Spotlight on hematology

Hairy Cell Leukemia

MQZH 2013-02

Introduction

Hairy cell leukemia (HCL) is a rare, malignant disease of the B-lymphocytes that is classified as the indolent (low-grade malignant) non-Hodgkin's lymphoma. The average age at which HCL is diagnosed is between 50 and 55 years, whereby men are affected four to five times as often as women. Classical hairy cell leukemia develops extremely slowly; splenomegaly and cytopenia are typical. The even rarer hairy cell variant (HCL-V) typically presents with lymphocytoses higher than 15.0 G/l.

The disease is often only diagnosed when the splenomegaly causes problems or the peripheral blood levels drop significantly, leading to anemia or infection symptoms.

Our current proficiency testing sample comes from a patient who was first diagnosed with hairy cell leukemia in the 1980s with the treatment starting with splenectomy and infrared therapy. Due to a recently developed infrared resistance, the number of hairy cells and the soluble interleukin 2 receptors (CD25) increased significantly in the peripheral blood. Our blood smears were made at that time. The therapy then successfully switched to Cladribine. Currently, the patient is already in full remission from the hairy cell leukemia.

Pathogenesis and Course

Neither the morphology nor the verifiable surface antigens of hairy cells are similar to any known sub-group of B-cells. Based on genetic research, there are, however, indicators that hairy cells originate from degenerated B-memory cells.

Hairy cell leukemia typically results in a prominent splenomegaly and cytopenia (reduced cell counts). These cytopenias originate in the bone marrow when normal hematopoiesis is inhibited due to leukemic cells on the one hand, and cytokines such as TNF alpha on the other. The consequence thereof is that with hairy cell leukemia, there is an increase of reticular fibers in the bone marrow which can suppress the hematopoietic marrow. In the diagnostic bone marrow puncture, this condition may only lead to a small amount or no bone marrow aspirating (punctio sicca; see also Blickpunkt Hämatologie (Focus Hematology) 2012-03 «Primäre Myelofibrose» (Primary Myelofibrosis)). When extracting the biopsy, it is important that as many roll-out medications as possible be made. Clinically, anemia symptoms and infections occur in the case of neutropenia and a bleeding tendency develops in the case of thrombocytopenia.

The course of hairy cell leukemia is relatively slow and, currently, can usually be treated very successfully. While a splenectomy used to be the only treatment option, Interferon has been used successfully since the 1980s. The chemotherapeutic Cladribine has been equally successful as has an antibody treatment with Rituximab in cases of recurrence.

Laboratory Findings for Classical Hairy Cell Leukemia

In cases of hairy cell leukemia, there are cytopenias of different sizes; approx. 50% of pancytopenias (reduction of all the three lines; Lc only neutrophiles and monocytes, Ec and Tc) or cytopenias of individual cell lines. A complete absence of monocytes („monocyte window") is quite typical. Hairy cells can wash out into the peripheral blood and be detectable in the blood smear.

Anemia

- Hemoglobin ↓
- MCH normal
- MCV sometimes slightly raised

Leukopenia

- Neutrophiles absolute ↓ (at < 0.5 G/l = Agranulocytosis)
- absolute monopenia
- relative lymphocytosis

Thrombocytopenia

Blood smear

Leukocytes	potential hairy cells
Red blood cells	potential tear drop cells, potential erythroblass, potential macrocytosis after splenectomy Howell-Jolly bodies and target cells *(see Spotlight on Hematology 2008-01 «Ec inclusions Howell-Jolly and Pappenheimer bodies»)*
Thrombocytes	potential macrothrombocytes *(see Spotlight on Hematology 2009-03 «Thrombocytes»)*

Fact sheet

Hairy cells in classical hairy cell leukemia

Zelle

Size	12-20 µm (larger than normal lymphocytes)
Shape	round to slightly ovoid

Nucleus

Shape	ovoid to bean-shaped, potential folded, slightly indented or dumbbell-shaped
Chromatin	regular, without larger compacted sites
Nucleoli	isolated, fine

Cytoplasm

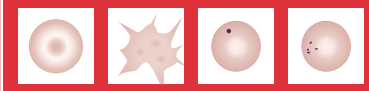
Size	medium-wide to wide
Color	light basophile-grayish
Shape	fine hair-like projections

Hairy Cells in the Hairy Cell Leukemia-variant (HCL-V)

The morphological properties are similar to those of classical hairy cells. However, the hairy cells often display a clear, bubbly nucleolus (similar to prolymphocytes).

Spotlight on hematology

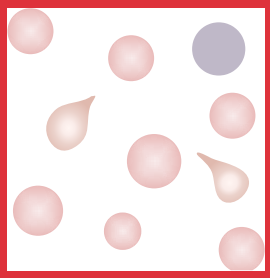
Red Blood Cells after Splenectomy



- Target cells
- Acanthocytes
- Howell-Jolly bodies
- Pappenheim bodies

Tear drops

(«Dakryocytes»)



These erythrocytes are tear drop-shaped whereby the tapered end of this cell is round or blunted at the end (not narrow, pointed or thread-shaped).
Tear drop shapes can be normo-, micro- or macrocytic / normo- or hypochromic.

They appear especially when there is an inhibition of hematopoieses in the bone marrow. One cause of this is the increasing fibrosis of the marrow that occurs with hairy cell leukemia. An additional cause can be, e.g. an inhibition process due to the metastasis of malign tumors. Occasionally, tear drop shapes are found alongside with hemolytic anemiae.

About
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Laboratory Findings for Classical Hairy Cell Leukemia

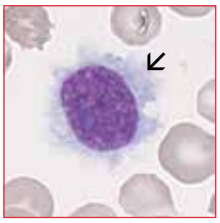
A bone marrow puncture is performed for a more detailed assessment. A cytochemical staining of the cells (TRAP) and the FACS analysis (identification of surface markers of the lymphocytes) can provide indications for identifying hairy cells.

Cytochemistry	FACS Analysis
tartrate-resistant acid phosphatase (TRAP)	• classical hairy cells CD103 pos. and CD25 pos. • hairy cell variant CD103 pos. and CD25 neg.

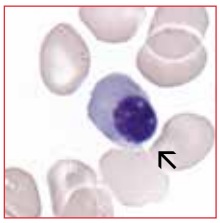
Genetic studies of malign cells are becoming increasingly important. This is also true for hairy cells in which the BRAF V600E mutation can be verified in the majority of classical HCL cases, while it is not present in HCL-V. Understanding of the underlying genetics is very important and will contribute to improved medical health care in terms of individualized therapies.

Pictures from our survey slides

Normal lymphocyte and target cell (arrow)

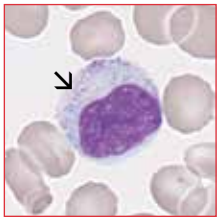


Hairy cell with pronounced, hair-shaped cytoplasm offshoots

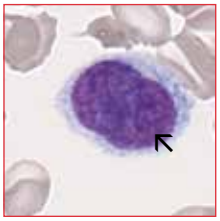


Polychromatic erythroblast

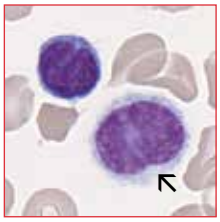
Hairy cell with a clearly dumbbell-shaped nucleus



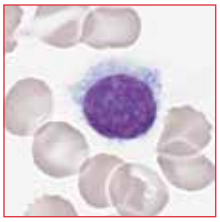
LGL cell (large granular lymphocyte) belongs to the normal lymphocytes.



Hairy cells with a fine nucleolus (arrow) and indicated indented/folded nucleus.

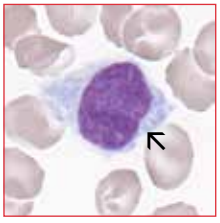


Hairy cell (arrow) next to normal lymphocytes



Small hairy cell with a round nucleus

Hairy cell with a fine nucleolus (arrow)



Hairy cell with indicated indented/folding nucleus (arrow)