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COMMENTARY

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Pancreatic Neuroendocrine Tumours: its Treatment and Symptoms

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Description

Pancreatic Neuroendocrine Tumors (PanNETs, PETs, or PNETs), often referred to as "islet cell tumors" or "pancreatic endocrine tumors," are neuroendocrine neoplasms that arise from cells of the endocrine (hormonal) and nervous systems in the pancreas. PanNETs are a type of neuroendocrine tumor that accounts for about one-third of Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs). Many PanNETs are benign, while some are malignant. Aggressive PanNET tumors have traditionally been called "islet cell carcinoma." PanNETs are quite different from the usual form of pancreatic cancer, most of which are adenocarcinomas that arise in the exocrine pancreas. Only 1% or 2% of clinically significant pancreatic neoplasms are PanNETs.

Therapy

In general, the treatment of PanNET includes the same range of options as other neuroendocrine tumors, as discussed in this main article. However, there are some specific differences that are discussed here. For functioning PanNETs, octreotide is usually recommended before biopsy or surgery but is generally avoided in insulinomas to avoid profound hypoglycemia. PanNETs in multiple endocrine neoplasia type 1 are often multiple and therefore require different treatment and follow-up strategies. Some PanNETs respond better to chemotherapy than gastroenteric carcinoid tumors. Several agents have shown activity. For well-differentiated PanNETs, chemotherapy is generally reserved for cases where there are no other treatment options. Combinations of several drugs have been used, such as doxorubicin with streptozocin and fluorouracil (5-FU) and capecitabine with temozolomide. Although cisplatin with etoposide is marginally effective in well-differentiated pancreatic neuroendocrine tumors, it has some activity in Poorly Differentiated Neuroendocrine Carcinomas (PDNEC), especially if the PDNEC has an extremely high Ki-67 score above 50%. Based on improved Progression-Free Survival (PFS), the Food and Drug Administration (FDA) has approved several targeted therapeutic agents in PanNETs:

1. Everolimus (Afinitor) is indicated for the treatment of progressive neuroendocrine tumors of pancreatic origin in patients with unresectable, locally advanced, or metastatic disease. The safety and efficacy of everolimus in carcinoid tumors have not been established.
2. Sunitinib (Sutent) is indicated for the treatment of progressive, well-differentiated neuroendocrine tumors of the pancreas in patients with unresectable locally advanced or metastatic disease. Sutent also has approval from the European Commission for the treatment of "unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumors with disease progression in adults." A phase III study of sunitinib in well-differentiated pNET that had worsened within the past 12 months (either advanced or metastatic disease) showed that sunitinib treatment improved progression-free survival (11.4 months *vs.* 5.5 months), overall survival, and objective response rate (9.3% *vs.* 0.0%) compared to placebo.

Symptoms

Some PanNETs cause no symptoms, in which case they may be discovered incidentally on a Computed tomography (CT) scan performed for another purpose. Symptoms such as abdominal or back pain or pressure, diarrhoea, indigestion or yellowing of the skin and the whites of the eye can result from a larger PanNET tumor, either locally or when it has metastasized. Approximately 40% of PanNETS have symptoms related to excessive secretion of hormones or

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active polypeptides and are therefore designated as "functional"; the symptoms reflect the type of hormone secreted as below. Up to 60% of PanNETs are nonsecretory or nonfunctional, in which there is no secretion or the amount or type of products such as pancreatic polypeptide (PPoma), chromogranin A, and neurotensin do not cause a clinical syndrome, although blood levels may be elevated. Overall, 85% of PanNETs have an elevated blood marker.