PANCREATIC CARCINOMA INDUCED BY 4-HYDROXYAMINOQUINOLINE 1-OXIDE AFTER PARTIAL PANCREATECTOMY AND SPLENECTOMY IN RATS

It was reported that a single injection of 4-hydroxyaminoquinoline 1-oxide (4-HAQO) induced a high incidence of pancreatic tumors in rats\(^1\) and the tumorigenicity of 4-HAQO was enhanced by ethionine.\(^3\) However, pancreatic tumors induced by 4-HAQO were often found to be hyperplastic nodules or adenomas and no clear observation was made on the induction of pancreatic carcinoma with metastasis in rats treated with 4-HAQO. In this communication, we report the induction of pancreatic carcinoma in rats given a single injection of 4-HAQO at 3 days, in DNA synthetic phase,\(^2\) after partial pancreatectomy.

A total of 29 male Wistar strain rats (Awazu Animal Farm, Osaka), weighing approximately 170 g, were given partial pancreatectomy by the method of Lehv and Fitzgerald.\(^4\) The spleen was removed with a part of pancreas to simplify the operation. 4-HAQO (Iwai Kagaku Yakuhin Co., Tokyo) was dissolved in 0.005N HCl. Injections were made into the saphenous vein under ether anesthesia 3 days after the operation. All the animals were divided into 2 groups: Group 1 given 0.3 ml of 0.005N HCl and group 2 given 7 mg/kg of 4-HAQO in 0.3 ml of 0.005N HCl solution. They were housed in wire cages in an air-conditioned room at 24° and fed a commercial stock diet Oriental MF (Oriental Yeast Ind., Tokyo). After 52 weeks, all the animals were fasted for 18 hr and sacrificed with ether. The residual pancreas of each animal was fixed in 10% neutral formaldehyde solution after macroscopic examination and sectioned routinely, stained with Hematoxylin and Eosin, and with Victoria Blue-Acid Fuchsin. Initial number of animals were 12 in group 1 and 17 in group 2, and effective number of those were 12 in group 1 and 15 in group 2.

Macroscopically, multiple pale or whitish yellow tumors were observed in the residual pancreas in all the animals from group 2. Histologically, hyperplastic nodules were seen in 13/15 (86.6%), adenomas in 14/15 (93.3%), adenocarcinomas including poorly and well-differentiated ones in 9/15 (60%), and \(\beta\)-cell islet tumor in 6/15 (40%) from group 2. Metastases were seen in 2 out of 9 animals. Poorly differentiated adenocarcinoma composed of cells containing pleomorphic nuclei and poorly developed interstitial elements and metastases were seen in the liver, in the mesenteric and para-aortic lymph nodes, and in the omentum. No pancreatic tumor was found in the animals from group 1 and no tumor of other sites was found in the animals from groups 1 and 2.

The present result indicated that pancreatic carcinogenesis initiated by 4-HAQO was enhanced by the regeneration induced by partial pancreatectomy. Experiments to study detailed histogenesis of the tumor and differentiation of cells in hyperplastic nodules, adenomas, and carcinomas of pancreas are in progress.

(Received September 2, 1976)

REFERENCES


Yoichi Konishi 小西陽一
Ayumi Denda 伝田阿由美
Shoji Inui 乾 松司
Seiichi Takahashi 高橋精一
Hiromu Kondo 近藤 弘

Department of Oncological Pathology
Cancer Center, Nara Medical University
840 Shijo-cho, Kashihara 634