Editorial

Carcinoma of the Exocrine Pancreas

Current Progress

Introduction

The incidence of carcinoma of the exocrine pancreas has been increasing, at least in the Western world, probably because of increased cigarette smoking during the past century. Hopefully, with continued health education, the incidence of pancreatic cancer may begin to subside after the next decade or so. This will be the finest type of advance.

Meanwhile, there is a sense of progress at the frontier. This sense of optimism has not yet spread throughout the clinical community. Much of the progress stems from work currently underway in Japan. Ozaki’s report, in this issue, deserves wider appreciation. The progress being made in Japan and to an extent in North America and Europe stems from perhaps four different initiatives. Not emphasized in his report, but of great importance, are the advantages to be gained to the individual patient and to the overall scientific field by the care of these patients in specialty centers.

Pooling Experiences

As outlined by Ozaki in this issue, during the past 10 yr, the Japan Pancreatic Cancer Registry has registered 11,317 patients with pancreatic cancer. Being treated in multiple institutions, the clinical information has been collected on a systematic basis. Diagnostic and treatment protocols often have been adopted on an interinstitutional basis. This permits the rapid accumulation of information and the early assessment of clinical results as new modalities of diagnosis and treatment are investigated. Similar inter-institutional efforts are underway elsewhere, but on a limited scale. One cannot escape the impression that one advantage of socialized medicine is that it makes collaborative efforts easier to organize.

Earlier Diagnosis

Jaundice is a late manifestation of pancreatic cancer, and yet it is the basis for initial recognition by the majority of clinicians. Ariyama and others (1) have demonstrated very small malignancies in the pancreas well before the initiation of common bile duct obstruction. The early syndrome is the result of pancreatic duct obstruction rather than of common bile duct obstruction in most patients. Pancreatic duct obstruction occasionally leads to acute pancreatitis as an early manifestation, but more likely, it leads to ductal hypertension and fibrosis of the obstructed segment of pancreas. Mild abdominal pain, backache, anorexia, and elevated blood glucose or amylase levels are the indications pointed out by Ozaki and colleagues as the early syndrome; and this is the group of patients that deserves intensive study. Measurement of the CA 19-9 antigen in the plasma is of significant help. Although not diagnostic and not approved by the Food and Drug Administration in the US for diagnostic use, its use is helpful in monitoring changes before and after resection of the cancer, and is particularly helpful in following the patient after resection for evidence of recurrence. The CA 19-9 titer is to the patient
with pancreatic cancer what the CEA titer is to the patient with cancer of the large intestine.

As Ozaki has indicated, of the 11,317 patients entered into the Japan Registry, 435 (3.8%) had a carcinoma 2 cm or less in diameter. The 5-yr survival rate of this group was 36.2%! Similarly, of the 3743 patients who underwent definitive resection of their pancreatic cancer, a resection rate of 33%, approx 12%, were found to have a cancer 2 cm or less in diameter. Of the patients with tumors 3 cm or less in diameter, only 10% had developed jaundice. The point that bears reemphasis is that the hallmark of early pancreatic cancer is distal pancreatitis caused by pancreatic ductal obstruction.

Radical Resection and Multimodality of Treatment

The low long-term survival rate demonstrated by many cancer centers following resection of pancreatic cancer has led many to the conclusion that resection may be part, perhaps the first part, of treatment. This has led to a multiple modality approach, beginning in most studies with resection as the centerpiece. Building on the pioneer work of Fortner (2), Japanese surgeons modified his radical approach to resection, emphasizing the systematic resection of the lymph nodes involved in the multiple pathways of lymphatic spread around the pancreas. Their operative approach, to which this author subscribes, includes anatomic resection of the lymph nodes along the celiac axis and its branches, the nodes along the splenic and portal veins, those along the common bile duct, the nodes along the superior mesentery artery and vein, the nodes along the adjacent aorta, and the lymphatics along the retropancreatic vena cava. The resection is entirely feasible in the nonobese patient and can be carried out in most obese patients. This extended radical operation is to the Whipple operation what radical mastectomy is to simple mastectomy. This may well be their major contribution to treatment at this time. Nevertheless, they have frequently combined this with intraoperative radiation as has been done in North America and Europe, our colleague Dobebower (3) being one of the pioneers in this modality.

Finally, the Japanese have utilized intraoperative chemotherapy, either directing the therapeutic agent toward the liver by way of intraportal injection or systemically by way of the celiac axis route. To this, perhaps, may be proposed an evaluation of sustained intraperitoneal infusions during and after laparotomy. Survival rates have been encouraging. Survival rates of 20–30% have been reported following multimodality approaches, but these have sometimes been an expression of projections by statistical analysis. Experience shows that actual survival sometimes falls short of projections. Nevertheless, their results are encouraging and the information deserves dissemination on a wider basis.

Subclassification of Pancreatic Adenocarcinoma of the Exocrine Pancreas

The description of mucinous ectatic adenoma or adenocarcinoma of the pancreas has been a contribution. Perhaps the best overall study so far presented of histologic review and subclassifications of pancreatic cancer has been made by Cubilla and Fitzgerald (4), based on their experience at Memorial Hospital in New York. The need for a new classification, however, was recognized by members of the International Pancreatic Cancer Study Group at the 1990 meeting of the International Association of Pancreatology in Japan. There, Pour (5) organized a meeting where physicians, surgeons, and pathologists from around the world gathered to propose an internationally accepted, clinically useful system of classification.

This is perhaps the first time that a multidisciplinary group has undertaken such a multifaceted approach. Realizing that neither morphology alone nor clinical presentation alone can adequately predict the biology of pancreatic cancer, other parameters need to be included: histomorphology, immunohistochemistry, metastatic growth, molecular biology, DNA analysis, flow cytometry, hormone receptors, antigen production, and genetic factors, as well as...