Chronic Myeloid Leukemia

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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

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