CELLOPHANE TUMORS OF THE SPLEEN

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Few investigations have been made of the role of plastics in tumor formation. Several authors [8, 9, 10, 13-17], by grafting layers of cellophane and other plastics subcutaneously in rats and intraperitoneally in mice and rats, have produced tumors of the type of sarcomas in these animals after 13-15 months. Recently some investigators, by wrapping the organs of rats, especially the kidney [2, 18] and muscle [7] with cellophane and other plastics, have produced tumors of these organs. However, notwithstanding these investigations, the problem whether the organs and tissues of the rat can undergo neoplastic degeneration as a result of wrapping in cellophane film remains unsolved.

In the present investigation the development of tumors of the spleen was studied after this organ had been wrapped with cellophane film. The spleen is known to undergo malignant degeneration relatively rarely, even when chemical carcinogens are injected directly into it.

EXPERIMENTAL METHOD

The spleen was wrapped with two or three layers of boiled cellophane film. In the region where the neurovascular bundle approaches the spleen the cellophane was cut to preserve the normal blood supply and innervation. Experiments were carried out on 22 noninbred albino rats weighing 85-95 g. The animals were divided into two series.

In 10 animals of series I the whole spleen was wrapped in cellophane, but not tightly, leaving a large free space so as not to compress the growing organ. In the 12 rats of series II only part of the spleen was wrapped in cellophane and the rest remained free. The spleen of normal rats was used as a control. The animals of series I were sacrificed when large tumors had been obtained, as revealed by external examination (13-17 months). The rats of series II were sacrificed after 20-22 months. The material was fixed in Zenker's fluid. Sections were stained with Regaud's iron-hematoxylin and counterstained by Mallory's and Giemsa's methods.

EXPERIMENTAL RESULTS

In the animals of series I, from the 8 investigated rats (2 animals died during the experiment) three tumors of the spleen, belonging to two types, were obtained after 13-17 months. One tumor was of the ascites-cystic type and the other two of the solid type (Fig. 1). At necropsy on these animals no cellophane could be found.

In the experiments of series II, no growth of the spleen could be found with the exception of a small visible enlargement, but slight proliferation of the pancreas of ascites-cystic type was always observed. The cellophane, covered with a very thin connective-tissue capsule, was found in all the animals.

The tumor of ascites-cystic type consisted of two large growths, each of them composed of large and small cavities and cysts, filled with dark yellow content. The content were fairly fluid, but in the middle of the tumor the cavities and cysts were found with contents consisting of jelly. The amount of exudate escaping from the cavities and cysts at necropsy was about 150 ml. Normal spleen tissue was almost completely absent from the tumor.

The results of a microscopic investigation showed that the tumor covered with a dense connective-tissue capsule. At the edge of the tumor, two or three layers of mast cells were present in the capsule. The walls of the cyst and cavities consisted of two layers. The outer layer was composed of coarse collagen fibers, staining an

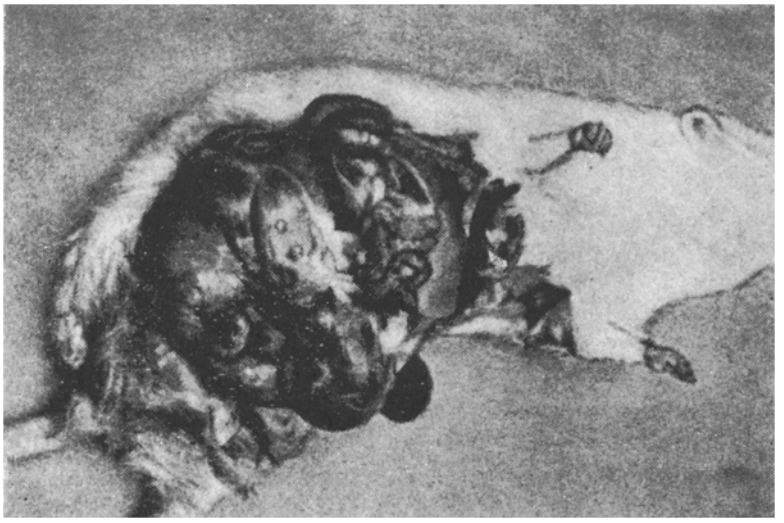

Fig. 1. General appearance of the solid tumors of the spleen.

intensive blue color by Mallory's method, and of small connective-tissue cells. Usually the outer layer bounded several cysts. The inner membrane of the cyst and cavities consisted of thin collagen fibers, staining pale blue by Mallory's method, and with very infrequent cells. Sometimes groups of between 3-5 and 10 mast cells were present here.

The cells composing the contents of the cysts and cavities were mature neutrophils with a fragmented nucleus, and a vacuolated cytoplasm staining from pink to violet by Giemsa's method. Lymphocytes and plasma cells with a highly modified cytoplasm and often with a pycnotic nucleus were rarely seen. All the cells mentioned above were situated in the spaces between the fibrin network. No mitoses were found in the central part of the tumor. The periphery of the tumor was denser than the center, and it had no cysts or cavities. The cell composition of the peripheral zone of the tumor differed from the contents of the cysts. It was composed of large connective-tissue cells with polymorphic nuclei (vesicular, laciniate, dark and light). The cells varied considerably in size. Besides fibroblasts, including giant-cell forms, fat cells and various lymphatic cells were found, while at the periphery there were far fewer neutrophilic myelocytes. At the periphery mitoses were rare and they were atypical in structure (Fig. 2).

The tumors of solid type were large (on the average 7.5 × 5 cm, 3 cm thick) and filled a large proportion of the peritoneal cavity. In color they resembled the normal spleen. Lighter spots could be seen on their surface. In one tumor a small cyst with dark blood-stained contents was found. In contrast to these ascites-cystic tumor described above, the tumors of solid type in the preparations had an ill-defined connective-tissue membrane. The tissue of the tumors was very loose and permeated with many blood vessels. The light spots seen on the surface of the tumor on macroscopic examination were necrotic areas containing large numbers of leukocytes (neutrophils). The zones of necrosis were sharply demarcated from the tumor tissue, consisting of fibroblasts and lymphocytes. The fibroblasts were larger cells, with processes and with oval, vesicular nuclei, containing between one and five nucleoli. The chromatin was concentrated into large granules and uniformly distributed throughout the nucleus. The cytoplasm of the fibroblasts sometimes contained coarse granules, staining violet by Giemsa's method. The lymphocytes appeared larger than normal, with polymorphic nuclei and often with vacuolated cytoplasm (Fig. 2). In the tumor atypical mitoses from the prophase to the telophase were often seen. In the marginal zone of the tumor sinuses were present, filled with blood. Migration of the connective-tissue cells in these sinuses could often be seen.

It may be concluded from this description that the growths obtained were most probably tumors. This was shown by the rate and character of their growth, the presence of mitoses, the ability of the tumor cells to migrate, and so on, and in addition, by the similarity of their structure with that of spleen tumors previously described [4, 12].

Many different opinions are held on the mechanism of action of the cellophane film grafted into the animal organism. Some authors [11] consider that the main cause of the development of a tumor in the body is the formation of active radicals at the border between the cellophane film and the body tissues. Other investigators [1, 2, 3, 8, 9] consider that the development of the tumor is associated with the appearance of a connective-tissue capsule

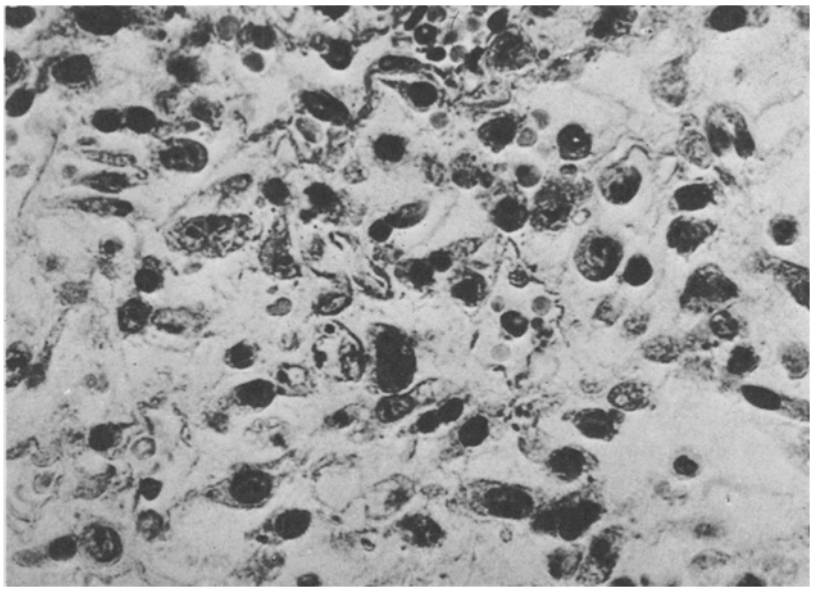

Fig. 2. Cellular composition of an area of a tumor of the spleen. Stained by Giemsa's method. Magnification 280 ×.

around the cellophane film as a result of proliferative inflammation. In the deep layers of the capsule selection takes place (probably by disturbance of the supply of nutritive substances and oxygen) of the more resistant and, consequently, of the malignant cells. On the grounds of the production of cellophane tumors of muscles, A. A. Studitskii [6, 7] suggests that tumors arising in organs when wrapped in cellophane are the result of a disturbance of the interaction between the tissue which, in the normal organism, is probably effected by means of specific chemical substances.

The production of tumors of the spleen in these experiments as a result of wrapping the organ completely cellophane film but preserving the normal lymph and blood supply and the normal innervation of the organs, the absence of cellophane in the center of the tumor, and of a firm capsule around the cellophane, and also the changes arising in the intestine and pancreas support the view that these tumors probably appear as a result of a disturbance of the relationship between the spleen and the organs of the abdominal cavity.

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