

A cell-free virus-like oncogenic agent is present in polyps and desmoid fibroids of patients with familial adenomatosis of the colon

Keywords: Familial adenomatosis of the colon, polyp, desmoid, cell-free agent, intestinal and oral cancer in rats

Introduction

15-20% of human tumors are caused by viruses. Among them are cervical cancer, Burkitt's lymphoma, liver cancer and a number of others. Oncogenic viruses are also detected in colon cancers, but the relationship is less defined. Familial adenomatosis of the colon (FAC) is an autosomal dominant hereditary syndrome, which is characterized by the development of multiple adenomas with their subsequent malignant transformation in 100% of cases. In some patients, many thousands of polyps replace the normal colon mucosa. Colon polyposis is also often combined with the development of desmoids and osteomas (Gardner's syndrome). The cause of the development of FAC are mutations in the APC (adenomatous polyposis coli) gene. This study was performed about 50 years ago at the National Medical Research Center of Coloproctology in Moscow during a period of high interest in the viral etiology of human tumors worldwide. We observed the development of intestinal and oral cancers in Wistar rats after the introduction of cell-free materials from tumors of patients with FAC. These data were published in Russian and remained unknown to English-speaking researchers.^{1,2} In this short article, we summarize the main results of the study.

Methods

The homogenates of polyps and desmoids were centrifuged at 7000xg. The supernatants (SN) were sequentially centrifuged at 35000xg and 100000xg. The sediment after the last centrifugation (SC) was dissolved in cell culture medium No. 199 (Polio Institute, Moscow): 3.0 ml of medium per 30.0 g of tumor tissue. The SC was sterilized through a Chamberlain bacterial filter. Primary cultures of human fetal intestinal fibroblasts and rat embryo fibroblasts were infected with filtrate of SC polyps and desmoid fibroids. SN, SC and medium from cultures fibroblasts of the 1-2 passages were administered to newborn Wistar rats and golden hamsters intraperitoneally in 0.3 ml. The control group of animals was injected with the same materials from the non-tumor mucosa of the colon resected in cancer patients. The incidence of tumors was determined among rats that survived the time of the first tumor.

Results

Tumors of the digestive tract developed in 19 of 62 (30.6%) rats who were injected with cell-free materials from polyps and desmoids. Intestinal and oral cancers were observed in 9 and 10 rats, respectively. The average age of rats with intestinal cancer was 13.1 (3.5-23) months and with oral cancer was 21.4 (17-23) months. After the introduction of the material from the polyps, tumors were observed in 12 out of 44 rats: SN-5/21 rats (in all oral cancer), SC-4/15 rats (small intestine cancer -2, colon cancer-1 and oral cancer-1),

fibroblast culture medium- 3/8 (colon and small intestine cancer-1, small intestine cancer-1, oral cancer-1). After the introduction of the material from desmoids, tumors were observed in 7 out of 18 rats: SN-4/13 (small intestine cancer-2, caecum cancer-1 and oral cancer-1), fibroblast culture medium- 3/5 (small intestine cancer-1, oral cancer-2). After the introduction of non-tumor mucosa material, tumor was observed in 1 of 51 (1.9%) rats: SN-0/12, SC-0/19, fibroblast culture medium-1/20 (small intestine cancer). Intestinal and oral tumors of rats had the structure of adenocarcinoma and keratinizing squamous cell carcinoma, respectively. In a group of 67 rats from this population that were not used in the experiment, no tumors of the digestive tract were observed. Tumors of other organs and tissues (mammary fibroadenoma, fibroma, sarcoma, paraganglioma, etc) occurred with the same frequency in the experimental and intact groups of rats. No intestinal and oral tumors were observed in golden hamsters after injection of SN polyps and desmoids.

Discussion

Cell-free oncogenic agent from polyps and desmoids of patients with FAC caused intestinal and oral cancer after injection to newborn rats. The agent has the properties of a virus: it precipitates during ultracentrifugation, passes through a bacterial filter and remains active in cell culture. Tumors of the digestive tract were not observed in this population of rats in their natural state. Intestinal cancer in one rat of the control group could be caused by an oncogenic agent that is located in the non-tumor intestinal mucosa, which is the natural habitat of many viruses. The oncogenic activity of the agent from polyps and desmoids confirms its presence in significant amounts compared with non-tumor mucosa. The identical spectrum of tumors that were observed in rats after the introduction of cell-free materials

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from polyps and desmoids suggests that the same oncogenic agent is present in them. The agent is associated with FAC and has a tropism to the intestinal and oral epithelium of rat.

Conclusion

Administration of a cell-free materials from polyps and desmoids in patients with FAC to newborn Wistar rats is accompanied by the development of intestinal and oral cancer. The oncogenic agent has the properties of a virus.

Acknowledgment

None.

Conflict of interest

None.

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