# ONCOLOGY

## NEW STRAIN OF TRANSPLANTABLE MOUSE LEUKEMIA

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In recent years, the interest of Soviet researchers in the problem of the etiology, pathogenesis and therapy of leukemias and, especially, in the experimental study of this disease [3, 5] has increased noticeably. The most convenient model for the study of some aspects of this problem, especially for experimental-therapeutic research, are the transplantable leukemias of mice. At present, only one strain of transplantable leukemia is being sustained and used in the laboratories of our country – the strain LIO-1, obtained and described by L. L. Malyugina [4]. Yet in carrying out experimental therapeutic research, comparative study of the action of this or that preparation on various strains of leukemia, which differ from each other in their properties, is important. On the basis of these considerations, we carried out a number of experiments whose purpose was to obtain a new strain of transplantable mouse leukemia.

In order to obtain a strain, we selected several mice of the afb variety with spontaneous leukemias and carried out hematological investigations. Test transplants were made of the leukemic tissue of these mice (enlarged lymph nodes and thymus) to young mice of the same variety. The leukemia which caused the sharpest leukemic changes in the blood of the original mouse and in the first generation after transplantation was selected for further work. The blood of the original mouse contained 90,000 leukocytes per 1 $mm^3$, its differential blood count was: lymphoblasts 54%, prolymphocytes 18%, lymphocytes 8%, polymorphonuclear neutrophils 19.5%, eosinophils 0.5%, monocytes 3%. The spontaneous leukemia we chose was fourth in number of those used in the tests, so our new strain was given the code designation LIV.

Later we carried this strain, by intraperitoneal (more rarely subcutaneous) transplants of a suspension of leukemic tissue, to mice of the variety afb for 1 – 1½ months. Before January 1, 1955, the strain was transplanted in 52 generations. With intraperitoneal transplant, local tumors did not appear in the mice, but generalized leukemia developed immediately, characterized by the same clinical symptoms as spontaneous mouse leukemia: general lassitude, more rapid respiration and enlargement of the peripheral (inguinal and cervical) lymph nodes. Usually the mice died no later than 1-3 days after the appearance of these symptoms. Small tumors at the place of transplantation appeared 7-10 days after subcutaneous transplantation of the leukemic tissue. However, these tumors did not have time to grow to a large size since generalization occurred in a few days and leukemia was found. It is interesting to note that the time in which the mice died of leukemia gradually decreased as the strain was transplanted (see Table). This increased speed of development of the leukemia, apparently, indicates that as it was transplanted, the strain gradually became more malignant. Such an increase in malignancy was observed repeatedly when various strains of malignant tumors were obtained [6]. Transplantable leukemias are no exception in this respect.

Usually hematological investigations of the blood were carried out on mice with already marked clinical symptoms of leukemia. The number of leukocytes in the blood of all the investigated mice was increased, very

considerably in the majority of cases. Thus, of 30 experimental animals, 7 were found to have from 30,000 to 50,000 leukocytes per 1 $mm^3$, 10 from 50,000 to 100,000, 6 from 100,000 to 200,000 and 7 over 200,000 per 1 $mm^3$.

Changes in the Time of Death of Mice When Strain LIV is Transplanted

| Time death of mice (in days) | Generation | | |
|---|---|---|---|
| | Minimum | Maximum | Average |
| 1—10 | 10 | 30 | 18.3±1.0 |
| 11—20 | 9 | 24 | 14.4±0.4 |
| 21—30 | 7 | 20 | 12.8±0.3 |
| 31—40 | 7 | 15 | 10.3±0.3 |
| 41—50 | 7 | 12 | 9.5±0.2 |

The differential blood count of all the mice disclosed immature cells of the lymphocytic series – lymphoblasts, which formed from 22-75% of all the leukocytes. More mature lymphatic cells, prolymphocytes and lymphocytes, composed 20-40% of all the leukocytes in the majority of cases. In some animals, polymorphonuclear neutrophils composed only a small part of the leukocytes (from 10-20%), but in approximately half of the leukemic mice investigated the percentage of these cells was increased to 30-50%. If the considerable increase in the total number of leukocytes in these mice is taken into account, and corresponding recalculations are made, then it is found that the absolute number of polymorphonuclear neutrophils in these animals was increased (to 40,000-50,000 per 1 $mm^3$) in comparison with the normal (from 2600 to 15,200 according to the data of Ginzburg [2]). At the same time, mature forms of neutrophilic leukocytes always predominated in the blood; the percentage of young neutrophils was small (from 0 to 3).

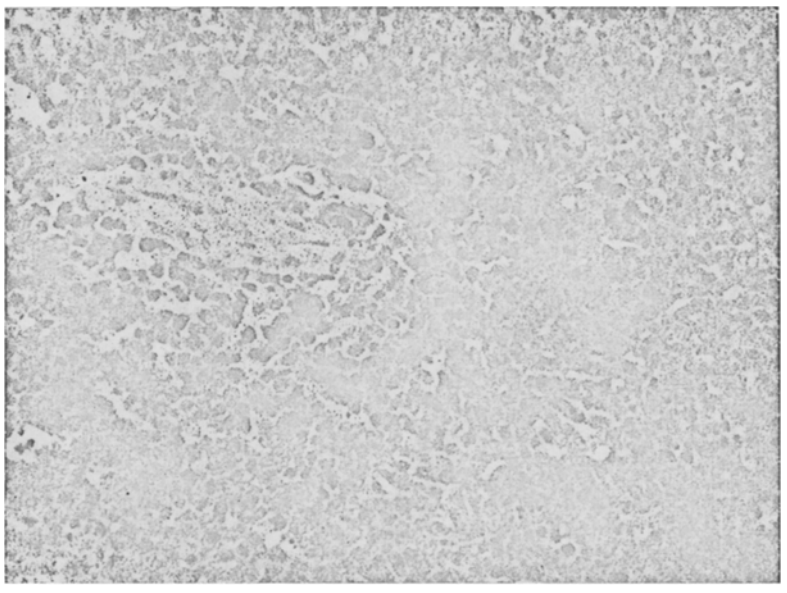

Fig. 1. Leukemic infiltration of the spleen, enlarged 400 X.

Thus, the blood changes were characteristic of the lymphatic type of leukemia. Along with this, an increase in the number of neutrophilic leukocytes in the blood was noted in part of the animals. It is known [7 that such a leukemoid reaction is occasionally observed in mice when lymphatic leukemia is developing. Undifferentiated cells of the lymphatic type also predominated in smears of bone marrow.

Autopsy of mice which died of leukemia disclosed considerable enlargement of all the lymphatic nodes (inguinal, cervical, mesenteric etc.), the thyroid gland, the spleen and the liver, as well as some enlargement of both kidneys. On histological examination it was found that the normal tissue of the spleen, lymph nodes

and thyroid gland was almost completely replaced by leukemic tissue, consisting of fairly large atypical cells of rounded or polygonal shape, with a thin layer of cytoplasm and large, rounded, lightly-staining nuclei containing one or several large nucleoli (Fig. 1). Remains of lymph follicles were found only occasionally in this tissue. Numerous growth foci of the same leukemic tissue were found in the liver, located perivascularly, close to the central veins of the hepatic lobes. In addition, individual leukemic cells and small groups of such cells were located between the liver ligaments (Fig. 2). Leukemic infiltration was also found in the kidneys, located between the renal canals and below the capsule (Fig. 3). Large infiltrations were occasionally located

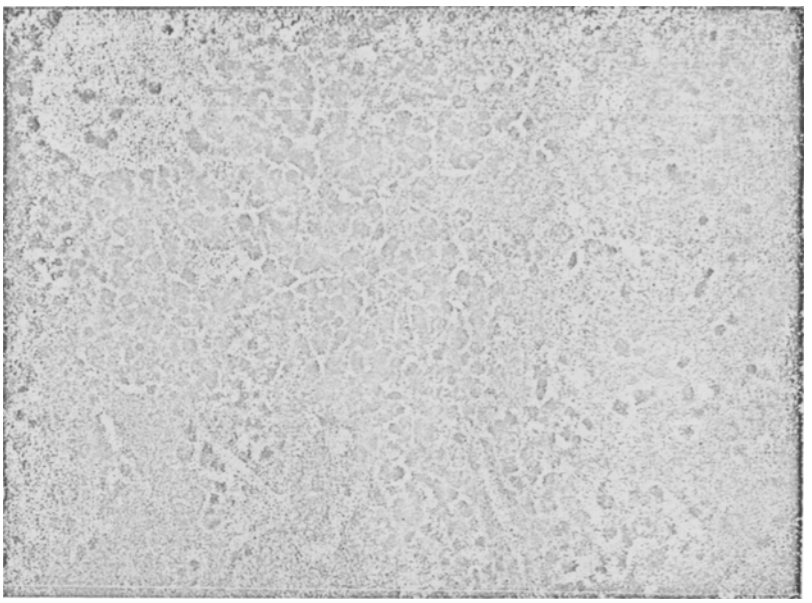

Fig. 2. Leukemic infiltration of the liver, enlarged 400 X.

Fig. 3. Leukemic infiltration of the kidney, enlarged 100 X.

in the perirenal fat. There was no leukemic infiltration of the lungs and cardiac muscle. We did not observe significant changes in the hematological and pathologic-anatomic picture of leukemia during transplantation of the new strain.

Thus, rapid development of generalized leukemic invasion of all the lymph nodes, liver, spleen and kidneys, as well as the sharp changes in the blood picture and bone marrow typical of lymphatic leukemia, are characteristic of the strain described above. Bacteriological control of seedings from the organs of the dead animals gave negative results. The fact that transplantation of leukemia requires a transfer of cells is also confirmed by the variety specificity of the strain: all attempts to transplant leukemia LIV to mice of other varieties (C57, CC57 etc.) gave negative results. Strain LIV differs somewhat in its properties from Strain LIO-I. The appearance of a large leukemic tumor at the place of transplantation is characteristic of the latter, while leukemic invasion of the organs and leukemic changes in the blood do not develop in all the mice and are not always sharply evidenced. It is probable that experiments with strain LIO-I and with strain LIV can complement each other in experimental therapeutic investigations: the first strain is more convenient to study the effect of a given substance on a local leukemic tumor, while the effect of the same preparations on generalized leukemic invasion can be studied in experiments with strain LIV, and changes in the blood picture can be one of the criteria of the effectiveness of the preparations.

## SUMMARY

Investigation of a new strain of transplantable lymphatic leukemia (LIO-I) in mice of the afb variety was carried out. The original leukemia arose spontaneously in the afb mice. After transplantation of LIO-I, leukemia in the form of a small local tumor appeared. In a few days, severe leukemic infiltration of lymphatic glands and internal organs developed. The number of leukocytes in the blood increased to 150,000-250,000.

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