MORPHOLOGY OF GROWTH OF HETEROGRAFTS OF HUMAN OVARIAN CARCINOMA IN DIFFUSION CHAMBERS

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The study of the morphology of growth of heterografts of human tumors in diffusion chambers is a necessary preliminary to their successful use for the study of sensitivity of these tumors to drugs. With respect to heterografts of ovarian tumors there have been only two communications whose authors have briefly stated that they observed growth of both epithelial and of fibroblast-like cells [3, 6].

EXPERIMENTAL METHOD

Heterografts of ovarian carcinoma were studied: seven serous papillary adenocarcinomas, three papillary cystadenocarcinomas, one mucinous cystadenocarcinoma, and four adeno-papillary carcinomas (altogether fifteen patients). Material for heterotransplantation was obtained from the gynecology operating department of the clinic of the Oncologic Scientific Center, Academy of Medical Sciences of the USSR. Chambers with tumor tissue were implanted into mice: either (CBA × C57BL)F_1 hybrids, of the BDF line, or noninbred. The technique of heterografting was described previously [5]. Microscopic investigation of the heterografts was carried out in the course of four weeks starting 1-5 days after transplantation. Altogether 4 to 6 grafts were studied at each time. Sections were stained with Carazzi's hematoxylin.

EXPERIMENTAL RESULTS

In all cases the heterografts consisted of a contact cluster of epithelial cells. In eight cases (7 serous and 1 mucinous carcinoma) the character of growth was identical and the only difference was in the rate of growth. In four of these eight cases, 3-5 days after transplantation migration of groups containing from 5 to 30 epithelial cells was observed along the edge of the graft (Fig. 1). The cells were round, angular, or oval in shape, with pale, frothy cytoplasm, and with a large, round, or irregularly shaped nucleus containing small granules of chromatin and a large nucleolus. The greater diameter of their nuclei in one of these preparations varied from 10 to 20 μ. Between 10 and 21 days after transplantation the whole surface of the filter was covered with a layer of compactly arranged epithelial cells, distinguished by considerable polymorphism (Fig. 2). In some parts these cells had a large nucleus of 20 μ in diameter and a wide pale cytoplasm around it, whereas in other parts the cells were smaller, the nucleus was under 10 μ in diameter, and it was surrounded by a narrow ridge of cytoplasm. They formed a characteristic pattern, being arranged in groups resembling rosettes, forming twists and turns. Some binuclear cells were seen. In one field of vision under low power (ocular 7, objective 10) one or two figures of mitotic division were counted.

In four other cases the surface of the filter was covered by a similar sheet of epithelial cells as early as 3-5 days after transplantation.

Mixed growth was observed on heterotransplantation of spleen serous and four adeno-papillary carcinomas. In the early stages (1-5 days) after transplantation, besides groups of 10 to 12 migrating epithelial cells, in some areas around the edge of the graft outgrowths of fibroblast-like cells could be distinguished. The epithelial cells were round, oval, or angular in shape, with a round or irregularly shaped nucleus containing fine granules of chromatin and a large nucleolus. The greater diameter of their nuclei varied from 8 to 12 μ. The fibroblast-like cells were long and ended in two thin, long processes running in opposite directions, and

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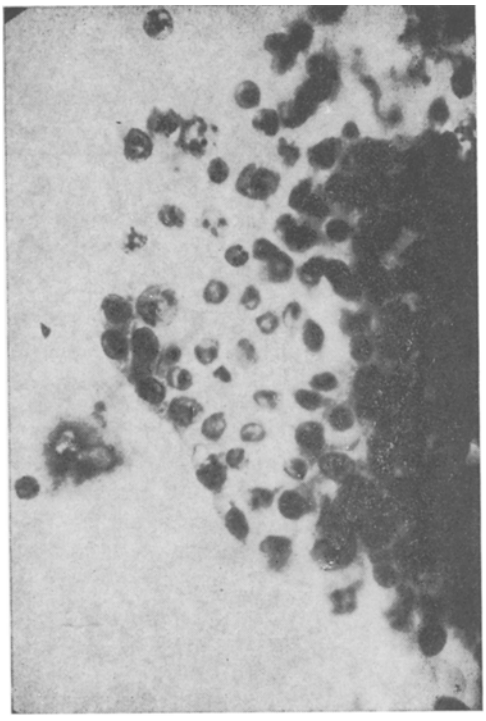

Fig. 1

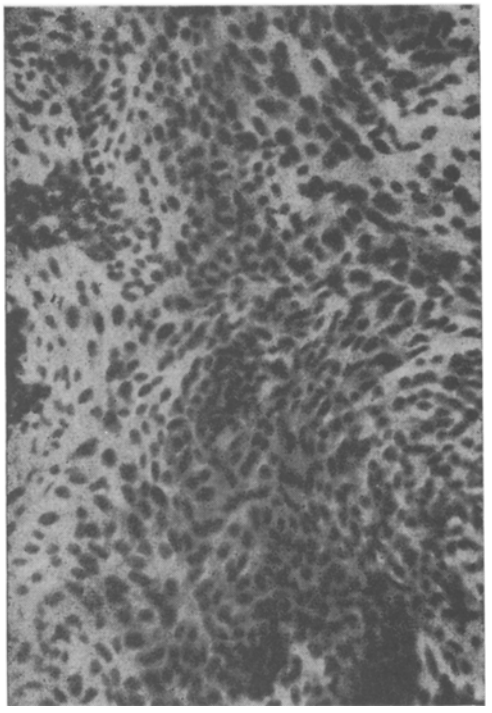

Fig. 2

Fig. 1. Migration of epithelial cells along border of graft. Serous papillary adenocarcinoma, 4 days. Ocular 10, objective 16.

Fig. 2. Layer of epithelial cells forming a complex pattern. Mucinous cystadenocarcinoma, 10 days. Ocular 10, objective 10.

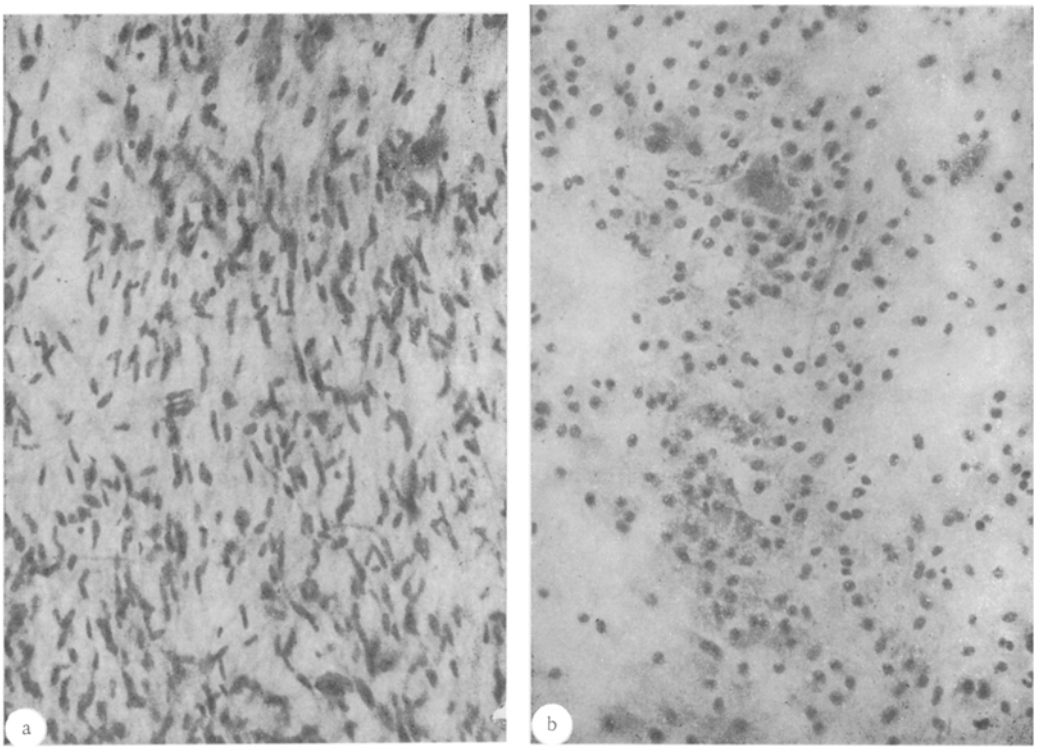

Fig. 3. Zone of growth formed around graft. Adeno-papillary carcinoma, 21 days. a) Fibroblast-like cells, compactly arranged around the graft; b) area of epithelial cells. Ocular 10, objective 9.

their nuclei were elongated oval-shaped; the cells were oriented in a radial direction. The length of their nuclei varied between 20 and 30 μ in the same specimens. Later, starting from the 7th day, a zone of growth occupying a large part of the filter was formed around the graft. It was formed by fibroblast-like cells, arranged compactly around the graft, and by areas of epithelial cells, distributed in its peripheral part and outside (Fig. 3). These latter areas were distinguished by greater polymorphism than at the previous times. Among them there were binuclear and polynuclear cells. In one field of vision under low power (ocular 7, objective 10) 2 or 3 figures of mitotic division were counted.

Investigations of heterografts of human ovarian carcinoma in diffusion chambers thus revealed two types of their growth. In some cases growth of epithelial cells covering the whole surface of the filter and forming a characteristic pattern took place. In other cases there was a mixed picture: growth of epithelial and fibroblast-like cells. These pictures are similar to those observed during culture of human ovarian carcinoma in vitro [1, 2, 4, 7].

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