

## Bölüm 36

# PANKREAS NÖROENDOKRİN TÜMÖRLERİ TANİ, FONKSİYONEL DEĞERLENDİRME VE TEDAVİDE CERRAHİNİN YERİ

Mehmet Kağan KATAR<sup>1</sup>

### GİRİŞ

Adacık hücresi tümörleri olarak da bilinen pankreas nöroendokrin tümörleri (PNET'ler), pankreasın endokrin dokularında ortaya çıkan nadir neoplazmlardır. İnsülin, gastrin, glukagon ve vazoaaktif intestinal peptid dahil olmak üzere çeşitli hormonları salgılayarak birçok klinik sendromla sonuçlanabilir. Bununla birlikte, modern klinik serilerde, PNET'lerin %50-75'i fonksiyonel değildir.

Bu bölümde, iyi diferansiye pankreatik NET'lerin sınıflandırılmasını, kliniği, lokalizasyonu, evrelemesi ve cerrahi tedavisi değerlendirilecektir.

### SINIFLANDIRMA

Pankreas nöroendokrin neoplazmlarının (NEN) isimlendirilmesinde son yıllarda değişim gözlemlenmiştir. Langerhans adacıklarında pankreatik NEN'lerin oluşumunu gösteren "Adacık hücresi tümörü" teriminin kullanımı azalmıştır. Son yıllarda, histolojik düzeyi ne olursa olsun iyi diferansiye tümörler için "pankreas nöroendokrin tümörü" terimi yaygın olarak kullanılmaktadır. Ayrıca "Pankreatik nöroendokrin karsinom" (NEC) terimi ise, kötü diferansiye histolojisi ve yüksek proliferatif oranı olan vakalar için kullanılmaktadır.

Vücuttaki farklı bölgelerde ortaya çıkan NEN'lar histolojik özelliklerine göre sınıflandırılır. Bu tümörlerin terminoloji ve derecelendirmesinde bazı farklılıklar bulunmasına karşın; yaygın olarak kullanılan tüm sınıflandırma sistemleri, iyi diferansiye tümörler ile klinik olarak akciğerin küçük hücreli karsinomu gibi davranan çok daha agresif, kötü diferansiye tipler arasında temel bir ayrımı ortaya koyar.

<sup>1</sup> Dr.Öğr.Üyesi, Yozgat Bozok Üniversitesi, drkagankatar@gmail.com

Bunlar, enükleasyondan pankreatikoduodenektomiye kadar tüm teknikler laparoskopik ve robotik olarak uygulanabilir.

**Anahtar Kelimeler:** pankreatik nöroendokrin tümör, pankreatektomi, pankreas

## **KAYNAKÇA**

1. Klimstra DS. Nodular neoplasms of the pancreas. *Modern pathology*. 2007;20(1):94-112
2. Hallett J, Law CHL, Cukier M, et al. Exploring the rising incidence of neuroendocrine tumors: a population based analysis of epidemiology, metastatic presentation, and outcomes. *Cancer*. 2015;121(4):589-597
3. Dasari A, Shen C, Halperin D, et al. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. *JAMA oncology*. 2017;3(10):1335-1342
4. Fesinmeyer MD, Austin MA, Li CI, et al. Differences in survival by histologic type of pancreatic cancer. *Cancer Epidemiology and Prevention Biomarkers*. 2005;14(7):1766-1773
5. Metz DC, Jensen RT. Gastrointestinal neuroendocrine tumors: pancreatic endocrine tumors. *Gastroenterology*. 2008;135(5):1469-1492
6. Leoncini E, Carioli G, La Vecchia C, et al. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. *Annals of Oncology*. 2015;27(1):68-81
7. Capurso G, Falconi M, Panzuto F, et al. Risk Factors for Sporadic Pancreatic Endocrine Tumors: A Case-Control Study of Prospectively Evaluated Patients. *The American journal of gastroenterology*. 2009;104(12):3034-3041
8. Hassan MM, Phan A, Li D, et al. Risk factors associated with neuroendocrine tumors: A US based case-control study. *International journal of cancer*. 2008;123(4):867-873
9. Halfdanarson TR, Bamlet WR, McWilliams RR, et al. Risk factors for pancreatic neuroendocrine tumors (PNETs): a clinic-based case-control study. *Pancreas*. 2014;43(8):1219
10. Hochwald SN, Zee S, Conlon KC, et al. Prognostic factors in pancreatic endocrine neoplasms: an analysis of 136 cases with a proposal for low-grade and intermediate-grade groups. *Journal of Clinical Oncology*. 2002;20(11):2633-2642
11. Zerbi A, Falconi M, Rindi G, et al. Clinicopathological features of pancreatic endocrine tumors: a prospective multicenter study in Italy of 297 sporadic cases. *The American journal of gastroenterology*. 2010;105(6):1421
12. Kasumova GG, Tabatabaie O, Eskander MF, et al. National Rise of primary pancreatic carcinoid tumors: comparison to functional and nonfunctional pancreatic neuroendocrine tumors. *Journal of the American College of Surgeons*. 2017;224(6):1057-1064
13. Falconi M, Plöckinger U, Kwekkeboom DJ, et al. Well-differentiated pancreatic nonfunctioning tumors/carcinoma. *Neuroendocrinology*. 2006;84(3):196-211
14. de Mestier L, Hentic O, Cros J, et al. Metachronous hormonal syndromes in patients with pancreatic neuroendocrine tumors: a case-series study. *Annals of internal medicine*. 2015;162(10):682-689
15. Li J, Luo G, Fu D, et al. Preoperative diagnosis of nonfunctioning pancreatic neuroendocrine tumors. *Medical Oncology*. 2011;28(4):1027-1031
16. Nomura N, Fujii T, Kanazumi N, et al. Nonfunctioning neuroendocrine pancreatic tumors: our experience and management. *Journal of Hepato Biliary Pancreatic Surgery*. 2009;16(5):639-647
17. Cheema A, Weber J, Strosberg JR. Incidental detection of pancreatic neuroendocrine tumors: an analysis of incidence and outcomes. *Annals of Surgical Oncology*. 2012;19(9):2932-2936
18. Cheslyn Curtis S, Sitaram V, Williamson R. Management of non functioning neuroendocrine tumours of the pancreas. *British Journal of Surgery*. 1993;80(5):625-627

19. Matthews BD, Heniford BT, Reardon PR, et al. Surgical experience with nonfunctioning neuroendocrine tumors of the pancreas/Discussion. *The American Surgeon*. 2000;66(12):1116
20. Chu QD, Hill HC, Douglass HO, et al. Predictive factors associated with long-term survival in patients with neuroendocrine tumors of the pancreas. *Annals of surgical oncology*. 2002;9(9):855-862
21. Riihimäki M, Hemminki A, Sundquist K, et al. The epidemiology of metastases in neuroendocrine tumors. *International journal of cancer*. 2016;139(12):2679-2686
22. Nikfarjam M, Warshaw AL, Axelrod L, et al. Improved contemporary surgical management of insulinomas: a 25-year experience at the Massachusetts General Hospital. *Annals of surgery*. 2008;247(1):165
23. Khashab MA, Yong E, Lennon AM, et al. EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. *Gastrointestinal endoscopy*. 2011;73(4):691-696
24. Wang SC, Parekh JR, Zuraek MB, et al. Identification of unknown primary tumors in patients with neuroendocrine liver metastases. *Archives of surgery*. 2010;145(3):276-280
25. Thoeni RF, Mueller-Lisse UG, Chan R, et al. Detection of small, functional islet cell tumors in the pancreas: selection of MR imaging sequences for optimal sensitivity. *Radiology*. 2000;214(2):483-490
26. Gibril F, Reynolds JC, Doppman JL, et al. Somatostatin receptor scintigraphy: its sensitivity compared with that of other imaging methods in detecting primary and metastatic gastrinomas: a prospective study. *Annals of Internal Medicine*. 1996;125(1):26-34
27. Pisegna JR, Doppman JL, Norton JA, et al. Prospective comparative study of ability of MR imaging and other imaging modalities to localize tumors in patients with Zollinger-Ellison syndrome. *Digestive diseases and sciences*. 1993;38(7):1318-1328
28. Rösch T, Lightdale CJ, Botet JF, et al. Localization of pancreatic endocrine tumors by endoscopic ultrasonography. *New England Journal of Medicine*. 1992;326(26):1721-1726
29. Anderson MA, Carpenter S, Thompson NW, et al. Endoscopic ultrasound is highly accurate and directs management in patients with neuroendocrine tumors of the pancreas. *The American journal of gastroenterology*. 2000;95(9):2271-2277
30. James PD, Tsolakis AV, Zhang M, et al. Incremental benefit of preoperative EUS for the detection of pancreatic neuroendocrine tumors: a meta-analysis. *Gastrointestinal endoscopy*. 2015;81(4):848-856.
31. Cadiot G, Lebtahi R, Sarda L, et al. Preoperative detection of duodenal gastrinomas and peripancreatic lymph nodes by somatostatin receptor scintigraphy. *Groupe D'étude Du Syndrome De Zollinger-Ellison. Gastroenterology*. 1996;111(4):845-854
32. Atiq M, Bhutani MS, Bektas M, et al. EUS-FNA for pancreatic neuroendocrine tumors: a tertiary cancer center experience. *Digestive diseases and sciences*. 2012;57(3):791-800
33. King C, Reznick R, Dacie J, et al. Imaging islet cell tumours. *Clinical radiology*. 1994;49(5):295-303
34. Vinik A, Delbridge L, Moattari R, et al. Transhepatic portal vein catheterization for localization of insulinomas: a ten-year experience. *Surgery*. 1991;109(1):1-11
35. Frucht H, Norton JA, London JF, et al. Detection of duodenal gastrinomas by operative endoscopic transillumination: a prospective study. *Gastroenterology*. 1990;99(6):1622-1627
36. Huai J-C, Zhang W, Niu H-O, et al. Localization and surgical treatment of pancreatic insulinomas guided by intraoperative ultrasound. *The American journal of surgery*. 1998;175(1):18-21
37. Rindi G, Klöppel G, Alhman x, et al. TNM staging of foregut (neuro) endocrine tumors: a consensus proposal including a grading system. *Virchows Archiv*. 2006;449(4):395-401
38. Strosberg JR, Cheema A, Weber JM, et al. Relapse-free survival in patients with nonmetastatic, surgically resected pancreatic neuroendocrine tumors: an analysis of the AJCC and ENETS staging classifications. *Annals of surgery*. 2012;256(2):321-325
39. Cho JH, Ryu JK, Song SY, et al. Prognostic validity of the American Joint Committee on Cancer and the European Neuroendocrine Tumors Staging Classifications for pancreatic neuro-

- endocrine tumors: a retrospective nationwide multicenter study in South Korea. *Pancreas*. 2016;45(7):941-946
40. Kulke MH, Anthony LB, Bushnell DL, et al. NANETS treatment guidelines: well-differentiated neuroendocrine tumors of the stomach and pancreas. *Pancreas*. 2010;39(6):735
  41. Åkerström G, Hellman P. Surgery on neuroendocrine tumours. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2007;21(1):87-109
  42. Pitt SC, Pitt HA, Baker MS, et al. Small pancreatic and periampullary neuroendocrine tumors: resect or enucleate? *Journal of Gastrointestinal Surgery*. 2009;13(9):1692-1698
  43. Falconi M, Bartsch DK, Eriksson B, et al. ENETS Consensus Guidelines for the management of patients with digestive neuroendocrine neoplasms of the digestive system: well-differentiated pancreatic non-functioning tumors. *Neuroendocrinology*. 2012;95(2):120-134
  44. Hill JS, McPhee JT, McDade TP, et al. Pancreatic neuroendocrine tumors: the impact of surgical resection on survival. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2009;115(4):741-751
  45. Gomez-Rivera F, Stewart AE, Arnoletti JP, et al. Surgical treatment of pancreatic endocrine neoplasms. *The American journal of surgery*. 2007;193(4):460-465
  46. Fernández-Cruz L, Blanco L, Cosa R, et al. Is laparoscopic resection adequate in patients with neuroendocrine pancreatic tumors? *World journal of surgery*. 2008;32(5):904-917
  47. Allendorf JD, Schrope BA, Lauerma MH, et al. Postoperative glycemic control after central pancreatectomy for mid-gland lesions. *World journal of surgery*. 2007;31(1):164-168
  48. DiNorcia J, Ahmed L, Lee MK, et al. Better preservation of endocrine function after central versus distal pancreatectomy for mid-gland lesions. *Surgery*. 2010;148(6):1247-1256
  49. Falconi M, Zerbi A, Crippa S, et al. Parenchyma-preserving resections for small nonfunctioning pancreatic endocrine tumors. *Annals of surgical oncology*. 2010;17(6):1621-1627
  50. Adham M, Giunipero A, Hervieu V, et al. Central pancreatectomy: single-center experience of 50 cases. *Archives of Surgery*. 2008;143(2):175-180
  51. Hirono S, Tani M, Kawai M, et al. A central pancreatectomy for benign or low-grade malignant neoplasms. *Journal of Gastrointestinal Surgery*. 2009;13(9):1659-1665