REGENERATIVE POWER OF THE STOMACH TISSUES IN ACUTE RADIATION SICKNESS

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UDC 616-001.28.036.11-092.9-07:616.33-003.93

Partial resection of the stomach, with removal of the full thickness of its wall, and subsequent closure of the defect with an omentum-muscle-aponeurosis graft, was performed on cats at various times after whole-body x-ray irradiation producing moderately severe acute radiation sickness in the animals. Histological investigation showed that the regenerative power of the stomach tissues in the irradiated animals was undisturbed.

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Investigation of reparative regeneration in animals exposed to the action of ionizing radiation can give some indication of the proliferative potential of different tissue cells [1, 4, 5].

In the present investigation regeneration in irradiated cats was studied histologically after excision of part of the stomach wall and replacement of the defect with an omentum-muscle-aponeurosis graft.

EXPERIMENTAL METHOD

Experiments were carried out on 96 cats, of which 6 received whole-body x-ray irradiation in a dose of 350 R, 4 in a dose of 250 R, and 66 in a dose of 208 R (conditions: RUM-3, 180 kV, 20 mA, filters 0.5 mm Cu + 0.5 mm Al, skin-focus distance 60 cm, dose rate 20.8 R/min). The dose of 208 R was optimal for our purposes. It produced moderately severe radiation sickness with death of most experimental animals within 3-30 days. Animals irradiated with doses of 250-350 R died on the 8th-13th days, and were disregarded when the results were analyzed.

On the 2nd day after irradiation, at the height of radiation sickness and in the recovery period, a full-thickness excision of part (measuring 2.5 × 3.5 cm) of the anterior wall of the prepyloric portion of the stomach was removed, and the defect subsequently closed with omentum on a pedicle fixed by an autograft consisting of muscle and aponeurosis, or by an equivalent homograft preserved in paraffin wax. In the control series 14 animals were irradiated in a dose of 208 R without undergoing the operation and 20 animals underwent the operation but were not irradiated.

Histological sections of the stomach were stained with hematoxylin-eosin, by van Gieson's method, with mucicarmine, and with Heidenhain's hematoxylin. Mucoids were detected by Hotchkiss' method.

EXPERIMENTAL RESULTS

In the control series of experiments all 20 unirradiated cats survived after operation.

Of the 30 cats undergoing operation 30 h after irradiation, 15 died on the 4th-27th day from acute radiation sickness. The surviving cats were sacrificed 48-445 days after the operation.

All 22 cats undergoing operation 7 days after irradiation except 1 died on the 8th-26th day, also from acute radiation sickness with manifestations of a hemorrhagic syndrome.

Of the 14 irradiated animals not undergoing operation, 8 died on the 4th-17th day after irradiation. Clinical and laboratory investigations of 6 cats on the 40th day after irradiation established recovery from acute radiation sickness. They underwent the operation at this time. All of these 6 cats survived and were sacrificed from 60-270 days after the operation.

Laboratory of Pathological Anatomy, Central Roentgeno-Radiological Research Institute, Ministry of Health of the USSR, Leningrad (Presented by Active Member of the Academy of Medical Sciences of the USSR A. P. Avtsyn). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 10, pp. 80-84, October, 1968. Original article submitted April 3, 1967.

Fig. 1. Area of stomach wall at site of former defect 5 days after autotransplantation performed in latent period of radiation sickness. Spreading of epithelium of a gastric gland over surface of omentum showing fibrotic changes. Van Gieson. Objective 40, ocular 5.

Operation during the latent period of action of the radiation had no significant effect on mortality of the animals, but if performed at the height of radiation sickness it adversely affected their condition and aggravated the radiation sickness.

Histological investigation of the unirradiated cats undergoing operation revealed the following changes.

On the 5th day, thin layers of cylindrical epithelial cells migrated from the edges of the mucous membrane toward the center of the defect. The omentum, aponeurosis, and muscle cells showed regressive changes. This was combined with proliferation of young fibroblasts and bundles of collagen tissue in the submucosa at the edges of the defect, providing the foundations for future regeneration of the mucous membrane.

On the 10th-15th day, the layers of epithelium continued to grow in from the edges of the gastric mucosa and to cover the peripheral portions of the graft. Sixty days after operation, the stomach wall was restored at the site of the plastic repair and consisted of a layer of connective tissue incorporating smooth-muscle cells, covered completely by regenerated mucous membrane, in which glands secreting mucus were formed.

In the animals undergoing operation during the latent period of radiation sickness, 1-3 days after plastic repair of the defect in the stomach wall the edges of the mucous membrane, submucosa, and muscular coat in the region of the wound were necrotic, and collections of leukocytes were present here and there. The omental part of the graft was adherent to the serous membrane of the stomach at the edges of the defect. On the 5th-7th days, thin layers of cylindrical epithelial cells spread out from the edges of the mucous membrane toward the defect, covering the peripheral parts of the floor of the former defect (Fig. 1). Ten days after the operation, a further ingrowing of mucous membrane from the edges of the defect was observed, with the formation of glands secreting mucus.

After 15-18 days the layers of epithelial tissue continued to spread from the edges of the gastric mucosa. Here and there in the regenerating tissue, atypical gland tubes could be seen lying directly on the fibrous connective tissue. After 26-32 days epithielization of the former defect continued. The regenerating tissue, gradually acquiring the structure of the glandular layer of the mucous membrane, contained haphazardly arranged islets of glandular tubes, racemose in shape.

On the 63rd day after the operation, a mucous membrane consisting of a true mucosa with properly formed glands producing mucus, containing mitoses in their cells, was observed directly on the fibrous connective tissue replacing the defect in the stomach wall.

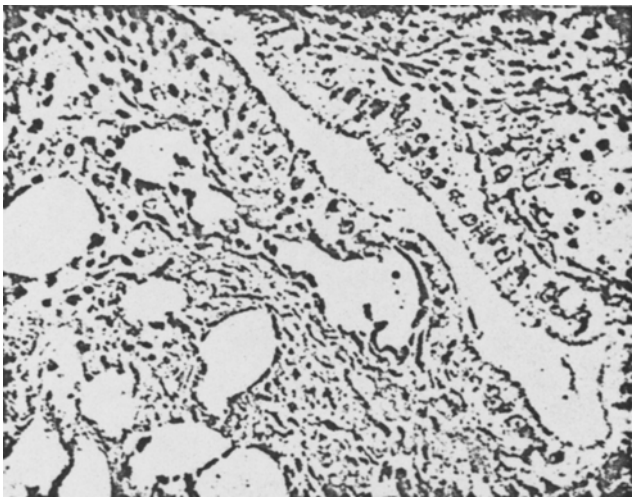

Fig. 2. Edge of defect in stomach wall 10 days after homotransplantation performed at the height of radiation sickness. Spreading of epithelium of gastric glands over surface of omentum. Large pale nuclei in epithelial cells in floor of gland. Small hyperchromic nuclei, crowded in epithelial cells in apical part of gland. Van Gieson. Objective 40, ocular 5.

In animals undergoing operation at the height of radiation sickness, necrosis of the edges of the gastric mucosa was found, together with hemorrhages in the thickened submucosa and muscular layers of the stomach wall. On the 2nd-3rd day, a mucous membrane was present with deformed gastric glands, secreting mucus. The omental part of the graft was adherent to the edges of all layers of the stomach wall.

On the 5th-7th day after the operation the submucosa showed proliferation in the form of young fibroblasts, with cylindrical epithelial cells creeping over it from the edges of the defect in the mucous membrane.

After 10 days solitary deformed glands and newly formed glands lying directly on the omentum, which had undergone fibrosis, were observed (Fig. 2).

On the 13th day after operation further spreading of functioning gastric glands from the edges of the defect in the mucous membrane could be seen.

After 19 days the ordinary gastric glands continued to proliferate, resting on the modified omentum and the proliferating submucosa containing collagen tissue and fibroblasts. On the 87th day after operation, a thick layer of bundles of fibrous connective tissue, covered with gastric glands of normal structure and secreting mucus, could be seen on the inner surface of the graft replacing the defect.

In the irradiated animals undergoing operation in the period of recovery from acute radiation sickness, 60 days after the operation the stomach wall at the site of the former defect consisted of mucous membrane with gastric glands of normal structure resting on a thick layer of bundles of fibrous connective tissue.

On the 180th-270th day after plastic closure of the defect in the stomach wall, a layer of fibrous connective tissue was found, containing smooth-muscle cells and covered with a mucous membrane containing gastric glands of normal structure.

The various types of tissue cells in the graft showed structural changes. Striped-muscle fibers showed cloudy swelling, so that in the late stages after the operation no muscle cells whatever remained. Bundles of fibers of the upper neurosis and, in particular, the omentum remained viable. They showed an intimate and early connection with subepithelial cells of the stomach wall at the edges of the defect, providing a foundation for the spread of the mucous membrane above it from the edges of the defect. The graft was soon replaced by a proliferating layer of connective tissue incorporating smooth-muscle cells, originating in the submucosa and, to a lesser degree, in the muscular layer at the edges of the defect.

Proliferation of epithelial cells at first took place irregularly, but eventually the mucous membrane acquired its normal structure, containing glands producing mucus.

Survival of the graft, followed by regeneration of the epithelium of the mucous membrane, took place in irradiated tissues. This happened because the tissues of the irradiated animal, despite injury by ionizing radiation, remained capable of regeneration after transplantation just as has been observed in other objects by other investigators [2, 3, 6].

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