Ductal Adenocarcinoma of the Pancreas

Histopathological Features and Prognosis

Andrea Tannapfel,† Christian Wittekind,*2 and Günther Huhufeld3

†Department of Pathology, Medizinische Hochschule Hannover, Hannover, Germany; *Surgical and Urological Pathology, Department of Surgery, Institute of Pathology, Friedrich-Alexander University, Erlangen, Germany; and 3Department of Surgery, Evangelisches Krankenhaus e. V., Göttingen—Weende, Germany

Summary

Between 1972 and 1987, curative surgical resection (RO) was performed in 81 patients with ductal adenocarcinoma of the pancreas. In this study, slides from surgical specimens were reviewed, and histopathological features of the carcinomas were retrospectively reevaluated. Tumor stage was the most important prognostic factor: In UICC stages I, II, and III, the median survival times were 13, 16, and 8 mo, respectively. Lymph node involvement and direct extension of the tumor into adjacent peripancreatic tissue, as well as invasion into peripancreatic organs were found to significantly influence survival. Tumor infiltration of the lymphatic vessels was present in 74% of the resected carcinomas and significantly correlated with survival time. There was no relationship between survival and tumor size; furthermore, histological grade of differentiation, age, and sex had no influence on prognosis.

Key Words: Exocrine pancreas; ductal adenocarcinoma; histopathological factors; prognosis; surgical treatment; resectability.

Introduction

The incidence of pancreatic exocrine carcinoma reported in Western countries has tripled during the last 50 yr (1); about 7000 new cases are diagnosed each year in the Federal Republic of Germany (2). This alarming increase is burdened by the fact that pancreatic cancer remains among the most lethal types of cancer. Surgical resection continues to be the only possibility of cure. However, the tumor is only rarely diagnosed at an early stage, and as a consequence, the overall resectability rate is low (5–10%), and the median survival time for patients undergoing resection is brief (17–20 mo) (3). Histopathological factors influencing the prognosis of pancreatic carcinoma may be related to tumor stage and differentiation. A valid prognostic assessment should therefore be based on an exact histological classification.

The data published so far are difficult to compare because previous studies have failed to ascertain the ductal origin of pancreatic adenocarcinomas by
histopathological means (2,4), and in addition, many reports do not present data regarding lymph node involvement or peripancreatic invasion (5,6). We report findings of a retrospective study on a large number of patients who underwent curative surgery for carcinoma of the exocrine pancreas between 1972 and 1987. The aim of our study was to determine which histopathological findings significantly correlated to survival.

Material and Methods

Patient Data and Statistics

Out of 267 patients with ductal adenocarcinoma of the pancreas who underwent surgery between 1972 and 1987, 81 (30%) were curatively resected (R0 resection): Whipple resection, 70%; total pancreatectomy, 15%; and left-sided hemipancreatectomy, 15%. In these 81 patients (52 male, 29 female, median age 58 ± 10.5 yr), the exocrine origin of the carcinoma was reevaluated by histological examination to ensure exclusion of all types of cystadenocarcinoma or acinar cell carcinoma.

In addition, size of the tumor, possible lymph node involvement, and tumor differentiation, as well as invasion of lymphatic vessels, perineural sheaths, and small veins were recorded. Further characteristics, such as local spread and anatomical location, were considered. Staging was based on the UICC-proposed TNM classification (7). Histological classification was performed according to the World Health Organization (WHO) classification system (8), as modified by Morohoshi et al. (9).

The grade of tumor differentiation was determined using Klöppel’s histological grading system (10), and at least 12 sections from each patient were evaluated.

All patients were available for follow-up. Survival times were measured from the date of operation. Five out of the 81 patients (6%) died within 1 mo after their operation (operative mortality).

Survival was calculated using the Statistical Package for Social Science life-table method (SPSS, Inc., Chicago, IL). This package uses the Cutler-Ederer analysis to compare cumulative survival function of different groups. Time intervals were chosen as small as possible (1 d) to achieve a maximum of precision. p Values of p < 0.05 were considered statistically significant.

Histopathological Samples

For histological evaluation of the primary tumor, sections obtained from at least 12 paraffin blocks stained with hematoxylin and eosin (H & E) were available. Additional sections were prepared from the paraffin blocks and stained with periodic-acid-Schiff (PAS), Alcian blue, Elastica van Gieson, and Azur-B-Eosin (11).

Immunohistochemistry

In order to evaluate definite ductal tumor origin, immunohistochemical studies using an avidin-biotin- peroxidase complex (ABC) or the peroxidase-antiperoxidase (PAP) technique were performed on sections of formalin-fixed, paraffin-embedded tumor tissue from 14 cases. Immunohistochemical studies were carried out only in those cases where there was reason to suspect a tumor origin other than ductal adenocarcinoma.

Antigens used to evaluate possible epithelial differentiation were keratin, cytokeratin 8, 18, and 19, carcinoembryonic antigen (CEA), and epithelial membrane antigen (EMA). Antigens used to identify nonspecific neuroendocrine differentiation were: chromogranin (CgA), S-100 protein, and neuron specific enolase (NSE). Insulin antigen was used to identify specific endocrine differentiation. Normal pancreatic tissue was used as the negative control. Five ascertained ductal adenocarcinomas served as positive controls.

The immunohistochemical pattern of the tumor was found to be highly variable. By immunocytochemical examination, the majority of cells were shown to contain immunoreactive material. As expected, in all tumors, we observed a variable number of cells that did not display immunoreactivity toward any of the applied antibodies. The distribution of the different types of pancreatic tumors investigated in this study is presented in Table 1.

After obtaining the results of immunohistochemical staining, we excluded all acinar cell carcinomas and mucinous cystadenocarcinomas from our study because their prognosis differs from that of other carcinomas. Thus, a total of 81 patients were examined.