WBN/Kob Rats

A New Spontaneously Occurring Model of Chronic Pancreatitis

Kazushi Ohashi, *•1 Joong-Hui Kim, 1 Hiroko Hara, 1
Ryoko Aso, 1 Toshio Akimoto, 2 and Kazumasa Nakama 2

1Clinical Pharmacology Center and 2Division of Laboratory Animal Science,
Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, 113, Japan

Received May 5, 1989; Revised August 3, 1989; Accepted August 19, 1989

Summary

Chronic pancreatitis-like lesions are observed in 100% of male Wistar Bonn/Kobori rats. At 3 mo of age, histopathologic examinations of the pancreas revealed a distinct infiltration of inflammatory cells with interstitial edema in the acini. At the same time, periductal and interstitial fibrosis and adenomatous hyperplasia of the ductular epithelium were observed. Extensive fibrotic exudation developed rapidly with age, and irregular destruction of the parenchyma was noted. The only abnormality, prior to the appearance of glycosuria, that could be detected clinically was lower levels, compared to Wistar rats, of BT-PABA excreted in the urine after oral ingestion. These lower levels indicate a decrease in enzyme secretion in WBN/Kob rats.

Ultrastructural observations in histologically normal areas at 2 mo of age showed a swelling of mitochondria, indicating that ischemia was associated with the early pancreatic lesions. Serial pancreatographies were performed at 2–8 mo of age. Irregular widenings of the main pancreatic duct and dilations of the smaller ducts were observed already at 2 mo of age, suggesting a stasis of pancreatic juice in the early stages of the disease. It seems that male WBN/Kob rats are a useful model of human chronic pancreatitis, with an unknown mechanism regulated by the sex hormones.

Key Words: Male WBN/Kob rats; spontaneously occurring animal model; chronic pancreatitis.

*Author to whom all correspondence and reprint requests should be addressed.

INTRODUCTION

Although models of acute and chronic pancreatitis, induced by cerulein (1), ethionine (2), alcohol feeding (3), partial or complete ductal occlusion by tissue glue (4) or surgical ligation (5), have been established, no naturally occurring model of chronic pancreatitis has been found. The pancreas of a WBN/Kob rat with spontaneous diabetes was found to undergo a series of pathological changes, prior to the development of diabetic symptoms, that resemble changes in human chronic pancreatitis (6). This study was designed to determine how the initial pancreatic exocrine damage is developed and evaluate the suitability of WBN/Kob as a model of spontaneous chronic pancreatitis.

MATERIALS AND METHODS

WBN/Kob is a Wistar strain derived in 1961 from a colony at the Institute of Experimental Gerontology (Basel) that was subsequently inbred through sister and brother matings at the Institute of Pathology, University of Bonn (7). The strain was developed as a model susceptible to gastric tumors (7). WBN/Kob were brought to Japan in 1976 by Kobori (Tokyo University), and the strain has been subsequently maintained at Shizuoka Laboratory Animal Center, Shizuoka, Japan. In a long-term study of the incidence of spontaneous tumors at the National Institute of Hygienic Sciences, Tobe and Kobayashi (personal communication) discovered that all male WBN/Kob had glycosuria after 9 mo of age. They also found that only male WBN/Kob rats manifested diabetic symptoms. Our coworker, Nakama (8), reported that the diabetic symptoms and pathological alterations in WBN/Kob rats were characteristic of a progressive fibrosis of the whole pancreas. Tsuchitani et al. (9) reported that histopathological lesions of the pancreas of WBN/Kob were somewhat different from previous reports of both types I and II diabetes mellitus in humans and animals.

In the present study, histopathological and exocrine pancreatic functional examinations were carried out on a total of 52 male WBN/Kob rats, ranging from 2-12-mo-old, and compared with age- and sex-matched Wistar rats and female WBN/Kob rats.

GENERAL OBSERVATIONS

General status and endocrinological examinations on another 40 male WBN/Kob rats, ranging from 2-20 mo of age, were carried out at the Division of Laboratory Animal Science of the Nippon Medical School by Nakama.

Morphological Examinations

Histopathology was conducted using conventional methods of light microscopy. Samples were stained with hematoxylin and eosin (H&E) or Gomori’s aldehyde-fuchs in. Electron microscopy was carried out in the conventional method. Epoxy sections were stained with uranyl acetate and lead citrate and