Epithelial Lesions of the Stomach Induced in Guinea Pigs by Intramural Implantation of 3-methylcholanthrene

By

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With 3 Figures in the Text
(Received April 16, 1962)

According to the latest reviews (Pfaltz and Lacour; Stewart) spontaneous adenocarcinoma of the stomach is very rare in mammals, with the exception of two species in which its frequency is very high, namely, an african multimammate rodent (Oepplé) and man. In the guinea pig, gastric carcinoma is practically non-existent (Warren and Gates; Dobberstein and Tamashke; Rogers and Blumenthal). The artificial production of gastric adenocarcinoma in rats and mice using polycyclic aromatic hydrocarbons is hampered, among other factors, by carcinomas and papillomas which arise from the squamous epithelium of the rumen, or by sarcoma and mixed malignant tumors originated in the mesenchymatous gastric tissues. Besides the percentage of induced malignancies is very low (Stewart). The guinea pig has the advantage to have a purely glandular stomach, which under the action of carcinogens could be expected to produce only or predominantly glandular lesions. However, the guinea pig did not develop gastric neoplasms when fed a methylcholanthrene suspension for periods up to 2 years (Lorenz). But, when crystals of the same carcinogen were administered intraperitoneally to the guinea pig, fibrosis and focal destruction of the muscularis propria of the stomach were observed in one case where the experiment lasted only 111 days (Kliwadenko). These observations prompted us to study the reaction of the gastric glandular epithelium after the intraperitoneal administration of methylcholanthrene crystals, deposited on the gastric serosa. We succeeded in inducing 9 epithelial lesions and 1 true adenocarcinoma in 66 treated animals (Zaldívar). The frequency of gastric lesions was low (15.1%), possibly due to the spreading of the carcinogen over the peritoneum. We therefore attempted to localize the activity of the carcinogen by implanting methylcholanthrene crystals into the gastric wall of the guinea pig. The present communication deals with the results of these experiments.

* The authors wish to thank Prof. O. Badénex, Department of Biology, University of Chile, and Prof. R. Barahona, Department of Pathologic Anatomy, Catholic University, for their assistance in the interpretation of some slides of the tissue sections, and Dr. R. Palacios, Bacteriological Institute, National Health Service, for the kind gift of 3-methylcholanthrene (Eastman Kodak Co., Rochester, N.Y.). They are also indebted to Drs. H. Maturana and S. Koren, Department of Biology, for their help during the preparation of this manuscript.
Materials and Methods

Guinea pigs of both sexes (21 males, 20 females), of unknown genetic constitution, with an initial body-weight of 400 to 700 g were used. The animals were numbered individually, housed in wooden cages, 6 per cage, and fed on wet bran, fresh carrot, cabbage and green grass. The temperature of the animal house was maintained at about 23°C.

The animals were fasted one day before operation in order to facilitate the reduction of the stomach after the implantation of 3-methylcholanthrene (MC). Under ether anesthesia and through a midline incision of the epigastric region, the stomach was delivered. Each animal received 3 mg of MC crystals which were implanted into a "pocket" of 4 × 5 mm in the subserosa of the ventral wall of the antrum, and some crystals were also implanted into the muscularis. The pocket, as the wound, were closed by a cotton thread suture.

The animals, including those ill from natural causes, were etherized and necropsied. In those found dead, special attention was paid to post-mortem changes in order to evaluate the lesions. At necropsy the stomach was opened and the implanted zone, together with the surrounding tissues was excised, carefully cleaned of any contents and gently distended, pinned on pasteboard and immersed in 10 per cent formaline. Paraffin blocks were sectioned at 6 μ and stained with hematoxylin and eosin, van Gieson, and Mayer's mucicarmine methods.

Results

1. Macroscopic observations

Adhesions, extending between the large omentum and laparotomy scar, and between the liver and the site of implantation, were common. Fibrosis also was seen at the site of implantation. Sometimes, at necropsy, the liver showed yellowish areas which were adhering to the implanted site of the stomach. These areas of hepatic tissue were removed for histological study.

2. Microscopic changes of the stomach

The gastric lesions induced by MC are summarized in the Table.

One animal was necropsied 6 days after implantation. The muscularis propria showed fibrosis; in the subserosa, acicular spaces with pale yellow material were observed. Granulation tissue around these spaces appeared. One animal examined at 56 days showed, at necropsy, the wall of the fundus considerably thickened. Microscopically, a focus of heterotopic pancreatic tissue with both exocrine and endocrine elements was found in the subserosa. Around this focus, strong fibrosis was observed. The liver of this animal showed a yellowish zone which consisted microscopically in a fatty change. The guinea pig examined at 107 days showed a glandular cyst between the muscularis and the subserosa of the stomach, which was lined by a single layer of flattened epithelium. The submucosa showed intense fibrosis; the muscularis was thickened, at the area of implantation, due to a massive fibrosis that markedly segmented the bundles of muscle fibers. In the subserosa, intense fibrosis was seen. The animal necropsied at 280 days showed, in one area of the stomach, an atrophic mucosa with a slight chronic inflammatory infiltrate. In this area a diverticulum appeared in the submucosa,

1 It was previously described as an adenocystic lesion (ZALDIVAR). Usually, the diverticulum shows a main lumen and a well-circumscribed growth zone, surrounded by a slight fibroblastic reaction (desmoplasia), it may involve the submucosa or muscularis propria. The glands lining the diverticulum appear normal, the interstitial spaces moderately infiltrated by chronic inflammatory cells. Diverticula with many small lumina were observed rather occasionally. Some diverticuli measured 8 mm in diameter, others being barely visible.