Newsletter

HemeInsights

Issue 1 | November 2024

Morphology Case Study

Patient Details
Female aged 64 presented at the hematology clinic after referral from GP. Anemic, excessive bruising, some bleeding.

FBC	Differential
WBC 65.11* (10^3/mm3)	Neutrophils 13.8%
RBC 2.11* (10^6/mm3)	Lymphocytes 15.9%
HGB 6.9* (g/dL)	Monocytes 6.5%
HCT 20.4* (%)	Basophils 0.7%
MCV 96.9 (fL)	Blasts 63.1%
MCH 32.8 (pg)	Large Platelets 1%
MCHC 33.8 (g/dL)	
PLT 48 (10^3/mm3)	

The blood smear was made and examined urgently.
Prior to the differential being performed a thorough examination of the smear was performed to ensure that no platelet clumps/aggregates/fibrin strands were found in order to validate the platelet count.
Numerous large mononuclear cells were noted.

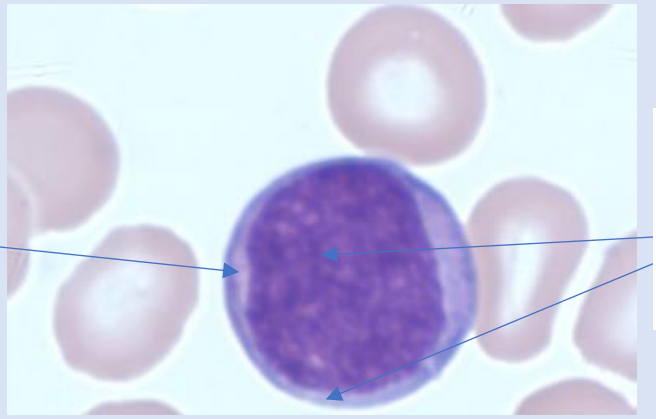
Smear comment
Blast cell count estimated at 41 G/L (63% of leukocytes).
Auer rods(+++): AML.

Comment for the attention of the expert
Please confirm "Auer rod cluster" appearance of the Auer rods on the framed image (in this case, can we suggest an AML3? The blasts are not granular, but we still observe certain? Bissac nuclei?
In short, perhaps AML3 (Acute Promyelocytic Leukemia) hypogranular variant...?

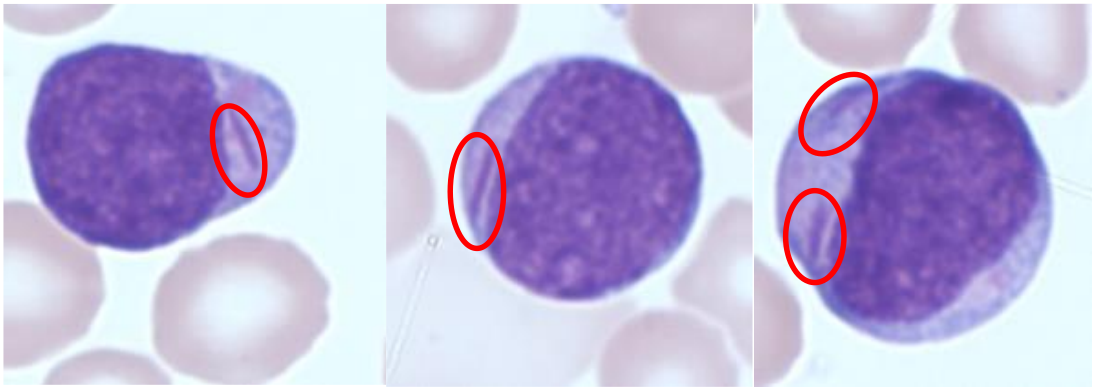
Expert Comment
(Not AML3). AML4 (Acute Myelomonocytic Leukemia) according with myelogram conclusions.

Blast cell or not blast cell

One of the first thing the morphologist has to determine is whether the abnormal-looking cell is a blast cell or not followed by the lineage.
Blast cells are, in general, larger than the normal mature cells e.g. mature Red Cell (Myeloblast 15-20 µm, Monoblast 12-20 µm, Lymphoblast 10-20 µm) have a high nuclear to cytoplasmic ration (N:C) – i.e. a large nucleus with a relatively small amount of cytoplasm, irregular nuclear contour, pale to deep blue cytoplasm, smooth or granular chromatin pattern, sometimes prominent single or multiple nucleoli.

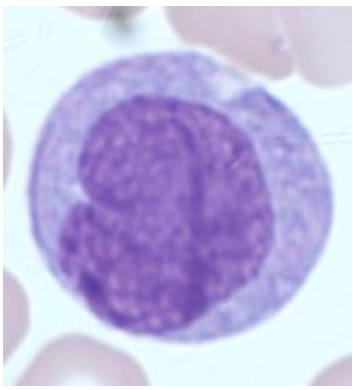
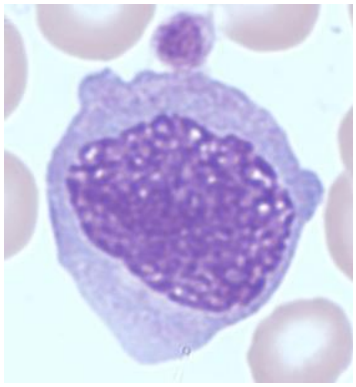
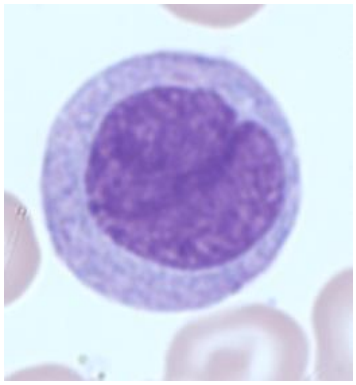


What Lineage?
A feature found in some of the blast cells were needle like crystals called Auer Rods that are specific and virtually diagnostic of myeloid clonal malignancy. Auer Rods are made up from peroxidase proteins normally expressed in **myeloid** cells. Therefore, we can say that with the presence of Auer rods and the general appearance, the majority of blast cells are almost certainly Myeloblasts. In myeloid leukemia, the percentage of cells with Auer rods and the number of Auer rods per cell varies greatly and is not known to be clinically significant (Auer Rod - an overview | ScienceDirect Topics). Auer rods are named after the American physiologist John Auer but were actually first described in 1905 by Thomas McCrae, both initially thought that the cells containing the Auer rods were lymphoblasts.
Blast cells containing Auer rods (circled):

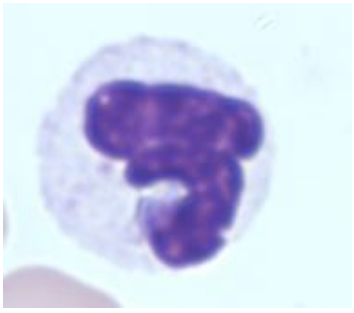
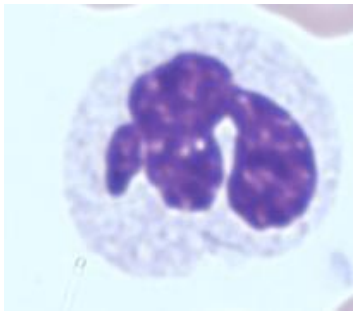
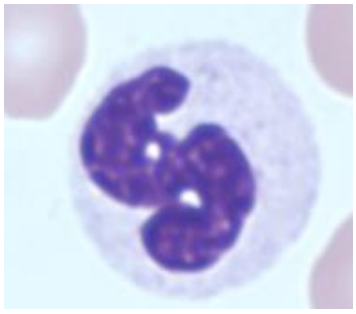


It is easy to just concentrate on the presence of blasts but the morphologist should always recognize the company they keep in terms of what other cells are present.

Abnormal cells which are not Myeloblast and are probably Monoblasts/Pro monocytes. Monoblast are large cells with more cytoplasm than Myeloblasts and which is light blue / gray. The nuclei is folded and or convoluted and has a lacy chromatin structure.

The Neutrophils which were present appeared agranular which are often seen in Myelodysplastic Syndrome (MDS) which often transforms to AML.

Additional tests such as immunophenotyping and molecular/cytogenetic studies will give a greater insight into the exact nature of the malignancy and also aid in the treatment and prognosis.

Hemoglobin – Structure and Function

Hemoglobin is a complex protein both in structure and function and its functions are still not fully understood. One of the main functions of Hemoglobin is to transport Oxygen from Oxygen rich tissues to Oxygen deficient areas as well as to transport Carbon Dioxide back to the lungs to exhale. Hemoglobin is contained within all red cells and is what gives blood its red color. Each red cell is estimated to contain 200 – 300 million molecules of Hemoglobin.
We now know that Hemoglobin is composed of 2 pairs of polypeptide globin chains known as alpha and beta (in normal adult hemoglobin HbA).

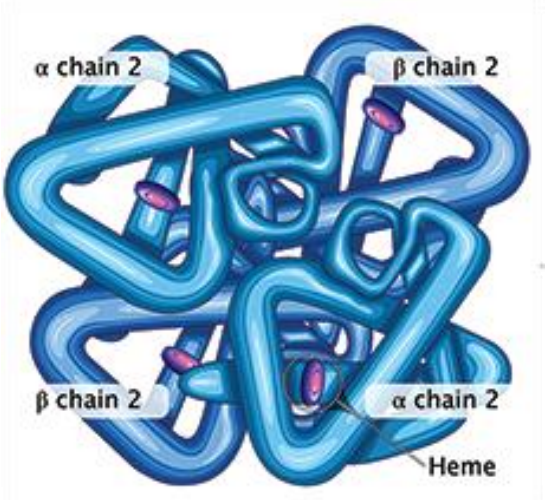
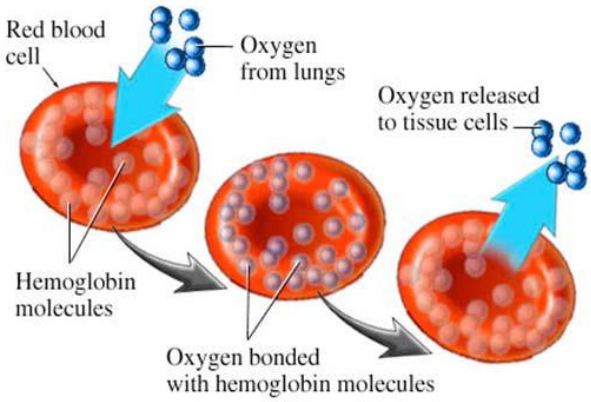


Diagram showing the structure of a normal Hemoglobin molecule

Each of the 4 chains surround a heme molecule in the so-called “heme pocket”. The heme molecule comprises a protoporphyrin ring made up of 4 pyrrole rings and a central iron ion in the Ferrous state (Fe^{2+}). Oxygen bind reversibly to the Fe^{2+}. A maximum of 4 Oxygen molecules can be transported per Hemoglobin molecule.

Hemoglobin is an allosteric compound in that binding of an Oxygen molecule causes a conformation change which causes an increase in the Oxygen affinity in the heme entities. In each Globin chain, the heme molecule is located in a deep crevice-like structure. The shape of the crevice determines how easily an oxygen molecule can access its binding site. When fully de-oxygenated the hemoglobin structure is described as in a tense or T form with small crevices making it comparatively difficult for Oxygen to access the Heme molecule. As Oxygen molecules bind to heme the hemoglobin molecule structure changes in such a way that the crevices open up allowing greater affinity for the Oxygen to bind. When fully Oxygenated with 4 Oxygen molecules the Hemoglobin is in its Relaxed or R form.

Whether Hemoglobin is in the T or R state determines the affinity for Oxygen in such a way that in high Oxygen concentration e.g. lungs the Hemoglobin has a high affinity for Oxygen and therefore allows Oxygen to bind to the Heme. Conversely in Low Oxygen concentration e.g. in peripheral tissue hemoglobin’s Oxygen affinity is low therefore enabling the release of Oxygen.



New Discoveries

HORIBA launches 3 new Yumizen H550E models with i-DoubleDiff and CoRA technology. 5-Part diff with ESR technology.

New Yumizen H550E uses i-DoubleDiff and CoRA technology.

What is i-DoubleDiff?

The double diff channel extends the standard 5-part diff to classify abnormal cells. The cells are measured at 2 intervals - the resistive aperture measures the size of the cell and a further measurement of optical extinction is made to determine the complexity and granularity of the cell. The i-DoubleDiff technology offers three immature populations of white blood cells and can detect Malaria and Dengue infections.

CoRA Technology (Correlated Rouleaux Analysis) technology.

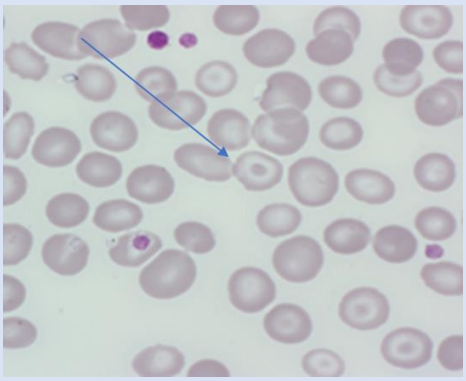
This technology is correlated to the Westergren method. The method uses optical analysis of rouleaux formation over time. The data is converted to ESR parameters (mm/h) by a dedicated processor.

- ESR capability inbuilt
- No increase in instrument footprint
- Correlation with reference method
- No additional reagents required except control

Yumizen H550E is available in auto loader, closed tube, and open tube models.

For further details: https://horiba.link/sdh

Cell Quiz



Look at this slide, can you name the cell?
What possible clinical details would this patient likely have?
Choose from the below options:

A) Glandular fever
B) Nothing abnormal
C) Thalassemia

Bibliography

- Slide 4, August 2024 QSP slide package
- Auer Rod - an overview | ScienceDirect Topics

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Read on website
https://horiba.link/6vy

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