Pancreatic Cancer

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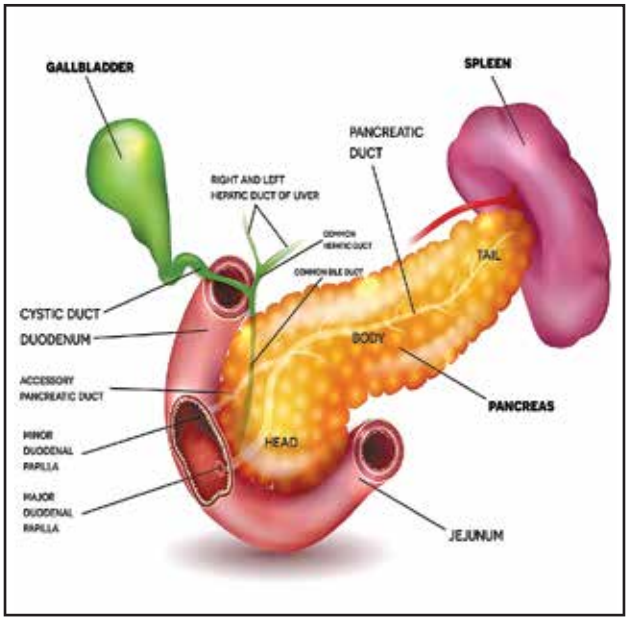
Key points

- Pancreatic ductal carcinoma - a type of carcinoma that develops from pancreatic duct cells
- Pancreatic cancer presentation symptoms
- Ras oncogene activated in pancreatic tumor
- Endoscopic retrograde cholangiopancreatography (ERCP) the treatment of choice

Pancreatic ductal carcinoma - a type of carcinoma that develops from pancreatic duct cells - is referred to as pancreatic cancer. In the US, it ranks as the fourth most common cancer-related death cause.1



An estimated 227 000 deaths from pancreatic cancer occur each year globally and are the fourth highest cause of cancer death in the United States.1 Smoking, advancing age, male sex, diabetes mellitus, obesity, non-O blood group, occupational exposures, African-American ethnicity, a high fat diet, diets high in meat and low in vegetables and folate, and possibly Helicobacter pylori infection and periodontal disease are risk factors for this malignant disease.2

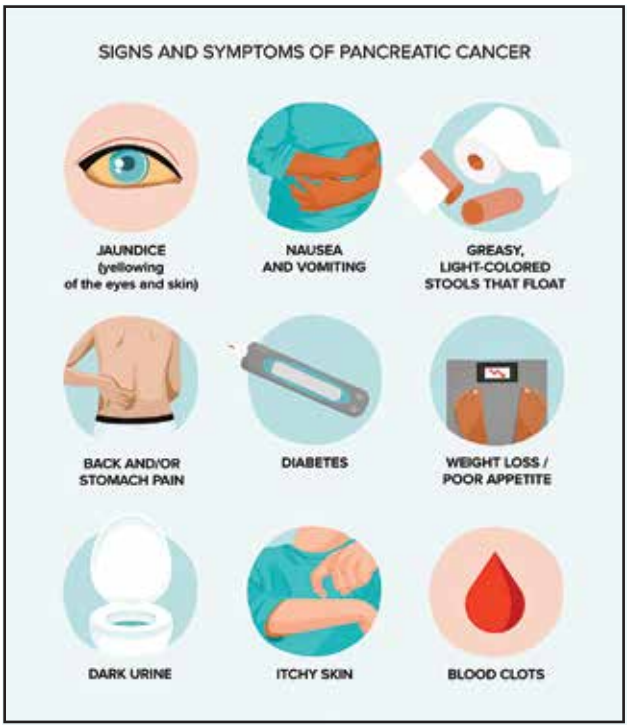
Activation of oncogenes & Inactivation of tumor suppressor genes

Point mutation and amplification are two alternative methods that might activate oncogenes. More than 90% of pancreatic tumours have been discovered to have the Ras oncogene activated. A 21-kDa membrane-bound protein from the Ras gene family is involved in signal transduction and causes a variety of pleiotropic effects, including cell migration and proliferation. Growth factor-mediated signal transduction pathways incorporate activated Ras. It has been discovered that codons 12, 13, and 61 in K-Ras have point mutations in about 80–90% of pancreatic tumours. A constitutively active version of Ras is created by the point mutation. Constitutively active Ras attaches to GTP and sends out-of-control stimulation impulses to downstream signaling cascades, which promotes unchecked cell growth.3 The K-ras mutation in pancreatic cancer typically manifests in the early stages of carcinogenesis, and patients who have the mutation live less than those who have the wild-type K-ras, indicating that the K-ras mutation plays a role in the development and spread of pancreatic cancer. Ras amplification is also frequently seen in pancreatic tumours together with point mutations, indicating that activation of the ras oncogene is a significant molecular event in pancreatic malignancies.

p16, p53, SMAD4, PTEN, and other tumour suppressor genes are targeted in pancreatic cancer. It is well known that p16 suppresses the activity of the CDK4/6 complex and cyclin D. The retinoblastoma (Rb) protein is typically phosphorylated by CDK4 and CDK6 in the presence of cyclin D. Rb's phosphorylation makes it possible for it to separate from a complex with elongation factor 2 (E2F), which then frees up E2F to activate the genes needed for DNA synthesis during the cell cycle. By blocking cyclin D and CDK4/6-mediated phosphorylation of Rb, which inhibits cell growth, p16 regulates cell cycle progression through the G1/S transition. 95% of people with pancreatic cancer have tumours that have inactivated p16 (40% deletion, 40% mutation, and 15% hypermethylation).3

Symptoms

Early-stage pancreatic cancer is typically clinically silent, and symptoms normally don't show up until the tumour has



spread to nearby tissues or distant organs. Weight loss, obstructive jaundice, and abdominal or mid-back pain are common pancreatic cancer presentation symptoms. Anorexia, malnutrition due to pancreatic ductal blockage, and cachexia can all cause weight loss. Attacks of pancreatitis may occasionally be brought on by pancreatic-duct blockage. At diagnosis, approximately 25% of pancreatic cancer patients have diabetes mellitus, and another 40% have impaired glucose intolerance.2

Endoscopic retrograde cholangiopancreatography (ERCP)

An upper endoscope is inserted into a second section of the duodenum during endoscopic retrograde cholangiopancreatography (ERCP), a combined endoscopic and fluoroscopic operation, allowing other equipment to travel through the main duodenal papilla and into the biliary and pancreatic ducts. These ducts can be given a contrast injection to enable radiologic visualisation and therapeutic interventions as needed. Through cannulation of the pancreatic and biliary ducts, ERCP was first performed as a diagnostic procedure, but it has since developed into primarily a therapeutic tool. It is suggested that difficult biliary cannulation be characterised as requiring at least two pancreatic guidewire passes and cannulation efforts lasting longer than five minutes or more than five. Cholangiopancreatoscopy allows for direct duct visualisation.4

References

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