



## BÖLÜM 53

### Somatostatinoma Tanı ve Tedavi Yaklaşımları

Ersoy TAŞPINAR <sup>1</sup>

#### ÖZET

Somatostatinomalar, aşırı miktarda somatostatin içeren ve bazen salgılayan D hücre kökenli, nadir görülen nöroendokrin tümörlerdir. Somatostatinomalı hastalarda kolelitiazis, safra kesesi kontraktilesini azaltan kolesistokinin salınımının inhibisyonundan kaynaklanabilmektedir. Azalan insülin sekresyonu, glukoz intoleransına/diyabete yol açmaktadır. Pankreatik enzim ve bikarbonat sekresyonunun inhibisyonu ve lipidlerin intestinal absorpsiyonu diyare ve steatoreye neden olmaktadır. Diğer nöroendokrin tümörlerde olduğu gibi cerrahi rezeksiyon tercih edilen tedavi yöntemidir. Yaygın bilobar tutulumu, bozulmuş karaciğer fonksiyonu veya yaygın ekstrahepatik metastazları olmayan, metastatik hastalığı olan hastalarda hepatik rezeksiyon düşünülebilmektedir. Hastalar metastatik hastalık ile başvurduğunda prognoz genellikle kötüdür.

#### Somatostatinoma Epidemiolojisi

Somatostatinomalar, aşırı miktarda somatostatin içeren ve bazen salgılayan D hücre kökenli, nadir görülen nöroendokrin tümörlerdir (1). Somatostatinomalar, yıllık insidansı 40 milyonda 1 olan nadir nöroendokrin tümörlerdir (2). Somatostatinomaların ortalama tanı yaşı, kabaca eşit bir cinsiyet dağılımı ile 50 ila 55 yıldır. Somatostatinomaların yaklaşık %55'i pankreastadır ve bunların üçte ikisi pankreasın başında ortaya çıkar. Geri kalanı duodenumun ampulla ve periampuller bölgesinde veya nadiren jejunumda ortaya

çıkarak. Diğer nadir primer bölgeler arasında karaciğer, kolon ve rektum bulunur (3-5). Somatostatinomaların yaklaşık %75'i maligndir ve %70 ila %92'si metastatik hastalık ile kendini gösterir. Somatostatinomaların %35 ila %45'i çoklu endokrin neoplazi (MEN)-1 sendromu veya diğer ailesel sendromla ilişkili olarak ortaya çıksa da, somatostatinomalar, MEN-1 sendromlu hastalarda en az görülen işleyen pankreas nöroendokrin tümörleri arasındadır ve hastaların %1'inden azında görülür (6). Nörofibromatoz I (NF-1; von Recklinghausen hastalığı) olan hastaların %10 kadarında somatostatinomalar gelişir. NF-1 ile ilişkili soma-

<sup>1</sup> Uzm. Dr. Ersoy TAŞPINAR, Özel Bursa Medica Hastanesi Genel Cerrahi Bölümü ersoytaspinar@gmail.com

**Tablo 3: Pankreas nöroendokrin tümörü rezeksiyonu yapılan hastalarda beş ve on yıllık sağkalım oranları (41).**

Stage	Gözlemlenen Survival*		Relative survival†		Median survival (ay)
	5-yıl (percent)	10- yıl (percent)	5- yıl (percent)	10- yıl (percent)	
I	61.0	46.0	75.6	71.1	112
II	52.0	28.8	64.3	45.8	63
III	41.4	18.5	60.5	33.1	46
IV	15.5	5.1	19.9	8.9	14

\* Her aşama grubu arasındaki karşılaştırmalar  $p < 0,0001$  için önemlidir.

† Sağkalım, 1990 Amerika Birleşik Devletleri Sayım Bürosu verileriyle eşleştirilerek hastanın yaşına göre ayarlanmıştır.

## Kaynaklar

- Friesen SR. Update on the diagnosis and treatment of rare neuroendocrine tumors. *Surg Clin North Am* 1987; 67:379.
- Jensen RT, Norton JA. Endocrine tumors of the pancreas. In: Slesinger & Fordtran's Gastrointestinal and Liver Disease: Pathophysiology/Diagnosis/Management, 7th ed, Feldman M, Scharschmidt BE, Slesinger MH (Eds), WB Saunders, Philadelphia 2002. p.988.
- Harris GJ, Tio F, Cruz AB Jr. Somatostatinoma: a case report and review of the literature. *J Surg Oncol* 1987; 36:8.
- Ohwada S, Joshita T, Ishihara T, et al. Primary liver somatostatinoma. *J Gastroenterol Hepatol* 2003; 18:1218.
- Doherty GM. Rare endocrine tumours of the GI tract. *Best Pract Res Clin Gastroenterol* 2005; 19:807.
- Garbrecht N, Anlauf M, Schmitt A, et al. Somatostatin-producing neuroendocrine tumors of the duodenum and pancreas: incidence, types, biological behavior, association with inherited syndromes, and functional activity. *Endocr Relat Cancer* 2008; 15:229.
- Jensen RT, Norton JA. Endocrine neoplasms of the pancreas. In: Textbook of Gastroenterology, Yamada T (Ed), JB Lippincott Co, Philadelphia 1995. p.2131.
- Snow ND, Liddle RA. Neuroendocrine Tumors. In: Gastrointestinal Cancers: Biology, Diagnosis and Therapy, Rustgi AK (Ed), Lippincott-Raven, Philadelphia 1995. p.585.
- Vinik A, Pacak K, Feliberti E, et al. Endotext, De Groot LJ, Chrousos G, Dungan K, Feingold KR, Grossman A, Hershman JM, Koch C, Korbonits M, McLachlan R, New M, Purnell J, Rebar R, Singer F, Vinik A. (Eds), MDText.com, Inc., South Dartmouth (MA) 2000.
- O'Brien TD, Chejfec G, Prinz RA. Clinical features of duodenal somatostatinomas. *Surgery* 1993; 114:1144.
- Pacak K, Jochmanova I, Prodanov T, et al. New syndrome of paraganglioma and somatostatinoma associated with polycythemia. *J Clin Oncol* 2013; 31:1690.
- Zhuang Z, Yang C, Lorenzo F, et al. Somatic HIF2A gain-of-function mutations in paraganglioma with polycythemia. *N Engl J Med* 2012; 367:922.
- Deppen SA, Liu E, Blume JD, et al. Safety and Efficacy of  $^{68}\text{Ga}$ -DOTATATE PET/CT for Diagnosis, Staging, and Treatment Management of Neuroendocrine Tumors. *J Nucl Med* 2016; 57:708.
- Ramage JK, Ahmed A, Ardill J, et al. Guidelines for the management of gastroenteropancreatic neuroendocrine (including carcinoid) tumours (NETs). *Gut* 2012; 61:6.
- Öberg K, Knigge U, Kwekkeboom D, et al. Neuroendocrine gastro-entero-pancreatic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2012; 23 Suppl 7:vii124.
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Head and neck cancer. Version 1.2021. Available at: [https://www.nccn.org/professionals/physician\\_gls/](https://www.nccn.org/professionals/physician_gls/) [https://www.nccn.org/professionals/physician\\_gls/](https://www.nccn.org/professionals/physician_gls/) (Accessed on January 29, 2020).
- Falconi M, Eriksson B, Kaltsas G, et al. ENETS Consensus Guidelines Update for the Management of Patients with Functional Pancreatic Neuroendocrine Tumors and Non-Functional Pancreatic Neuroendocrine Tumors. *Neuroendocrinology* 2016; 103:153.
- Nikou GC, Toubanakis C, Nikolaou P, et al. VIPomas: an update in diagnosis and management in a series of 11 patients. *Hepatogastroenterology* 2005; 52:1259.
- Hope TA, Bergsland EK, Bozkurt MF, et al. Appropriate Use Criteria for Somatostatin Receptor PET Imaging in Neuroendocrine Tumors. *J Nucl Med* 2018; 59:66.
- Rindi G, Klöppel G, Alhman H, et al. TNM staging of foregut (neuro)endocrine tumors: a consensus proposal including a grading system. *Virchows Arch* 2006; 449:395.
- Strosberg JR, Cheema A, Weber JM, et al. Relpase-free survival in patients with nonmetastatic, surgically resected pancreatic neuroendocrine tumors: an analysis of the AJCC and ENETS staging classifications. *Ann Surg* 2012; 256:321.
- Strosberg JR, Cheema A, Weber J, et al. Prognostic validity of a novel American Joint Committee on Cancer Staging Classification for pancreatic neuroendocrine tumors. *J Clin Oncol* 2011; 29:3044.
- 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 Neuroendocrine Tumors: A Retrospective Nationwide Multicenter Study in South Korea. *Pancreas* 2016; 45:941.

24. Bergsland EK, Woltering EA, Rindo G. Neuroendocrine tumors of the pancreas. In: AJCC Cancer Staging Manual, 8th ed, Amin MB (Ed), AJCC, Chicago 2017. p.407. Corrected at 4th printing, 2018.
25. House MG, Yeo CJ, Schulick RD. Periampullary pancreatic somatostatinoma. *Ann Surg Oncol* 2002; 9:869.
26. Rinke A, Wittenberg M, Schade-Brittinger C, et al. Placebo-Controlled, Double-Blind, Prospective, Randomized Study on the Effect of Octreotide LAR in the Control of Tumor Growth in Patients with Metastatic Neuroendocrine Midgut Tumors (PROMID): Results of Long-Term Survival. *Neuroendocrinology* 2017; 104:26.
27. Glazer ES, Tseng JF, Al-Refaie W, et al. Long-term survival after surgical management of neuroendocrine hepatic metastases. *HPB (Oxford)* 2010; 12:427.
28. Eriksson B, Oberg K. An update of the medical treatment of malignant endocrine pancreatic tumors. *Acta Oncol* 1993; 32:203.
29. Swärd C, Johanson V, Nieveen van Dijkum E, et al. Prolonged survival after hepatic artery embolization in patients with midgut carcinoid syndrome. *Br J Surg* 2009; 96:517.
30. Christante D, Pommier S, Givi B, Pommier R. Hepatic artery chemoinfusion with chemoembolization for neuroendocrine cancer with progressive hepatic metastases despite octreotide therapy. *Surgery* 2008; 144:885.
31. de Baere T, Deschamps F, Teriitheau C, et al. Transarterial chemoembolization of liver metastases from well differentiated gastroenteropancreatic endocrine tumors with doxorubicin-eluting beads: preliminary results. *J Vasc Interv Radiol* 2008; 19:855.
32. Rhee TK, Lewandowski RJ, Liu DM, et al. 90Y Radioembolization for metastatic neuroendocrine liver tumors: preliminary results from a multi-institutional experience. *Ann Surg* 2008; 247:1029.
33. Arrese D, McNally ME, Chokshi R, et al. Extrahepatic disease should not preclude transarterial chemoembolization for metastatic neuroendocrine carcinoma. *Ann Surg Oncol* 2013; 20:1114.
34. Memon K, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for neuroendocrine liver metastases: safety, imaging, and long-term outcomes. *Int J Radiat Oncol Biol Phys* 2012; 83:887.
35. Moug SJ, Leen E, Horgan PG, Imrie CW. Radiofrequency ablation has a valuable therapeutic role in metastatic VIPoma. *Pancreatol* 2006; 6:155.
36. Shimata K, Sugawara Y, Hibi T. Liver transplantation for unresectable pancreatic neuroendocrine tumors with liver metastases in an era of transplant oncology. *Gland Surg* 2018; 7:42.
37. Yao JC, Shah MH, Ito T, et al. Everolimus for advanced pancreatic neuroendocrine tumors. *N Engl J Med* 2011; 364:514.
38. Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 Trial of (177)Lu-Dotatate for Midgut Neuroendocrine Tumors. *N Engl J Med* 2017; 376:125.
39. Kunz PL, Catalano PJ, Nimeiri H, et al. A randomized study of temozolomide or temozolomide and capecitabine in patients with advanced pancreatic neuroendocrine tumors: A trial of the ECOG-ACRIN Cancer Research Group (E2211). Paper, American Society of Clinical Oncology; American Society of Clinical Oncology, Chicago, IL 2018.
40. Kulke MH, Anthony LB, Bushnell DL, et al. NANETS treatment guidelines: well-differentiated neuroendocrine tumors of the stomach and pancreas. *Pancreas* 2010; 39:735.
41. Bilimoria KY, Bentrem DJ, Merkow RP, et al. Application of the pancreatic adenocarcinoma staging system to pancreatic neuroendocrine tumors. *J Am Coll Surg* 2007; 205:558.