

Malignant Argyrophilic Gastric Carcinoids of *Praomys (Mastomys) natalensis*

Abstract. Cells of carcinoid tumors which arise in the glandular stomach of old male and female *Praomys (Mastomys) natalensis* contain argyrophil granules when tissues fixed in formalin are colored with solutions of silver salts. The carcinoids metastasize in about 25 percent of cases, and are transplantable to other *Mastomys*. Tumor-bearing animals may show gastric and duodenal ulcers and multiple endocrine adenomas.

Tumors of the glandular stomach occur spontaneously in about two-thirds of old male and one-third of old female *Praomys (Mastomys) natalensis*. Fifty-six such tumors fixed in Zenker's solution had the histologic characteristics of carcinoids (Fig. 1), but because this material was unsuitable for silver methods, we could not reveal the specific granules. Therefore ten primary gastric tumors, mesenteric lymph node metastases from two of these, and a second-generation transplant from an 11th animal were fixed in dilute formalin, treated with reducing substances, and colored with solutions of silver salts according to the methods of Sevier and Munger (1) and of Azzopardi and Pollock (2). The cells of these 11 tumors, which were histologically identical to the 56 other carcinoids,

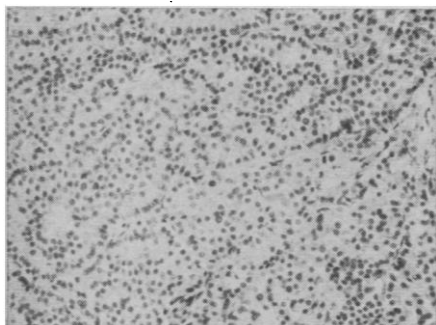


Fig. 1. Section of a malignant carcinoid showing the solid masses and coarse trabeculae of rather uniform cells (hematoxylin and eosin, $\times 340$).

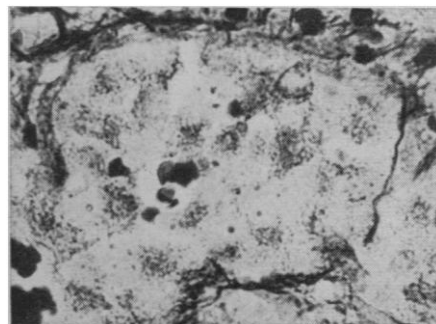


Fig. 2. Gastric carcinoid showing the fine, uniform, coal-black granules in the cytoplasm as demonstrated by the method of Sevier and Munger (1) ($\times 1260$).

contained the coal-black granules diagnostic of argyrophilic carcinoid tumors (Fig. 2). Argentaffin granules were absent with the Fontana and methenamine silver methods and the diazo reaction. No cells containing argentaffin granules were seen in normal control stomachs, but scattered argyrophil cells were present within all levels of the mucosa except the surface.

The carcinoids of *Mastomys* are located in the body or fundus of the glandular stomach along the greater curvature. The large tumors are polypoid and ulcerated and may measure 2 cm in greatest dimension. The neoplastic process begins as a focal or multicentric proliferation of argyrophil cells, usually deep within the mucosa. The foci enlarge, coalesce, penetrate the muscularis mucosae, and infiltrate the submucosa where the main mass of the neoplasm is ultimately located. Lymphatic and blood vessels are invaded early, and at least 25 percent of the carcinoids metastasize to the mesenteric and other lymph nodes, liver, pancreas, and lung, sometimes before the neoplasm has penetrated all coats of the wall of the stomach. The area of gastric mucosa within which the carcinoid develops becomes populated with hyperplastic, atypical glands lined with cells that are enlarged, hyperchromatic, pseudostratified, intestinal-like, and often in mitosis. It has been assumed that the small cells seen between, around, and within the gastric glands are neoplastic derivatives of the epithelial cells, and it has been reported that the tumors are undifferentiated adenocarcinomas (3). We have found that these neoplastic cells are derivatives of argyrophil cells, and we can trace no transitions from the cells of the glandular mucosa. The atypicality of the glands represents a secondary response to the proliferation of the argyrophil cells, the blockage of lymph and blood vessels by tumor thrombi, and associated inflammation.

In man, carcinoid tumors arise from Kulitschitsky cells in the mucosa of the tracheobronchial tree and alimentary

tract. While the gastric and bronchial carcinoids (foregut origin) are less likely to give an argentaffin reaction than those of the ileum, appendix, and cecum (midgut origin), the gastric carcinoids, as demonstrated by Black and Haffner (4), may give an argyrophil reaction. Thus at least some gastric carcinoids of man, like those of *Mastomys*, arise from argyrophil rather than from argentaffin cells. In man, carcinoids of foregut origin are often of trabecular pattern and sometimes secrete 5-hydroxytryptophan, a precursor of serotonin, while those of midgut origin are of the solid nest pattern and secrete and store 5-hydroxytryptamine (serotonin) (5). Areas of the carcinoids of *Mastomys*, particularly in the metastases and transplants, reproduce a trabecular pattern, and since the cells contain argyrophil granules, these experimental tumors should be useful for studying the association between argyrophil cells and the formation of 5-hydroxytryptophan (6). In man, peptic ulcers with chronic iron-deficiency anemia (7) as well as multiple endocrine adenomas (8) have been reported in association with carcinoid tumors. Four of eight *Mastomys* bearing large transplanted carcinoids have developed ulcers of the duodenum, and many animals with primary carcinoids have ulcers of the duodenum and glandular stomach and adenomas of the pituitary and adrenal glands and pancreatic islets. The carcinoid tumors of *Mastomys*, therefore, offer a promising experimental tool for study of the relationship of morphology and the biochemical effects on the host.

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References and Notes

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