Pancreatic Adenocarcinoma:
A Review for Primary Care Physicians

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Adenocarcinoma of the pancreas is becoming an increasingly common disease. The differential diagnosis of pancreatic adenocarcinoma is that of obstructive jaundice. Suspicious findings on history and physical examination can be confirmed with appropriate laboratory and radiologic testing. Approximately 20% of patients with small lesions and no metastatic disease may be cured with resection. The operative mortality and morbidity for major pancreatic resections is now sufficiently low to warrant a more aggressive approach to these patients.

Adenocarcinoma of the pancreas was first described in 1769 by Morgagni. The first operation for this disease was done by Von Winivarter in 1882. For reasons that may be related to the primary risk factors associated with pancreatic cancer, the incidence of this disease has risen dramatically over the past twenty years and it now is the second ranking cause of death among gastrointestinal cancers. These risk factors are advancing age and smoking. Molecular biologists have identified at least one oncogene associated with pancreatic adenocarcinoma, the Ki-ras gene, and work is proceeding to better understand the genetic alterations which lead to this disorder. Primary care physicians will continue to see increasing numbers of patients with pancreatic adenocarcinoma. The purpose of this paper is to review the current management of these patients in light of recent advances in diagnosis and therapy.

Presentation
The majority of patients with adenocarcinoma of the pancreas develop the tumor in the head of the pancreas and present with obstructive jaundice. There is initially little to no pain and the patient may delay seeking medical attention until pain, weight loss, or gastric outlet obstruction become prominent. Patients with tumors in the body or tail of the gland usually present late with pain as their primary symptom. When pain occurs it is usually severe and radiates from the epigastrium to the back. Physical examination usually reveals evidence of icterus and commonly a vague mass in the right upper quadrant of the abdomen representing a distended gallbladder. Signs of recent weight loss, malnutrition, or evidence of ascites all indicate advanced disease. Occasionally, a palpable left supravacular node (Virchow's node), periumbilical nodule (Sister Mary Joseph node), or Blummer's shelf may be detected, all indicating advanced disease.

The differential diagnosis of pancreatic adenocarcinoma is that of jaundice. Gallstone disease with common duct obstruction, ductal obstruction due to either proximal or distal bile duct adenocarcinoma, or perianpillary adenocarcinoma are the most likely alternative diseases. Sclerosing cholangitis, usually in the setting of inflammatory bowel disease, is unusual but is seen. Primary liver disease with jaundice is also a consideration.

Work-Up
Work-up of the patient with jaundice includes appropriate laboratory and radiology testing. It is important to select appropriate studies and obtain appropriate interpretation.

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tant to select tests in a logical sequence and avoid costly duplication of diagnostic studies. Laboratory examination should include a complete blood count and liver function tests with additional serum total protein and albumin studies to assess nutritional state. Patients with an obstructive pattern, that is, elevated total bilirubin with elevated alkaline phosphatase and only mildly elevated transaminase, need to be further evaluated to determine the site and probable cause of their obstruction. While ultrasound may be used to confirm obstruction by the finding of dilated intrahepatic ducts, it does not preclude the need for further studies. Its usefulness lies in its ability to detect common duct stones as a cause of obstructive jaundice.

Computed tomographic scanning of the abdomen confirms dilated biliary ducts and can usually determine the level of obstruction, i.e., proximal or distal. In addition, the obstructing lesion in the head of the pancreas is usually identified. Presence of metastatic disease in the liver or in peripancreatic nodes, when seen, is helpful in planning treatment. Many authors advocate celiac and superior mesenteric arteriography with portal venous images to aid in the staging of the tumor and identify potentially important anomalies. We have not found it necessary to routinely add this expensive, uncomfortable, and potentially risky procedure to the work-up of these patients. Anomalous arterial structures can be detected and protected intraoperatively by experienced surgeons. The accuracy in detecting portal venous or superior mesenteric involvement with tumor has not been sufficient to safely deny potentially beneficial surgery to patients who may be resectable.

If the cause or the location of the obstruction remains in doubt after computed tomographic scanning, then endoscopic retrograde cholangiopancreatography (ERCP) is the next diagnostic step. Peripanillary tumors may be seen and can be biopsied to provide helpful information. Obstruction of both the common bile duct and the pancreatic duct, the double duct sign, if seen, is further evidence for pancreatic cancer as the cause of the jaundice. If ERCP is unsuccessful or fails to adequately indicate the uppermost level of biliary duct obstruction, then percutaneous transhepatic cholangiography (PTC) is indicated.

In the past, PTC and drainage of the obstructive bile ducts prior to definitive operation was routine, but recent data indicate that this increased morbidity and mortality and is not indicated. In most patients, computed tomographic scanning provides adequate information to allow for appropriate treatment, and further studies are not needed. Patients with tumors of the body and tail who present with pain are best evaluated with computed tomography. Unfortunately, the pain usually indicates advanced disease and is not specific enough to lead to an early computed tomographic scan in many cases.

The clinical, laboratory, and radiologic picture of pancreatic adenocarcinoma, especially involving the head of the pancreas, is characteristic enough that therapy can reasonably be instituted in the absence of a tissue diagnosis. In patients with advanced disease or complicating diseases making operation contraindicated, fine needle aspiration cytology using ultrasound or CT guidance usually is able to confirm the diagnosis. This should be avoided in patients who are candidates for operation as it is expensive, uncomfortable, and adds no information that can not be gained at operation. In some cases, a false negative aspiration could delay resection in an otherwise resectable patient.

**Therapy**

It is now clear that patients presenting with small tumors in the pancreas can be cured with appropriate operations. Tumors less than 2 cm in size and with negative nodes have a 3-year survival rate of over 20% in several series. In addition, it is difficult to distinguish preoperatively and even at operation between distal common duct or periampullary adenocarcinomas and pancreatic adenocarcinomas. The former have a nearly 30% 3-year survival rate. The operative mortality rate of the Whipple procedure, which once approached 30%, is now less than 5% in centers with experienced pancreatic surgeons. For these reasons, the oncologic attitude towards patients with pancreatic adenocarcinoma is no longer warranted. Patients who are unresectable based on preoperative studies or who are otherwise poor candidates for surgery can be palliated either by endoscopically placed biliary stents or stents placed at PTC. Endoscopically placed stents are preferred as they obviate the need for an external catheter and simplify the patient’s care but are not always technically possible. Gastric outlet obstruction is more difficult to palliate nonoperatively, but in a patient with very advanced disease, a percutaneously placed endoscopic gastrostomy tube is helpful.

Patients who are in reasonable medical condition and have no preoperative evidence of unresectability should be offered an attempt at resection of their tumor. In patients who are unresectable, usually due to invasion of the portal vein or superior mesenteric artery, biliary and gastric bypass and chemical celiac ganglion block can be accomplished and allow for ef-
The most distressing and fearsome problem associated with pancreatic cancer is pain. Epigastric pain radiating to the back due to involvement of splanchinic nerves occurs relatively early in the course of the disease and tends to be severe. A number of techniques are now available which can significantly attenuate the pain in these patients. Tumor ganglion block, done either at laparotomy or by the percutaneous approach, will provide effective, although often short-lived pain relief.

In patients with limited disease but severe pain, a morphine spinal pump offers good pain control. The expensive and invasive nature of this approach makes it unreasonable for most patients with a limited life expectancy. Patient-controlled analgesia administered at home via infusaport devices can be very successful in most patients. Finally, narcotic transdermal patches (fentanyl patches) are now available and are being evaluated in this setting. It is important to emphasize to the patient early in the course of their disease that pain control can be achieved and that every effort be made to do so. This can significantly improve the attitude of patients who are facing a terminal illness.

Summary

In summary, patients with adenocarcinoma of the pancreas are being seen with increasing frequency. While most patients will succumb to their disease, resection is now a safe and reasonable alternative in appropriate patients and offers the only hope for cure and the best form of palliation. Resection is best accomplished by surgeons with experience in pancreatic surgery. Nonoperative stenting of the bile ducts can provide palliation in inoperable patients. Currently, chemotherapy and radiation therapy are of limited benefit in this disease. Techniques for pain control are now sufficient to be able to allow the patients in their terminal stages to be relatively pain free.

References


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