Tips in Pancreatic Neuroendocrine Tumors (P-Nets)

Danilo Coco* and Silvana Leanza

1Department of General Surgery and Surgical Pathology, Augusto Murri Hospital, Italy
2Department of Surgery, Carlo Urbani Hospital, Italy

Abstract

A neuroendocrine tumor seems to arise from neural and endocrine cells. The most common are carcinoid tumors and neuroendocrine tumors of the pancreas (P-NETs). Most pancreatic tumors are sporadic but they also can arise from genetic syndrome such as MEN 1, MEN 2, VHL syndromes. They account for approximately 1% of pancreatic cancer in a range of age between 30-60 years. They can divide in Functional (F-PNETs) and non Functional tumors (NF-PNETs). Approximately 10% to 20% is functional. Functional P-NET may or may not have hormonal syndrome based on the hormone secretion: gastrin, insulin, glucagone, VIP, somatostatin. About 70% are insulinomas, 15% glucagonomas, 10% gastrinomas and somatostatinomas, which have a risk of metastases of 80% to 90%. Very rare is Vipomas, ACTHoma, GRFoma. Non functional PNET may have not any kind of symptoms and they are discovered in advanced stage. Appropriate diagnosis requires multidisciplinary team evaluating biochemical, radiological, endocrinological and surgical findings.

Pathogenesis

P-NETs have two probable origins of pancreatic NET: mature endocrine cells in the pancreas and multipotent stem cells. Ki-67 index, mitotic count and differentiation are the major components of P-NETs grading system (WHO) (Table 1) [1-4].

Biochemical, Clinical and Diagnostic Features

Insulinoma

It’s the most common P-NET. Betcha cells. Hormon secretion: Insulin. It’s a benign type in almost 80%. Hepatic metastases inferior of 5%. Clinical symptoms: hypoglycemic symptoms, Whipple triad. Biochemical findings: Insulin level more than 3 mcLU/ml, C-peptide >0.6 ng/ml, pro-insulin >5 pmol/L. Dinamic tests: Calcium injection (Imamura test).

Gastrinoma


Glucagonoma

Rare Malignant. 80% risk of metastase. Clinical signs: Recent-onset diabetes, cachexia, necrotic erythematous skin rush. Biochemical findings: elevated glucagone in blood.

VIPoma


Somatostatinoma

Rare D cells. Hormone: somatostatin. Malignancy 70%. Clinically: diabetes mellitus, cholelithiasis, diarrhea.

Diagnostic Evaluations

CT/MRI are the most common techniques for the diagnosis of pancreatic NET with a sensitivity and specificity >90%. CT/MRI can also be used for preoperative staging, follow-up and evaluation of treatment efficacy. EUS is a highly sensitive for small lesions with diameters from 0.3 cm to 0.5
cm. Somatostatin Receptors Scanner (SRS) can detect tiny primary lesions and distant metastases. PET may be suitable for the detection of poorly differentiated tumors. The role of serum tumor markers in diagnosing pancreatic NET is limited. Tumor markers: Chromogranin A (CgA), synaptophysin and/or neuron-specific enolase (NSE).

**Treatment**

Surgical resection is the only curative strategy for pancreatic NET. 6 Furthermore, cytoreductive surgery can control the secretion of activated hormones and improve the survival for patients with advanced pancreatic NET and can be an optional strategy for physically fit patients with metastatic, well-differentiated pancreatic NET with an overall survival (OS) of 60 months versus 30 months in non cytoreductive or not fit patients. Somatostatin analogues or CHT are the first or second line approach in advanced diseases.

**Conclusion**

Pancreatic NET are a group with high heterogeneity and a better prognosis than exocrine pancreatic cancer. The incidence of pNETs is increasing and the majority of pNETs are nonfunctional. The prognosis worsens in patients with metastatic tumors or poorly differentiated pancreatic NET. Surgical treatment is the first choice treatment. Somatostatin analogue or cytotoxic CHT are the alternative. The efficacy of sunitinib and everolimus support the role of targeted agents as a new option in the first- or second-line treatment of pancreatic NET.

**Summary**

Evaluate CgA, NSE, hormone features (Table 2), symptoms and signs, radiologic findings (CT, MRI, SRS, PET, EUS), decide after a multidisciplinary team planning, analyze histopathological findings (Ki-67, mitotic count, differentiation).

**References**