THE SIGNIFICANCE OF THE LYMPHOID APPARATUS OF THE BRONCHIAL TREE IN THE DEVELOPMENT OF LEUKEMIC FOCI IN THE LUNGS ASSOCIATED WITH TRANSPLANTED LEUKEMIA IN MICE

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In works on experimental leukemia in mice, diverse data has been presented on the frequency of lung involvement in the leukemic process. N. P. Voshchanova [1] observed the appearance of leukemic infiltrates associated with spontaneous and transplanted leukemia of mice. According to her data, the leukemic infiltrates were always nestlike in character, and were located along the course of vessels and bronchi. However, leukemic changes apparently do not always arise in the lungs. Thus, A. Ya. Krashilina [4], working with transplanted leukemia in mice, did not observe these changes up to the 6th day of transplantation.

Studying the morphogenesis of leukemic cells during transplanted hemocytoblastic leukemia in mice, we undertook to follow the changes in the lymphoid apparatus of the bronchial tree and to elucidate the pattern of lung involvement in the leukemic process.

EXPERIMENTAL METHOD

The lungs were studied in 55 mice of the high-leukemia Afb line, in the 2-3.5 month age range, from the first day of development of leukemia up to the death of the animals on the 12th-14th day. As a control, we used 10 mice of this line, in the same age groups. The preparations were fixed in Bouin's solution, and stained with eosin-azure, hematoxylin-eosin, by the method of Van Gieson, and with fuchselin.

EXPERIMENTAL RESULTS

In the different mice of the control series, the degree of patency of the bronchial lymphoid apparatus was varied. Around the vessels and bronchi of large caliber, and in the precorneal zone, as a rule, we observed single, solitary follicles, without manifest centers of multiplication. In the membrane proper of the small bronchi, and in the respiratory portion, the lymphoid accumulations were very scanty, and sometimes absent. In 2 mice, with a background of residual symptoms from spontaneously arising pneumonia (chance finding), we noted flourishing lymphoid infiltrates around the large vessels and bronchi, and also in the respiratory portion of the lung. They consisted of lymphoblasts, lymphocytes, and a small number of hemocytoblasts.

Out of the 55 mice with transplanted leukemia, leukemic infiltrates were observed in the lungs in only 16 animals. In the remaining 39 mice, the lymphoid apparatus of the bronchial tree was manifested weakly, and in a number of the cases we observed complete disappearance of lymphocytes from the perivascular and peribronchial seams in the late stages of the transplantation. These seams appeared as fibrous tissue, in which we sometimes observed single cells or chains of hemocytoblasts. In the period of generalization of the leukosis associated with leukemia, leukemic hemocytoblasts were observed only in the lung capillaries, in the form of passing cells.

As chance findings, in the lung tissue of 16 mice we observed small leukocytic or fibrinous-hemorrhagic foci of spontaneously arising pneumonia, and also residua of pneumonia in the form of accumulations of macrophages in the alveoli. In the lungs of these mice we noted markedly apparent hyperplasia of the lymphoid apparatus. Around the vessels and bronchi, and often also in the respiratory portion of the lung and in the subpleural region, there were large cellular accumulations, and the cellular composition of these foci varied, depending on the stage of transplan-

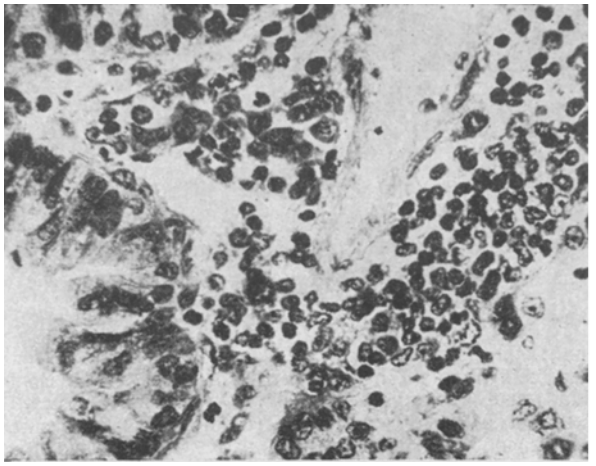

Fig. 1. Hyperplasia of the reticular cells of a lymphoid follicle (peribronchial) on the 2nd day of transplantation. Stained by the method of Van Gieson. Obj.40, ocul. 10.

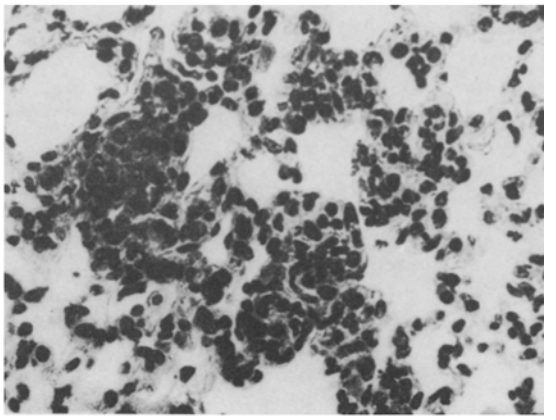

Fig. 2. Leukemic infiltrate composed of hemocytoblasts, in the respiratory portion of the lung, on the 8th day of transplantation. Stained with azur-eosin. Obj. 10, ocul. 15.

tation. Thus, on the 1st-3rd day of transplantation (6 mice) the cellular foci consisted of lymphocytes, lymphoblasts, and large, sedentary reticular cells of elongated or oval form, with a wide zone of protoplasm and light-blue nucleus. Among these cells we encountered solitary and large, spherical cells, with heavily basophilic protoplasm and a light nucleus containing a nucleolus (Fig. 1).

On the 5th-6th day of transplantation (5 mice), within the lymph follicles we observed an increase in the number of young, indifferent cells, with a basophilic ring of protoplasm, and a light nucleus and nucleolus. They no longer were arranged individually, but in whole groups, and made up the basic mass of the follicle. The mature lymphocytes were arranged in small mounds. Isolated mitoses were noted. According to morphological form, the cells in the follicles that had the light nucleus completely corresponded to hemocytoblasts.

In the subsequent days of the transplantation (5 mice), mature lymphocytes became absent from the lymphoid accumulations of the bronchial tree, the cellular infiltrates consisted of monotypic hemocytoblasts, and the number of mitoses rose.

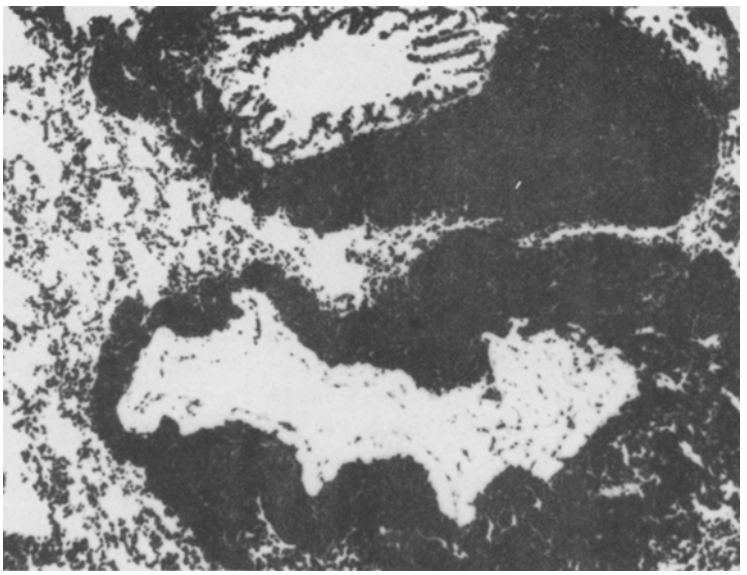

Fig. 3. Wide sleeves of hemocytoblasts around the vessels and bronchi, on the 13th day of transplantation. Stained by the method of Van Gieson. Hand lens.

Leukemic infiltrates in the respiratory portion of the lung, markedly thickening the wall of the alveolus, led to partial atelectasis of the lungs (Fig. 2). In one case, the leukemic infiltrate occupied an entire lobe of the lung. Staining for elastic tissue made it possible to demonstrate complete atelectasis of this pulmonary lobe, and to establish the pseudodiffuse character of the infiltrate.

By the 12th-14th day of transplantation, the alveoli in the lungs were distended, and filled with macrophages; in the interalveolar capillaries we observed passing hemocytoblasts. Around the vessels and bronchi of all calibers there appeared wide, cellular sleeves of hemocytoblasts (Fig. 3). The hemocytoblasts infiltrated the wall of the bronchus, and formed accumulations in the subpleural zone. As a result of this, the lung looked like an hematopoietic organ with multiple foci of blood formation, located throughout the entire parenchyma of the lung and consisting of hemocytoblasts.

Our attention was drawn to the lack of a parallel relationship between the extent of the leukemic process in the subcutaneous focus of the transplant and the extent of the process in the lungs, as observed at varying stages. Thus, on the 1st-2nd day after the transplantation—when the focus itself showed nonspecific hyperplasia of the recipient's tissue and necrosis of the transplanted material—in the lungs, with the presence of an inflammatory process, we sometimes observed a markedly manifested hyperplasia of the lymphoid apparatus of the bronchial tree and the respiratory division.

In other cases, at later stages of the transplantation (8th-12th day), when a more or less large nest of hemocytoblasts had formed in the transplant focus, and generalization of the leukemic process throughout the entire organism had begun, we failed to observe leukemic changes in the lungs, the lymphoid follicles of the large bronchi were weakly apparent, and we did not find any foci of hyperplasia in the respiratory division.

Thus, we observed participation of the lungs in the generalized leukemic process in only 16 of the 55 mice, i.e., in less than 1/4 of the cases.

In the remaining 39 mice, no leukemic infiltrates formed in the lungs. In this case, we did not even observe the lymphoid accumulations of the bronchial tree [3, 5], characteristic for healthy mice. We believe that in the development of leukemic foci in the lungs, associated with transplanted leukemia, a chief role is played by the condition of the lymphoid apparatus of the mouse's lung at the moment of the transplantation. It is known that in mice, during infections and intoxications, extensive foci of hematopoiesis arise in the lungs, liver, and other organs, which undergo reverse development upon removal of the causative agents [1, 2, 6].

However, in our observations, there was no reverse development of these foci in the course of the leukemic process. The young, polypotential cells in the lymphoid apparatus of the perivascular and peribronchial seams differentiated toward the hemocytoblast side, while the mature lymphocytes disappeared. The leukemic infiltrates in the lung were localized at the site of usual situation of the lymphoid apparatus, in the form of isolated foci around vessels and bronchi, under the pleura, and in the respiratory division of the lung around the capillaries; associated with partial atelectasis of the lung tissue, they showed a pseudodiffuse appearance.

On the basis of our data, one can apparently conclude that, in the lungs of mice, leukemic infiltrates associated with transplanted leukosis only form in those cases where there is manifest hyperplasia of the lymphoid apparatus and the reticular cells in the lung tissue, related to inflammation of the lungs. In the absence of such a "preparatory" period, one does not observe leukemic infiltrates in the pulmonary tissue of mice associated with transplanted leukemia.

SUMMARY

In studying the transplantable hemocytoblastic leukemia in mice changes in the lungs were traced from the 1st to the 12th day of the development of this affection. As a rule, no leukemic infiltrates occurred in the lungs in leukemia of affected mice. Leukemic infiltrates from hemocytoblasts are formed only in cases when there is a marked hyperplasia of lymphoid follicles of the bronchial tree in the presence of inflammatory process in the lungs. Leukemic infiltrates are nestlike in nature, are located in the usual sites of lymphoidal accumulations and with a partial atelectasis of the lungs may acquire a pseudodiffuse appearance. There was no conformity between the development of leukemic changes in the transplantation focus and in the pulmonary tissue.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
