

LECTURE 10

Diseases of Blood System

Leucoses

•are systematic tumouric diseases of hematopoietic tissue (blood-forming tissue) which are characterized by the progressive overgrowth of tumouric cells-leukemia cells. First tumouric cells increase in hematopoietic organs (marrow, lymph nodes, spleen) and then hematogenously spread in whole organism with infiltration of some organs; and also appear in peripheral blood.

•In contrast to aplastic anemia, leukemia results in a highly cellular marrow. The marrow between the pink bone trabeculae seen here is nearly 100% cellular, and it consists of leukemic cells of acute lymphocytic leukemia (ALL) that have virtually replaced or suppressed normal hematopoiesis. Thus, though the marrow is quite cellular, there can be peripheral cytopenias. This explains the complications of infection (lack of normal leukocytes), hemorrhage (lack of platelets), and anemia (lack of red blood cells) that often appear with leukemia.

Leucoses

- Progressive overgrowth of leukemia cells leads to
- anaemia,
- hemorrhagic syndrome,
- dystrophic changes in parenchymal (parenchymatous) organs,
- immunity oppression,
- ulcero-necrotic and septic complications

Leucoses *etiology*

Leucoses classification

is based on the morphologic and cytochemical peculiarities of tumouric cells of marrow.

There divide

- the **acute** and
- **chronic** leucoses according to the level of differentiation of tumouric blood cells and their development (non-malignant or malignant)

Leucoses classification

Acute leucoses

- are characterized by proliferation of non-differentiated
- or differentiated,
- blastic cells and have malignant development.

Chronic leucoses

- are characterized by proliferation of differentiated leukemic cells and
- relative non-malignant development.

Leucoses classification

• As to the quantity of leucocytes and leukocyte cells there are the next variants of leucosis: **leukemic** (dozens and hundreds thousands of cells per 1mcl (microliter) of blood), **subleukemic** (not more than 15-25 thousands cells),

•**leukopenic** (lowering of leucocytes quantity but with their presence),

•**aleukemic** (no leucoses in peripheral blood).

Acute leucoses

•as to morphologic and cytochemical peculiarities of leucocytes are divided into

- lymphoblastic* and
- myeloblastic* leucoses or
- lymphoblastic and
- non-lymphoblastic.

•As to nowadays knowledge of hematosis among the **acute leucoses** there are:

- non-differentiated,
- myeloblastic with blasts maturation,

- promyelocytic,
- myelomonocytic,
- monocytic,
- monoblastic,
- erythroleucosis,
- megakaryoblastic variants which develop from spinal cell or cell precursors of class II-IV.
- Among the lymphoblastic leucoses according to immunal and cytogenetic characteristics there are 3 morphologic forms: L1, L2, L3.

Clinicopathologic characteristic of Acute leucoses.

- 1 The first manifestation of the acute leucosis is the presence of blastic cells in punctation of marrow of breast bone
- 2 marrow of breast bone changes its painting and consistence :
 - red,
 - succulent,
 - sometimes with grey shade under non-differentiated form;
 - pyoid under myeloblastic form;
 - raspberry-red under lympholeucosis).
- 3 In the peripheral blood the leukemic (leucemic) hiatus develops.
- It is a great number of blastic cells, too little of mature, and total absence transferring cell forms.
- 4 There is a substitution of marrow with the new blastic leukemic cells.

Clinicopathologic characteristic of Acute leucoses.

- 5 Gradually leukemic infiltration appears in the spleen,
 - liver,
 - lymph nodes,
 - kidneys,
 - meninx (brain tunic) (neuroleukemia under lymphoblastic leucosis),
 - mucous tunics of gastrointestinal tract,
 - lungs (leukemic pneumonitis under myeloleucosis) and other organs.
- 6 There develops anaemia, thrombocytopenia, and

Clinicopathologic characteristic of Acute leucoses.

Hemorrhagic syndrome on

- skin,
 - mucous tunics,
 - serous tunic,
 - internals,
 - cerebrum,
- necrotic tonsillitis (angina), septic complications, dystrophic changes in parenchymatous organs.

Clinicopathologic characteristic of Acute leucoses.

- Children* have acute leucoses more often;
- there can be inherited forms of disease.
- There are nodular infiltrations in different organs.
- The most common is T-dependent lymphoblastic leucosis,
- the less common is myeloblastic leucosis.

•The WBC's seen here are lymphocytes, but they are blasts--very immature cells with larger nuclei that contain nucleoli. Such lymphocytes are indicative of acute lymphocytic leukemia (ALL). ALL is more common in children than adults. Many cases of ALL in children respond well to treatment, and many are curable.

Causes of death:

- septic complications (especially often met under non-differentiated form),
- ulcero-necrotic complications,

- hemorrhages (especially dangerous into cerebrum which are often met under promyelocytic leucosis, progressive disease).

Medical pathomorphism of Acute leucoses:

- under the influence of therapy under leucoses
- the hemorrhagic diathesises,
- necrotic changes in mucous tunic of decreased mouth (oral) cavity;
- more often there met ulcero-necrotic changes in tunics of gastrointestinal tract;
- leukemic pneumonics,
- leukemic meningitis.

Chronic leucoses

are divided into

- leucoses of myelocytic origin,
- leucoses of lymphocytic origin,
- and leucoses of monocytic origin (myelomonocytic leucosis and histiocytosis).

- These mature lymphocytes are increased markedly in number. They are indicative of chronic lymphocytic leukemia, a disease most often seen in older adults. This disease responds poorly to treatment, but it is indolent.

Chronic leucoses of myelocytic origin or myeloproliferal diseases

are represented generally by

- chronic myelosis or chronic myeloid leucosis,
- chronic erythromyelosis,
- polycythemia,
- erythromia,
- myelofibrosis.

Chronic myeloid leucosis

- has two stages: monoclonal non-malignant and polyclonal malignant.
- The first stage lasts several years and is characterized by progressive increasing of neutrophilous leucocytes with transfer to myelocytes.
- At the later stage in 3-6 months there develops polyclonism,
- blastic cell form appear (myeloblasts, erythroblasts, monoblasts and other), blast crisis appears, the quantity of erythrocytes in blood increases to several millions per 1mcl, all manifestations of acute leucosis develop.

Morphology of Chronic myeloid leucosis

- Here is another view of a peripheral blood smear in a patient with CML. Often, the numbers of basophils and eosinophils, as well as bands and more immature myeloid cells (metamyelocytes and myelocytes) are increased. Unlike AML, there are not many blasts with CML.

Morphology of Chronic myeloid leucosis

- the spleen is abruptly increased to 6-8 kg (13,22-17,64 lbs),
- of grey with brown painting,
- atrophied follicles,
- sclerosis and hemosiderosis of pulp,
- leukemic infiltrates,
- leukemic thrombi in vessels;
- the liver is increased to 5-6 kg (11,02-13,22 lbs),
- of grey with brown painting,
- leukemic infiltration along the sinusoid,
- fatty dystrophy of hepatocytes,
- hemosiderosis;
- lymph nodes are diffusely very increased, soft, of grey with red painting.

Myelofibrosis

- is characterized by presence of myeloid leucosis manifestations
- and change of marrow to connective or bone (osseous) tissue.
- Thus the disease has a prolonged non-malignant course.

Erythromia

- is met among the elderly people
- and is characterized by increasing of mass of erythrocytes, thrombocytes, granulocytes in peripheral blood,
- increased blood (arterial) pressure,
- inclination to thrombosis, splenomegaly.

Chronic leucoses of lymphocytic origin

Chronic lympholeucosis

- develops among elderly people,
- appears from B-lymphocytes,
- but with abrupt lowering of immunoglobulin formation,
- development of autoimmune reactions,
- increased quantity of leucocytes in peripheral blood to 100 thousands per 1 mcl,
- leukemic infiltrates are present in all organs.

Morphology of Chronic lympholeucosis

- the marrow is red;
- the *spleen* is increased to 1 kg (2,2 lbs), of red painting,
- follicles are increased due to leukemic infiltrations;
- the *liver* is increased, of grey with brown painting,
- leukemic infiltration along the portal tract, fatty dystrophy of hepatocytes;
- *lymph nodes* are abruptly increased, thick, in the form of bags,
- can squeeze the neighbouring organs, of grey with pink painting;
- the *kidneys* are greatly increased, leukemic infiltration abruptly disturbs parenchymal structure.
- *Infectious* complication and hemolytic statuses are typical.

Infectious complication of Chronic lympholeucosis-pneumonia

Lympholeucosis (mesenterial nodes).

• On the macropreparation the intestine and increased mesenterial lymphnodes of bag shape are represented. Diameter of some nodes is reaches 5 cm The nodal pulp is homogeneous, of white painting. The nodes are increased because of extramedullar hematosis. The bag of abruptly increased mesenterial lymphnodes can press the vessels, nerves, which clinically manifest the tumour.

Tumours of plasmatic cells or paraproteinemic leucosis

- develop from B-lymphocytic system, the precursors of plasmatic cells.
- These cells synthesize the pathologic proteins, paraproteins. To this group of leucoses are numbered: *myeloma* (myelomatosis, plasmocytoma, Kahler's disease),
- *Valdenstrem's macroglobulinemia*,
- *Franklin's disease* of heavy chains.

Myeloma

- is characterized by spread of tumouric cells of lymphoplasmocytic line – myelomic cells in marrow with bones destruction.
- In peripheral blood there accumulated the pathologic proteins (paraproteins), which segregates into urine through the kidneys (Bens-Jones's protein).
- As to the character of myelomic infiltrates in marrow and bones there divide
- -diffusive,
- -diffusive-nodal,

- multiple forms of disease.

Myeloma

- The most affective there are the flat bones (skull and ribs), vertebrae, more seldom tubal with the development of bone tissue destruction. In the bones there develop osteolysis and osteoporosis.
- Myelomic infiltration is also observed in the internals: spleen, liver, kidneys, lungs, lymph nodes.
- Complications:*
- paraproteinemic nephrosis,
- myelomically wrinkled kidneys,
- renal amyloidosis (amyloidosis nephrosis),
- inflammatory changes as pneumonia, pyelonephritis. The other forms of paraproteinemic leucosis are seldom accompanied with bones destruction.

Renal amyloidosis

- The kidney is increased, of homogenously white painting, the edges between organ areas is absent. Renal amyloidosis complicates myeloid leukemia.

Renal amyloidosis

- plasmocytes product a great number of plasmaglobulines which go out via kidneys (Bence-Jones protein) and constipate them. Besides destruction products of bone tissue also of protein nature go out of the organism via kidneys and constipate the renal filter – the walls of glomerule capillaries

Tumour diseases of lymph nodes or lymphomas

- To this group are numbered:
- lymphosarcoma,
- mycosis fungoides,
- Caesary's disease,
- reticulosarcoma,
- Hodgkin's disease (lymphogranulomatosis).

Lymphomas.

- There are Hodgkin's and non-Hodgkin's lymphomas.
- They can be B- and T-cellular.
- Lymphomas or lymphocytomas are ectomarrow tumours which consist of
- different lymphocytes or of lymphocytes and
- prolymphocytes.
- They appear in lymph nodes or lymphoid tissue of the other internals.
- They are characterized by the local growth and non-malignant course.
- The first manifestation of lymphomas are increased peripheral lymph nodes,
- they become thicker, mobile, non-painful.
- Later there appear the manifestations of intoxication, general weakness, weight loss, night sweat, which is the manifestation of tumouric process.
- Transformation into lymphosarcoma is met seldom and after the long time.

Lymphosarcoma

- is a malignant lymphoma of mediastinal, extraperitoneal, inguinal lymph nodes, and lymph tissue of gastrointestinal tract.
- The nodes increase with the necrotic and hemorrhagic areas.
- Process generalization courses lymphatically and hematogenously.
- To this group are numbered: Burkitt's lymphoma (Burkitt's tumor) - endemic disease of African children when facial skeleton bones are damaged.
- The cause is the herpetiformis virus.

Metastases lymphoma in kidney

Lymphosarcoma of kidney

Hodgkin's disease (lymphogranulomatosis)

- is a chronic recurrent lymphoma with affection of cervical, mediastinal, extraperitoneal, inguinal lymph nodes.
- There are isolated (local) and spread (generalized) forms.

- The *spleen* is often affected (necrosis niduses of white with yellow painting, sclerosis, lymphocytic infiltration), that's why it turns to variegated and porphyric look.
 - In *lymph nodes* there appear proliferation of leucocytes, histiocytes, reticular cells, eosinophils, plasmatic cells, neutrophilic leucocytes, necrosis and sclerosis niduses, atypical mononuclear small and big Hodgkin's cells, polynuclear giant Reed-Berezovsky-Stenberg's cells.
- This is a high power view of a Reed-Sternberg cell seen with Hodgkin's disease. Note the large, prominent nucleoli.
- This is Hodgkin's disease, mixed cellularity type. A mixed cell population is present. This form of HD tends to be disseminated.
- This is Hodgkin's disease, lymphocyte depletion type. Many Reed-Sternberg cells and variants are present, as seen here at medium and high magnification. This type of HD is not common.

Hodgkin's disease (lymphogranulomatosis)

- There are *four clinicopathologic forms* of disease:
 - predominance of lymph tissue (lymphohistiocytic) variant – I-II stages of disease, its localized form,
 - nodular sclerosis is met under non-malignant course of disease,
 - mixed-cellular variant appears under disease spread and corresponds to the II-III stages, oppression of lymph tissue variant is typical for the generalized form
 - and has a malignant course, sometimes called Hodgkin's sarcoma.
- thanks