is generally curative (aimed at a cure).

Age distribution of acute leukemias

In adults, around 80% are acute leukemias of a myeloid origin (AML). They affect the stem cells or precursor cells of granulocytes, monocytes, platelets, or erythrocytes. The new classification is provided by the WHO description – FAB is still provided as a supplement

In children, acute leukemia is the most common cancer with approximately 35%. The predominant type of leukemia, around 80%, is acute lymphatic leukemia (ALL). The disease can originate both from the B cell line (common-ALL) and from the T cell line.

Clinical aspects of acute leukemias

Patients suffering from acute leukemia describe nonspecific symptoms that have been persisting for days or a few weeks.

These include general symptoms such as:
- Flu-like symptoms
- Infections of the upper respiratory tract
- **Fever, fatigue, drop in performance**
- More rarely nosebleed, bleeding into the skin and mucous membranes (suffusions and petechia)

Good to know:
- Patients who suffer from cushion-like infiltrates of leukemic cells in the gums (gingival hyperplasia) often visit the dentist first
- In acute lymphatic leukemia diffused bone and variable joint pain is often increased. Small children can therefore present with an unwillingness to move (up to refusal of moving). Marked lymph node swelling and splenomegalies may also appear.

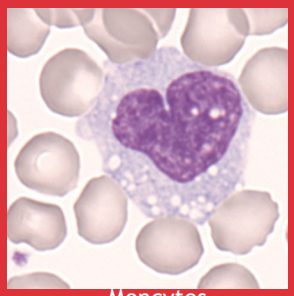
Hemogram findings with acute leukemia

Quantitative changes in the hemogram (counts)
- Leukocyte number very variable
- (normal, elevated, or reduced)
- Accompanying normochromic- normocytic anemia, frequently from the start (hb reduced)
- Platelet number frequently reduced from the start
- Absolute neutropenia

Good to know:
Although the term leukemia (gr. "white blood") indicates a highly elevated number of leukocytes, normal or even reduced number of leukocytes can actually be found just as frequently in acute leukemias (aleukemic presentation).
The clonal proliferation of malignant degenerated precursor cells leads to the formation of a quite uniform cell population in terms of appearance. In addition, the number of normally matured blood cells is in part dramatically decreased (hiatus leukemicus). Frequently, the leukemia cells cause erythropoiesis and thrombopoiesis to decrease in the bone marrow from the start, which leads to low counts of these cells in the peripheral blood.

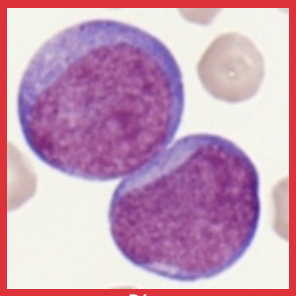
Comparison with other preparations

Monocytes (Spotlight 2011-2)



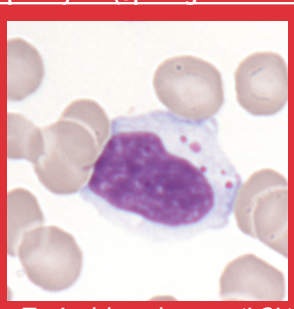
Moncytes

Blasts (Spotlight 2009-4)

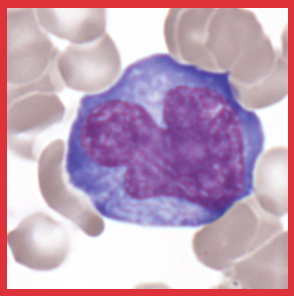


Blasts

Lymphocyte (Spotlight 2014-3)



Typical lymphocyte (LGL)



Atypical lymphocyte, most likely reactive

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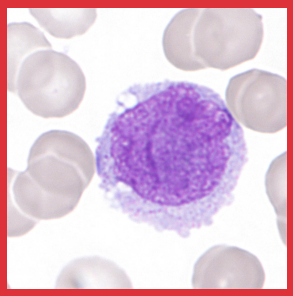
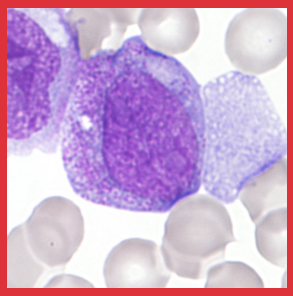
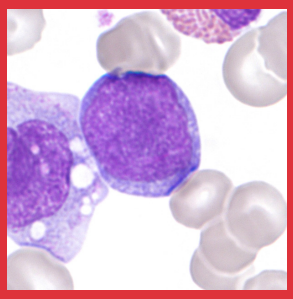
MQ 2017-2 H3B Examples



Monocytes



Promyelocytes



Blasts

Further diagnostics with suspected acute leukemia

Ideally, with respect to hemato-oncology the finding is further clarified directly at a specialized center. Under certain circumstances it is reasonable to first send the sample to the external laboratory. However, the sample must be preregistered as an emergency there and picked up by courier service in order to avoid unnecessary loss of time. In the praxis blood smears of perfect quality should have already been prepared which are enclosed together with the EDTA blood in a protective cover.

About
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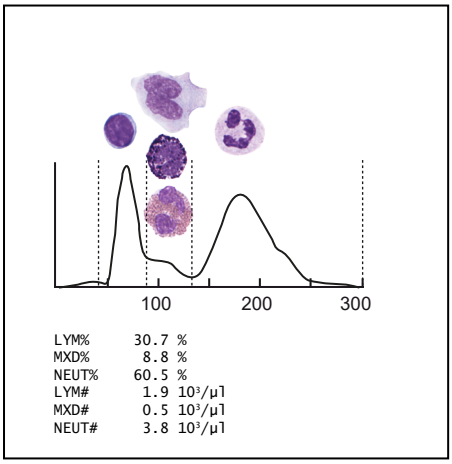
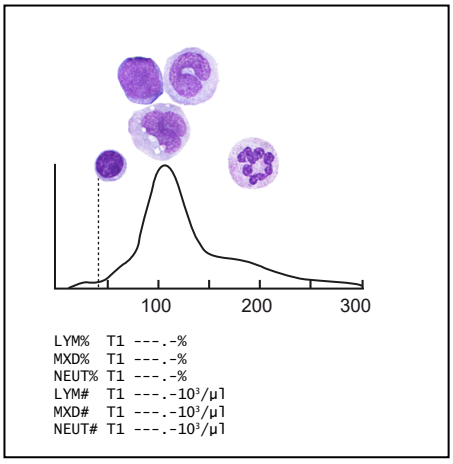
The leukocyte histogram (WBC histogram)

The WBC histograms of healthy people generally show a population of small, medium, and large cells, which the instrument can adequately separate from each other using discriminators.
In acute leukemias, however, malignant degenerated cells develop, which often appear uniform due to their clonality. These cells are seen as an atypical single peak that often overlays the normal boundaries (discriminators). In addition, even the smaller hematology instruments generally recognize that an atypical cellular distribution of potentially immature cells is present and display corresponding warnings (flags). Some instruments completely block the output of the histogram when these findings are found.



WBC histogram Sysmex, MQ 2017-2 H3A WBC



histogram Sysmex, MQ 2017-2 H3B

Checklist for the evaluation of hematogram findings

1. Counts

- ☐ Values within the reference range? Mark deviations with ↑↓ .
- ☐ Test plausibility-extreme values? Plausibility with previous findings or clinic?

2. Istogrammi (curve)-WBC, RBC, PLT

- ☐ Curva anomala? Se sì, di che tipo? (marcare, annotare)
- ☐ WBC: sono riconoscibili i tre sottogruppi normali?
  Se no: è visibile un picco singolo sospetto? Lo strumento utilizza i discriminatori soliti (linee di demarcazione)? Marcare e annotare ogni anomalia.
- ☐ Appaiono messaggi d'allarme (flags) per alcuni parametri? O ne viene rifiutata la stampa?
  Se sì: cercarne il significato preciso nel manuale dello strumento, annotare.
  Eventualmente effettuare le azioni previste dal manuale, secondo le istruzioni (per es.: diluire il campione)

3. Troubleshooting

Preanalytical error?

- ☐ Problems with blood withdrawal? Coagulation, over- or under filling?
- ☐ Correct vials taken/measured?
- ☐ Sample material unambiguously assignable to the patient?
- ☐ Sample correctly prepared for the measurement? Sample cooling down time after withdr at least 5 minutes? Careful, repeated sample mixture along the vial lid?

Analytical error?

- ☐ Sufficient amount of sample aspirated into the instrument? Correct vial filling and adapter properly positioned below the suction needle?
- ☐ General alarm on the day of the measurement? E.g., during instrument startup?
- ☐ Internal quality control (control blood) measured for the current day? Results okay?
- ☐ Were reasonable values (within the reference range) already measured for other patients on the instrument?

4. Further procedure

- → Repeat sample measurement, observing all instructions for correct measurement
- → Repeat measurement of the internal quality control

The values are confirmed by the second measurement, pre-analytical and analytical errors were ruled out -> inform the doctor immediately about the raised findings. The further procedure can then be clarified.