CERTAIN DATA ON THE NATURE OF DEVELOPMENT OF THE PATHOLOGICAL PROCESS IN THE GASTRO-INTESTINAL TRACT FOLLOWING Ce^{144} ADMINISTRATION

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The study of the condition of the gastrointestinal tract under the effect of radioactive substances on the organism is of interest in connection with the possibility of elicitation of certain peculiarities of its reaction and ascertaining its dependence on the character of distribution of isotopes in the organism.

The aim of the present work was to investigate morphological changes in the stomach and intestines in radiation sickness, induced via introduction of the Ce^{144} isotope, and the comparison of these changes with the lesions which originate upon the exposure to the external action of x-rays.

Ce^{144} is a β and γ emitter (β radiation equal to 0.3-0.7 mev, and γ radiation equal to 0.03-0.13 mev) with a half life of 282 days. Upon entering the organism, Ce^{144} is retained mainly in the liver (55%) and skeleton (25%). It is poorly absorbed in the gastrointestinal tract (about 0.5% according to the data of Hamilton [6] and Yu. I. Moskalev [1]), and upon oral introduction it causes mainly a local injury to the digestive organs [2].

METHOD

Experiments were conducted on 30 white rats to which Ce^{144} had been administered via gastric sound at the rate of 12-15 $\mu C/g$ of body weight. The examination was carried out atperiods from one to 30 days. The material was fixed in a 10% solution of neutral formalin and placed in celloidin and celloidin-paraffin. The histological slides were stained with hematoxylin-eosin, mucicarmine according to Meyer, and picrofuchsin according to van Giesen. In addition, the mitoses in the epithelium of the crypts of the small intestine were counted and the isotope distribution in the gastrointestinal tract was studied by the method of autoradiography.

RESULTS

Following administration of Ce^{144}, the animals manifested a liquid stool, sluggishness, thirst, anorexia, loss of weight, and emaciation. Death usually occured in the 3rd-4th week from the beginning of the experiment. At the autopsy of animals killed or perished within the first five days an atony of the stomach and large intestine was observed. In all examined rats, a liquid bloody gastric content was noted as well as an enlargement of the lymph nodes of the mesenterium; in the cecum, sigmoid and, less frequently, the distal section of the jejunum,small focal necroses were found covered with purulent secretion; sometimes adhesions with the loops of the small intestine were observed. Also dryness of the serous membranes, liver degeneration, and at times pulmonay hemorrhages.

Upon microscopic examination of the stomach, it was found that in the majority of rats there were infiltrates in the basal section of the mucosa and the submucous layer which consisted of lymphoid cells and, less frequently, of eosinophile and neutrophile leucocytes. The submucous layer in some animals was hypertrophied. In some rats killed at the end of the 4th week after the isotope administration, no morphological changes in the stomach were observed.

In the jejunum during the first five days from the start of the experiment, a reduction of mitotic activity of the mucous membrane epithelium by approximately 47% of the initial level was observed. In the crypts, in the stroma of the mucosa, and in the lymphatic follicles of Peyer plaques, products of cellular disintegration were encountered which were incorporated by macrophages. In addition, during the first three days, a considerable swelling of the nuclei of the crypt epithelium took place.

In rats killed on the 4th-5th day, in addition to changes in the structure of the basal sections of the mucous membranes, considerable changes were found in the cilia,which appeared shortened and covered with flattened

epithelium containing large vesicle-like nuclei. Scanty beaker-like cells were enlarged and had a cricoid form. The mucosa was hyperemic and a large number of lymphoid cells were present in its stroma.

On the 7th day a gradual restoration of the mucose structure began to take place. Together with crypts lined with flattened epithelium and containing products of cellular disintegration, crypts appeared of the usual structure and the number of mitoses rose to the initial level. The ciliary epithelium reverted to its usual form. Within 10 days after the administration of Ce^{144}, the epithelial structure of the mucosa was fully restored. During this period only an increase in the number of lymphoid cells and a reduction in the size of lymphatic follicles of Peyer plaques could be noted.

In the iliac epithelium a consecutive development of morphological changes analogous to the disturbances in the jejunum was observed. Microabscesses were encountered in the mucosa. The submucous layer and mesenterium in many animals became infiltrated with neutrophile leucocytes and lymphoid cells. More pronounced changes occured in the distal end of the colon, where necroses and ulcers of the mucosa were found.

The large intestines were the most affected; as early as within 24 hours following administration of the isotope, a considerable destruction of the epithelium was observed, and on the 2nd-3rd day extensive necroses and ulcers of the mucosa appeared (Fig. 1). The epithelium of areas adjacent to the ulcers was in a state of dedifferentiation. Microabscesses were present in the crypts. A large number of leucocytes were present in the granulation tissue which filled the bottom of the ulcers. Within $1\frac{1}{2}$ - 2 weeks after administration of the isotope, in addition to the above-mentioned cellular forms, isolated fibroblasts began to appear in the granulation tissue; later, within three weeks, macrophages and eosinophile leucoytes appeared, and formation of collagen fibers was observed. The number of newly formed vessels was slight. A considerable quantity of fibroblasts and collagen fibers was found also in the mesenterium of the large and, sometimes, the iliac intestines.

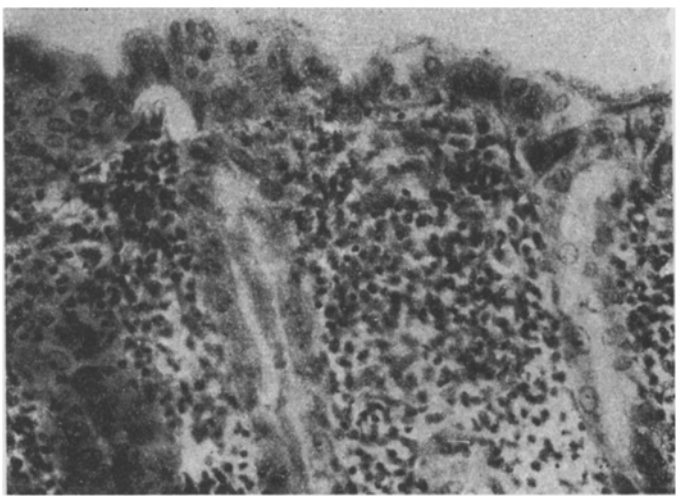

Fig. 1. Destruction of the epithelium of the mucosa of the large intestine of a rat and an increased quantity of cellular elements in the stroma, 24 hours after the introduction of 12 μC/g of Ce^{144}. Photomicrograph. Stained with hematoxylin-eosin; magnification 200 ×.

Microabscesses were sometimes found in the newly formed mucous membrane at the edges of ulcers (Figs. 2 and 3).

In some rats killed or perished within 3-4 weeks after the affection, a focal hyperplasia was observed of the mucous membrane as well as formation of displaced and distended crypts. The vessels of all sections of the intestinal tract had thickened, swollen walls and the lumen of the large arteries was constricted. Many neural cells of the Auerbach plexus situated in the ulcerated areas stained intensively with hematoxylin or had the appearance of dark clots. Lymphocytes and some lymphostasis were found in the enlarged lymphatic nodes of the mesenterium, and in some cases foci of myeloid hemopoiesis were observed in the lymph nodes.

Upon autoradiographic examination, the largest amount of the isotope was elicited in the smears of the contents of the large intestine during the first 48 hours after the isotope administration. The activity of the wall of the stomach and small intestine, apparently on account of isotope absorption, proved to be somewhat higher when compared to the activity of the wall of the large intestine. Subsequently, during the entire period of investigation, the highest Ce^{144} content was found in the liver.

The obtained results indicate that the affection of the gastrointestinal tract following a single oral administration of Ce^{144} had a nonuniform character. The morphological changes increase from the proximal to the distal

Fig. 2. Ulcer of the large intestine on the 23 rd day after the introduction of 12 μC / g of Ce^{144}. Photomicrograph. Hematoxylin-eosin; magnification 15 X.

Fig. 3. Microabscesses in the regenerated mucosa of the large intestine in a rat on the 23rd day after the introduction of 12 μC/g of Ce^{144}. Photomicrograph. Hematoxylin-eosin. Magnification 70 X.

end of the gastrointestinal tract, the greatest impairment taking place in the large intestine.

The stomach shows a mild inflamatory reaction, which in some animals disappears toward the end of the 1st month.

The involvement of the jejunum presents the picture of a radiation burn and is similar to the lesions observed following external irradiation [4,5,8,9]. As in the case of external irradiation, the changes are most pronounced in the crypts, and later in the cilia. A period of reparation follows the phase of destructive changes and, approximately within 10 days, the epithelial structure of the small intestine becomes fully restored. However, in contrast to the effect of external irradiation the morphological changes following internal administration of Ce^{144} proved to be less marked and more prolonged. The greatest changes following direct total irradiation with x-rays usually manifest themselves in the small intestine, whereas during the early stages after Ce^{144} administration the large intestine shows greater pathological changes with the formation of extensive necroses and ulcers accompanied by a prolonged inflammatory process. In addition, in the small intestine, especially in its distal section, there appear phenomena of inflammation after Ce^{144} introduction which are absent in the case of total x-ray irradiation. The leucocytic reaction, generally absent in x-ray irradiation, is well marked on Ce^{144} administration.

Thus, the radiation injury is combined in this case with the picture of an acute inflammation. The insignificant impairment of bone marrow hemopoiesis in peroral administration of Ce^{144} is, apparently, one of the basic reasons responsible for the presence of a large number of leucocytes in the tissues.

This unique affection of the gastrointestinal tract depends on the physicochemical properties and the method of introduction of the isotope.

As we know from the data in the literature, Ce^{144} is absorbed in very small quantities (0.05%) in the gastrointestinal tract and is excreted basically within 1-2 days after its introduction. The faster movement of the contents along the small intestines causes a lesser injury to this section, whereas the detention of food in the iliac and especially in the colon apparently represents the basic cause of the radiation burn of the distal segment of the digestive tract. Thus, the basic reason for the development of mosphological changes is, presumably, the direct effect of radiation on the structures of the gastrointestinal tract.

The results of autoradiographic examinations and toxicological data permit us to assume that upon introduction of the isotope the intestines are basically affected as the result of a relatively short action of massive radiation doses.

The obtained data correspond to the scanty reports in the literature which mention the peculiarities of the reaction of structures of the gastrointestinal tract, depending on the properties of the radiation action. Thus, Hulse

[7] reports the emergence of an inflammatory reaction and microabscesses in the intestines following irradiation of the abdomen with β-particles of Sr^{90} in a dose of 9400 rad. M. V. Svyatukhin [3] describes the development of fibrinous necrotic colitis under conditions of peroral administration of a mixture of poorly absorbed β-emitters, and assumes that the basic role in the development of morphological changes is due to the local radiation effect. Sommers and Warren [10] note the formation of abscesses in the large intestine and distal part of the small intestine in parabiotically united rats following irradiation of one of them with a 400-1600 r dose.

SUMMARY

A study was made of morphological changes occurring in the gastrointestinal tract of rats after Ce^{144} administration(12-15 μC/g of body weight). Destructive and necrobiotic changes in the mucosal epithelium accompanied by inflammatory reaction were characteristic of gastrointestinal tract lesions. The degree of these changes increased toward the distal end of the digestive tract, the large intestine being most affected.

After external x-ray irradiation and Ce^{144} administration, certain features specific to the reaction of the gastrointestinal tract could be observed. These depended on the physicochemical properties and the method of isotope administration.

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