Myeloproliferative diseases

Myeloproliferative diseases are a group of sharply demarcated disease units that are expected to transform a pluripotent stem cell . This results in uncontrolled proliferation and differentiation of this transformed cell. A pathological clone often suppresses the production of hematopoietic cells from normal clones. There is also a significant increase in blood elements in one row and at the same time a less significant increase in other rows.

Myeloproliferative diseases include the following units: chronic myeloid leukemia , polycythemia vera, essential thrombocythemia, primary myelofibrosis, systemic mastocytosis.

Classification of myeloproliferative diseases

The difference between these diseases lies in the hematopoietic lineage into which the cells differentiate. There is no sharp line between clinical units.

FAB classification includes among myeloproliferative diseases:

- **Chronic myeloid leukemia (CML)**;
- **True polycythemia (PV)**;
- **Essential thrombocythaemia (ET)**;
- **Primary myelofibrosis (PMF)**.

In addition, the WHO classification according to new findings includes:

- Chronic neutrophilic leukemia (CNL);
- Chronic eosinophilic leukemia (CELL, NOS)).

Polycytemia vera

Polycytemia vera

Chronic myeloid leukemia

CML is a chronic myeloproliferative disease caused by fault in the pluripotent stem cells, **affected** blood lineages are both **myeloid**, and **lymphoid**.Faulty granulopoiesis is predominant (often combined with a failure in thrombocytopoiesis).

A characterisitic sign of tumour cells in CML is the **presence of Philadelphia chromosome Ph[1]** (translocation of a part of the 9. chromosome – carries protooncogene c-abl) on the 22. chromosome (gen bcr) – creating fused gene bcr/abl, which can be demonstrated even in cases where the Ph-chromosome cannot be determined (about 10 % CML). Proliferation of pathological clones gradually extrudes normal hematopoiesis and leads to multiple increase total granulocyte mass, presence of Ph-chromosome leads to further mutations resulting in malignant clones with greater proliferative activity (dedifferentiation of malignant cells) – this new population gradually replaces the original „benign“ leukemic clone and finally completely predominates – **i.e. blastic change** (course line in AML with massive blast leaching – more than 30 % of monoblasts in the bone marrow or in the blood, bleeding, susceptibility to infections, anaemia).

Microscopical picture

Bone Marrow

- Hypercellular bone marrow with an evident prevalence of granulopoietic elements, oppression of erythropoiesis,
- replacing of megakaryocytes is variable (CML can be divided to **CGL** – granulomatous and **CGML** – granulocytomegakaryocytic),
- changes of stroma include occurence of special scavenger macrophages (so called **Gaucher cells**) or macrophages with a hexagonal crystaloid departments in the cytoplasm (macroscopically: bone marrow is pyoid – tj. similar to pus),
- megakaryocyte proliferation is often seen with reticular fiber enlargements, even myelofibrosis, massive tumour hemopoiesis leads to secondary thinning of the bone trabeculae.

Extramedullar tissue

- **Spleen** – sinuses infiltrated with elements of granulopoiesis, or megakaryocytes, evident **splenomegaly** (up to 10 kg – the most evident splenic enlargement is in CML),
- **Liver** – infiltration predominantly **in sinuses** (unlike in CLL, where the infiltrate is mainly in the portobilii),
- **Nodes** – diffuse infiltration of leukemic cells (only in later stages).

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Findings in peripheral blood

- **High leukocytosis** (50–250×10^9/l), ***hiatus leucaemicus*** which is typical for AML **is missing** (in the differential count one can see all developmental stages of granulocytes).

    High amount of leukocytes increases the blood viscosity, which causes the decrease of flow and can even cause a complete blood arrest (leukostasis).

- The leukomioid reaction (a condition resembling leukemia, in which there are few mature white blood cells in the blood due to infection) is distinguishable due to the low activity of leukocytic AF and the presence of the Ph-chromosome.
- **Amount of platelets** can be normal, increased or decreased.

Clinical picture

Clinically we differentiate between **3 stages** of the disease: **chronic phase, acceleration phase, blastic change phase.** Symptoms of CML are non-specific, they include weight loss, fever, anorexia/loss of appetite and sweating.Up to 40% of cases are diagnosed accidentally, usually according to blood tests. From the physical examination the presence of splenomegaly is usually determined (in over 50 % of cases). In the case of successfukl treatment, the size of the spleen goes back to normal. Serious anemia is rarely presence, in the contrary, we usually find thrombocytosis.

Therapy

Busulfan, hydroxyurea and interferon-α have been used in the past to treat CML. Hydroxyurea Template:HVLP is still sometimes used in the pre-treatment phase of therapy to rapidly reduce the amount of circulating tumor elements. A revolution in CML therapy was the discovery of "imatinib" Template:HVLP, the first tyrosine kinase inhibitor. It specifically inhibits the still active BCR-ABL tyrosine kinase, thus stopping the growth of the tumor clone. Other drugs have been approved for therapy: *nilotinib* , *dasatinib* .

Links

Related articles

- Hairy cell leukemia
- Philadelphia chromosoem
- Imatinib

Source

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Kategorie:Patologie Kategorie:Hematologie Kategorie:Onkologie Kategorie:Patofyziologie Kategorie:Vnitřní lékařství

Primary myelofibrosis

Primary idiopathic myelofibrosis, also known as myeloid metaplasia, is a myeloproliferative disease with an incidence of 0.5-1.5 per 100,000 population. Approximately 10-20% of patients then develop AML. Younger patients (under 55 years of age) live after the diagnosis of myelofibrosis live for more than 10 years, older than about 5 years.

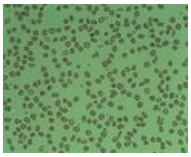
Etiology

The origin of this disease is not yet known. However, a primary disorder at the stem cell level is presumed. This theory is confirmed by the cure of some patients through bone marrow transplantation.

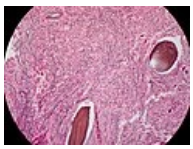
Pathogenesis and diagnostics

In primary myelofibrosis, there is a gradual attenuation of hematopoiesis in the bone marrow with its simultaneous fibrotization. **Collagen III** begins to accumulate in the tissue. This change is **reversible** and is likely to be caused by the production of excessive amounts of the growth factors **PDGF** and **bFGF** and the cytokine **TGF-β,** which is produced by megakaryocytes. **Fibroblasts** in the bone marrow are normal.

Simultaneously with this change, **extramedullary hematopoiesis** (formation of blood elements outside the bone marrow) is activated, which causes a small part of immature forms of blood elements (erythroblasts, myelocytes and promyelocytes) to be released into the blood. This is used in diagnostics. At the same time, we can find teardrops in erythrocytes in the blood. Extramedullary hematopoiesis leads to splenomegaly and hepatomegaly.



Poyclocytosis - erythrocyte in the shape of a drop

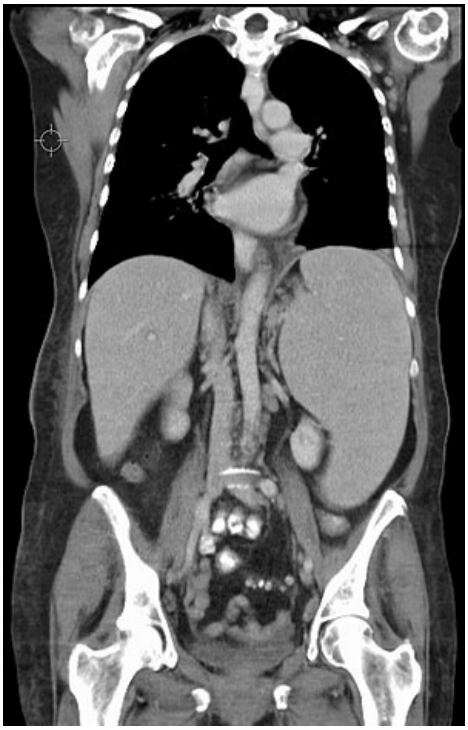


Myelofibrosis (reticular fiber staining)

Clinical picture

This disease consists of two phases. The first, so-called prefibrotic, is accompanied by only mild reticular fibrosis with hypercellular bone marrow. In the second, so-called fibrotic, phase, massive reticular and collagen fibrosis already occursApproximately 30% of patients do not have any symptoms and myelofibrosis is diagnosed at random. The most common symptoms include:

- B symptoms (weight loss, subfebrile to febrile, night sweats);
- fatigue;
- nausea.



Expressive splenomegaly in late stages

Therapy

Most methods are only palliative, the only curative option is **allogeneic transplantation.** Palliative approaches include cytoreductive therapy (interferon α, hydroxyurea), splenectomy, androgen and EPO or JAK kinase inhibitors.

Links

Related articles

- Myeloproliferative diseases
- Splenomegaly

Literature

- NEČAS, Emanuel. *Patologická fyziologie orgánových systémů.* - vydání. Karolinum, 2009. 379 s. ISBN 9788024617114.
- ČEŠKA, Richard. *Interna.* - vydání. Stanislav Juhaňák - Triton, 2015. ISBN 9788073878856.

Essential thrombocythemia

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This article has been translated from WikiSkripta; the **translation** needs to be checked.

Essential thrombocythemia, is caused by pathological monoclonal hematopoiesis , which is manifested by increased number of platelets. These platelets are dysfunctional and, in addition to the risk of microthrombosis, they can also cause bleeding conditions.

Patogenesis

Pathological monoclonal hematopoiesis in the bone marrow is characterized by an increased number of megakaryocytes and megakaryoblasts.

Platelets may have reduced sensitivity to thrombopoetin and therefore we register elevated levels of thrombopoetin , which secondarily causes increased formation of megakaryoblasts and megakaryocytes.

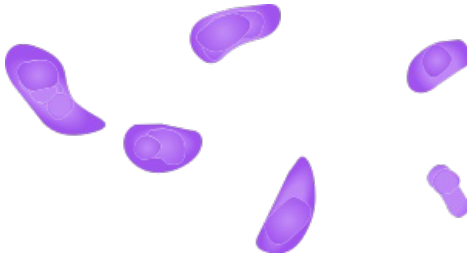
Platelets are dysfunctional, which causes bleeding conditions.

Signs and symptoms

- thrombosis
- bleeding conditions

Prognosis

Essential thrombocytosis can progress to acute myeloid leukemia (in 3-4% of cases).



Thrombocytes

Related articles

- Neonatal Thrombocytopenia
- Thrombocytopenia
- Erythropoiesis
- Thrombocytes

Bibliography

- NEČAS, Emanuel. *Patologická fyziologie orgánových systémů : Část I.* 2. edition. Karolinum, 2009. pp. 379. ISBN 978-80-246-1711-4.

- NEČAS, Emanuel – ŠULC, Karel – VOKURKA, Martin, et al. *Patologická fyziologie orgánových systémů. Část I.* 1. edition. Karolinum, 2006. pp. 0. ISBN 978-80-246-0615-6.

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Systemic mastocytosis

Systemic mastocytosis