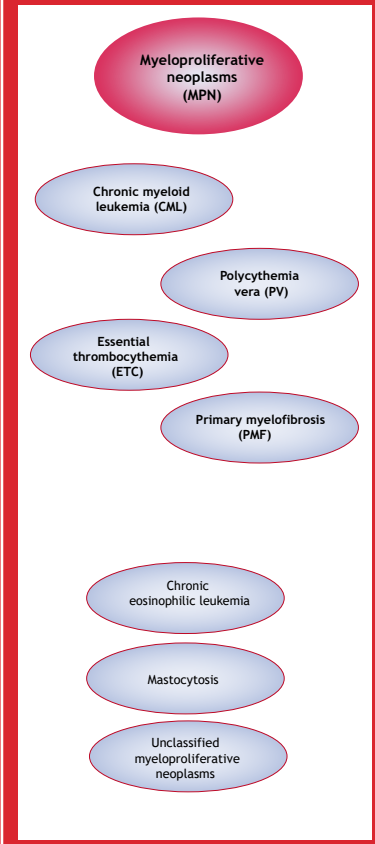
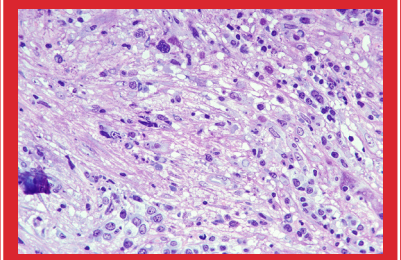
Spotlight on hematology

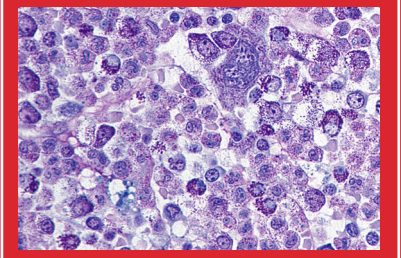
WHO Classification 2008

Myeloproliferative neoplasms (MPN)





Bone marrow with strong fibrosation with myelofibrosis



Bone marrow without fibrosation in a reactive finding

Primary myelofibrosis (PMF)

MQZH 2012-03

osteomyelofibrosis (OMF), idiopathic myelofibrosis (IMF)

Introduction

Primary myelofibrosis (PMF) is a rare malignant disorder of hematopoiesis that belongs to the group of myeloproliferative neoplasms (MPN per WHO 2008). Over the course of the disease, a clonal defect of myeloid stem cells causes increasing displacement of the blood-forming bone marrow with reticulin fibers. Externalization of blood formation (extramedullary blood formation) in the spleen and liver results with hepato-splenomegaly.
The patients are often initially asymptomatic, often causing the change of the blood picture to be determined for the first time in the course of a routine blood test. In the initial phase, slight anemia, thrombocytosis and a mostly moderate neutrophilic leukocytosis are often present. Over the course, increasing pancytopenia (reduction of leukocytes, erythrocytes and platelets) develops with a leukoerythroblastic blood picture and increased appearance of teardrop erythrocyte forms. This pancytopenia then also determines the clinical symptoms (anemia, susceptibility to infections, bleeding tendency).
Transformation of PMF into acute leukemia is possible. To secure the diagnosis, bone marrow examinations and molecular analyzes (especially JAK2-Mutation) are performed. Our proficiency testing survey sample 2012-03 H3b is from a 52-year-old patient with primary myelofibrosis.

Pathophysiology

As with the other myeloproliferative disorders, the underlying disorder is a clonal defect on the level of the myeloid stem cell. It is assumed that the cause for the progressive fibrosation of the bone marrow is that decomposition and deposition of atypical megakaryocytes and platelets leads to the secretion of fibroblast-activating cytokines.

Diagnosis

During the bone marrow examination, usually only a small amount of bone marrow can be aspirated
(punctio sicca). In the histological examination of the bone marrow biopsy, an increased cellular density with propagation of atypical megakaryocytes can be detected in the initial stage. In addition, precursors of granulopoesis are found and many, in part atypical, erythroblasts. In the later stages, the distinct fibrosation is seen in the medullary cavity.
Molecular genetics mainly tests for the JAK2(V617F) mutation (JAK = Janus kinase) which is positive in approx. 55% of the patients.

Hematological findings

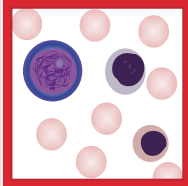
Finding	initial	advanced stages
Anemia	minor	increasingly pronounced
Erythroblasts	few	many
Erc-morphology	aniso- and poikilocytosis potentially basophilic stippling and polychromasia teardrop forms (+) to +	aniso- and poikilocytosis, possible basophilic stippling and polychromasia. teardrop forms ++ to +++
White blood cell count	potentially increased to approx. 10-14 g/L	increasing decrease
neutrophil count	increased	normal, reduced or increased
abnormal left shift blasts, promyelocytes, myelocytes, metamyelocytes	present	increasing
basophilia	possible	possible
platelets	normal to slightly increased	reduced
platelet morphology	anisozytosis	anisozytosis pronounced, atypical forms, nuclear megakaryocyte fractions
Bone marrow special	minor reticulin fiber fibrosis	pronounced reticulin-/ collagen fiber fibrosis and extramedullary hematopoiesis in spleen and liver

Spotlight on hematology

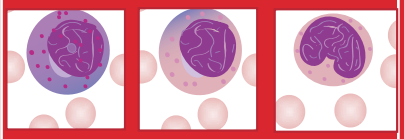
Typical diagnosis constellation and morphological aspects of primary myelofibrosis

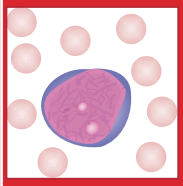
Leukoerythroblastic blood picture

Leukoerythroblastosis = washing out of myeloid precursors and erythroblasts



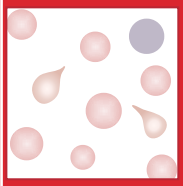
Erythroblasts
When > 4 erc / 100 WBC in the differential blood picture, the instrument WBC number must be corrected:
100xWBC no. device / 100+number Ebl/100 WBC = WBC corr.





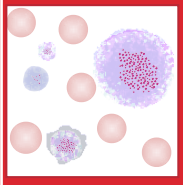
Blasts leukocytes
A sudden increase in the number of blasts over the course of the disease can be indicative of transformation to acute leukemia.

Erythrocyte morphology



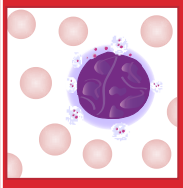
Teardrop forms
The tapering part of this cell is round or truncated at its end (not narrow, pointy or thread-like). The cells must be pointing in different directions.

Platelet morphology



Atypical platelets
Normal platelets are 1-3µm in size. Platelets between 4-7 µm are referred to as macroplatelets and those > 7 µm as giant platelets.

Size comparison:
Normal erc = 7 µm



Megakaryozyten-Kernrest

About
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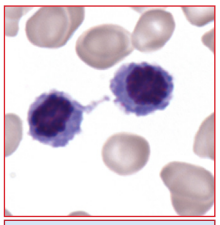
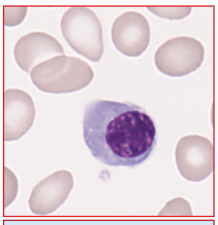
Morphological aspects in the proficiency testing survey sample 2012-03

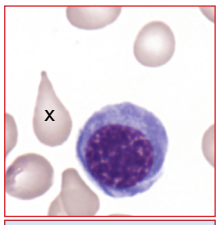
Red blood picture - erythroblasts and erythrocyte morphology



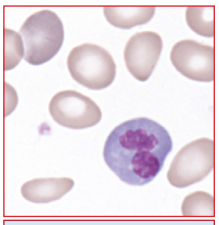
2 Erythroblasts



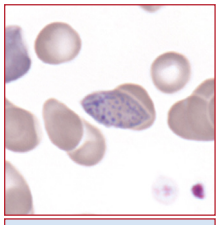
Erythroblast



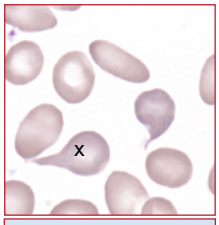
Erythroblast and Teardrop form



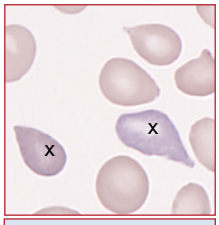
Erythroblast (karyorrhexis form)



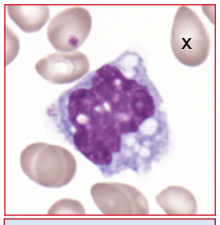
basophilic stippling



teardrop form (x)

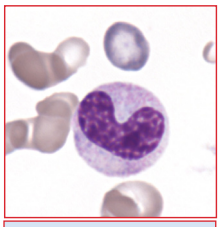


teardrop forms (x)

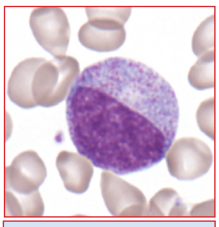


teardrop form (x) and monocyte

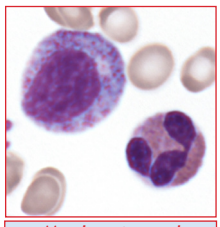
White blood picture - precursors of granulopoesis, eosinophils and basophils:



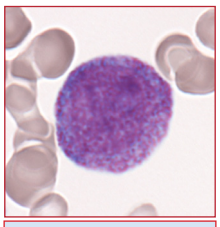
Metamyelocyte



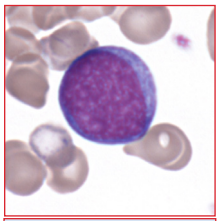
Myelocyte



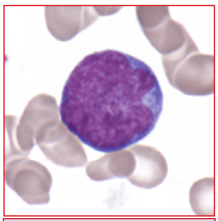
Myelocyte and Eosinophilic



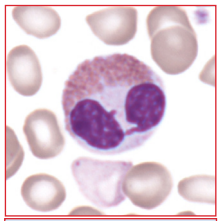
Promyelocyte



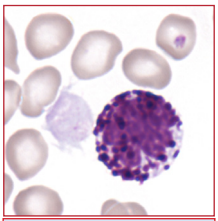
Blast



Blast

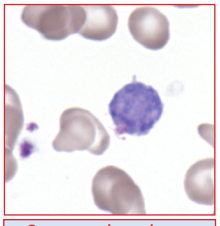


atypical eosinophilic

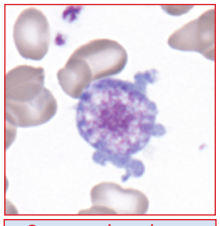


basophilic

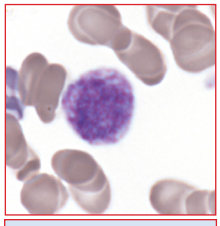
Thrombozyten - atypische Thrombozytenmorphologie, Megakaryozyten-Kernreste



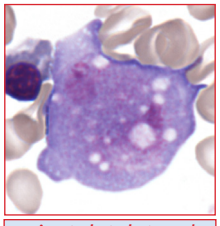
2 normal and one macrothrombocyte



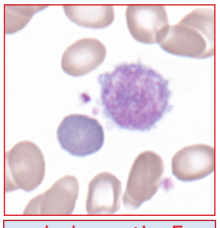
2 normal and one giant platelet



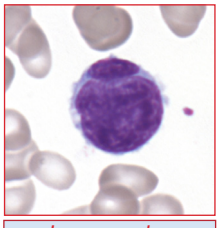
1 giant platelet



giantplatelet and Erythroblast



polychromatic. Erc and giant platelet



nuclear megakaryocyte fragments