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EFFECT OF ESTROGENS ON THE BLOOD SERUM LEVEL OF CARCINO-EMBRYONIC ANTIGEN IN RATS WITH NEOPLASMS OF THE INTESTINE AND NONSPECIFIC INJURIES OF ITS MUCOSA

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UDC 616.34-006-092.9-07: 616.15-097.5-078:615.357.651

Carcino-embryonic antigen (CEA) was detected in the blood serum of 70% of rats with tumors of the large intestine induced by 1,2-dimethylhydrazine and with posttraumatic regeneration of the mucosa of the large intestine. After injection of estrogen (diethylstilbestrol propionate, 0.57 μg daily for 6 days) the frequency of appearance of CEA in such animals increased, as also did the CEA level in the blood serum. In rats with injury to the mucosa of the large intestine, injection of estrogen prevented the natural decrease in the CEA concentration as the intensity of the regenerative process diminished.

KEY WORDS: carcino-embryonic antigen; large intestine; estrogens.

An antigen which, in some of its physicochemical features, is analogous to the carcino-embryonic antigen (CEA) of similar tumors in man has been found in the blood serum of rats with induced tumors of the large intestine and in the tumor tissue itself [1]. This antigen is also found with high frequency (about 70%) in rats with chronic nonspecific lesions of the intestinal mucosa [5].

During the study of the role of the endocrine system in experimental carcinogenesis in the intestine [4], the writers found CEA with high frequency and in a high titer in animals receiving injections of estrogens. The investigation described below was carried out to study this phenomenon.

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(Presented by Academician of the Academy of Medical Sciences of the USSR V. I. Ioffe.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 83, No. 5, pp. 582-583, May, 1977. Original article submitted November 19, 1976.

TABLE 1. Dynamics of Detection of CEA in Rats with Regenerating Mucosa of the Cecum

Rat	CEA in blood serum				
	before operation	after operation*			
		1st day	5th day	14th day	26th day
1	—	++++	++++	+	++
2	—	++++	+++	+—	++
3	—	+++	++++	++	++++
4	—	++++	+	—	++++
5	—	—	—	—	—
6	—	++++	++++	++++	++++
7	—	+++	—	—	+
8	—	—	—	—	—
9	—	++	++++	+	++++

*Injection of DESP into animals began on 14th day after operation.

EXPERIMENTAL METHOD

Experiments were carried out on 70 female rats bred at the Rappolovo nursery, Academy of Medical Sciences of the USSR. The experiments of series I and II were performed on 20 and 41 rats, respectively, in which tumors of the large intestine were induced by injection of 1,2-dimethylhydrazine (DMH) for 4 or 6 months, as described previously [2]. One half of these animals, during the week before determination of CEA, received daily injections of 0.57 μg of diethylstilbestrol propionate (DESP). The animals were killed on the day after the sixth injection of the estrogen and the CEA determined in their serum. The method described previously [1, 5] was used for semiquantitative assessment of the results of the immunodiffusion test.

In the experiments of series III a purse-string suture was applied to the cecum, thus producing prolonged posttraumatic proliferation of the enterocytes [3, 6]. The CEA in the blood serum of these rats was determined on the day before the operation and 1, 5, 14, and 20 days thereafter, for which purpose 0.1-0.2 ml blood was taken from the caudal vein. For 6 days after the 14th postoperative day the animals of this series also were given DESP in the same dose as those in series I and II.

EXPERIMENTAL RESULTS

In the experiments of series I the blood serum of 20 animals receiving DMH for 4 months was investigated. At autopsy on all the rats adenocarcinomas were found, mainly in the descending portion of the large intestine.

The CEA was discovered in 6 of the 9 rats receiving the estrogen and in 4 of the 11 rats not receiving it. The mean CEA concentration in the blood serum of the two groups of animals, estimated semiquantitatively, was almost identical (2+ and 1.75+ respectively).

In the experiments of series II the serum of 41 rats receiving the carcinogen for 6 months was investigated. At autopsy multiple large tumors were found in the large intestine; in about half of the animals, neoplasms also were found in the duodenum and proximal part of the small intestine. In their histological structure most of these tumors were adenocarcinomas, and cricoid-cell and mucous carcinomas were much less frequent.

CEA was discovered in 14 of 19 rats receiving the estrogen and in 13 of 22 rats not receiving it. However, in rats receiving DESP, the blood level of CEA was estimated mainly at 3+ or 4+, whereas in animals not receiving DESP the CEA level did not exceed 2+, except in four cases in which it reached 4+.

In the experiments of series III CEA was detected in the rats before insertion of the purse-string suture into the intestine, and 1, 5, 14, and 20 days after the operation. As will be judged from the results given in Table 1, CEA was found in seven of the nine rats on the day after the operation.

A significant decrease in the CEA level in the blood serum of these animals was observed 2 weeks after the operation, in agreement with results obtained previously [5]. Meanwhile, injection of estrogens led to a definite increase in the quantity of CEA detected.

The results thus indicate that estrogens can increase the CEA concentration in the blood serum of animals with tumors or with regenerative processes in the large intestine. In the writers' opinion, this can be explained either by the nonspecific anabolic action of estrogens on CEA synthesis (in particular, by proliferating cells), or by an increase in the permeability of the cell membrane of the proliferating enterocytes for CEA. Whatever the true explanation, the results are of considerable practical interest as a possible clinical test for a CEA carrier state in cases suspected of a proliferative process in the large intestine when no such changes can be detected by the ordinary immunological methods. Naturally, its use for such purposes must be preceded by detailed experimental investigations.

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