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PANKREAS NÖROENDOKRİN TÜMÖRLERİ

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GİRİŞ

Pankreatik nöroendokrin tümörler (PNET), eski adıyla "adacık hücreli tümörler", nadir, heterojen bir tümör grubudur. Bu tümörlerin hücresel orijini konusunda henüz bir fikir birliği sağlanamamıştır [1]. Fonksiyonel ve fonksiyonel olmayan PNETler olmak üzere ikiye ayrılır. Büyük çoğunluğu nonfonksiyoneldir ve fonksiyonel PNETler salgıladıkları hormonlara göre isimlendirilir. Gastrinoma en sık görülen PNET olup bunu insülinoma takip eder. Glukagonoma, somatostatinoma (SSoma), vazoaktif intestinal peptid salgılayan tümörler (VIPoma) ve pankreatik polipeptid salgılayan tümörler (PPoma) ise daha nadir görülen fonksiyonel PNETlerdir [2].

EPİDEMİYOLOJİ

PNETler tüm nöroendokrin tümörlerin yaklaşık %7 sini ve tüm pankreatik tümörlerin %1-2 sini oluşturur [1, 3, 4]. Bu tümörlerin insidansı son 30 yılda 0,17/100000'den 0,43/100000'e yükselmiştir. Her iki cinsiyette de aynı oranda görülmektedir ve genellikle 60-80 yaş arasında tanı almaktadır [5]. Hastaların %5 inde altta yatan multipl endokrin neoplazi tip 1 (MEN1), von Hippel-Lindau (VHL), tüberoz skleroz (TS) veya nörofibromatoz tip 1 (NF1) gibi familyal bir sendrom PNET gelişimine yatkınlık yaratmaktadır. Böyle familyal sendromlu hastalar daha genç yaşta tanı almaktadırlar [4]. PNET gelişimi konusunda iyi ortaya konulmuş olan tek risk faktörü aile hikayesi olmasıdır [6]. Sigara içimi, obezite, tip 2 diyabet, kronik pankreatit gibi pankreatik adenokanser için olan risk faktörleri PNET ile ilişkili olduğu gösterilememiştir [7].

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SÜRVEYANS VE TAKİP

PNET li hastalar rezeksiyon sonrası her 3 ila 12. ayda CT/MR ve biyokimyasal markerlar ile takip edilmelidir. Rekürrens saptanmıyorsa 10 yıl boyunca yılda 1 veya 2 kez muayene, kromogranin A, pankreastatin düzeyi bakılmalı ve CT/MR ile takibi önerilmektedir [47].

KAYNAKLAR

1. Kuo, J.H., J.A. Lee, and J.A. Chabot, Nonfunctional pancreatic neuroendocrine tumors. Surgical Clinics, 2014. **94**(3): p. 689-708.
2. Yao, J.C., et al., Population-based study of islet cell carcinoma. Annals of surgical oncology, 2007. **14**(12): p. 3492-3500.
3. Franko, J., et al., Non-functional neuroendocrine carcinoma of the pancreas: incidence, tumor biology, and outcomes in 2,158 patients. Journal of Gastrointestinal Surgery, 2010. **14**(3): p. 541-548.
4. Schimmack, S., et al., The diversity and commonalities of gastroenteropancreatic neuroendocrine tumors. Langenbecks Arch Surg, 2011. **396**(3): p. 273-98.
5. Fraenkel, M., et al., Epidemiology of gastroenteropancreatic neuroendocrine tumours. Best practice & research Clinical gastroenterology, 2012. **26**(6): p. 691-703.
6. Hassan, M.M., et al., Risk factors associated with neuroendocrine tumors: A US-based case–control study. International journal of cancer, 2008. **123**(4): p. 867-873.
7. Ryan, D.P., T.S. Hong, and N. Bardeesy, Pancreatic adenocarcinoma. New England Journal of Medicine, 2014. **371**(11): p. 1039-1049.
8. Jiao, Y., et al., DAXX/ATRX, MEN1, and mTOR pathway genes are frequently altered in pancreatic neuroendocrine tumors. Science, 2011. **331**(6021): p. 1199-1203.
9. Charlesworth, M., et al., Pancreatic lesions in von Hippel–Lindau disease? A systematic review and meta-synthesis of the literature. Journal of Gastrointestinal Surgery, 2012. **16**(7): p. 1422-1428.
10. Thakker, R.V., Multiple endocrine neoplasia type 1 (MEN1) and type 4 (MEN4). Molecular and cellular endocrinology, 2014. **386**(1-2): p. 2-15.
11. Yachida, S., et al., Small cell and large cell neuroendocrine carcinomas of the pancreas are genetically similar and distinct from well-differentiated pancreatic neuroendocrine tumors. The American journal of surgical pathology, 2012. **36**(2): p. 173.
12. Zhang, J., et al., Current understanding of the molecular biology of pancreatic neuroendocrine tumors. J Natl Cancer Inst, 2013. **105**(14): p. 1005-17.
13. Baudin, E., et al., Malignant insulinoma: recommendations for characterisation and treatment. Ann Endocrinol (Paris), 2013. **74**(5-6): p. 523-33.
14. Klöppel, G., A. Perren, and P.U. Heitz, The gastroenteropancreatic neuroendocrine cell system and its tumors: the WHO classification. Annals of the New York Academy of Sciences, 2004. **1014**(1): p. 13-27.
15. Rindi, G., et al., Gastroenteropancreatic (neuro) endocrine neoplasms: the histology report. Digestive and Liver Disease, 2011. **43**: p. S356-S360.
16. Bosman, F.T., et al., WHO classification of tumours of the digestive system. 2010: World Health Organization.
17. Edge, S.B., AJCC cancer staging manual. Springer, 2010. **7**: p. 97-100.
18. Halfdanarson, T.R., et al., Pancreatic neuroendocrine tumors (PNETs): incidence, prognosis and recent trend toward improved survival. Annals of oncology, 2008. **19**(10): p. 1727-1733.

19. Strosberg, J.R., et al., Prognostic validity of a novel American Joint Committee on Cancer Staging Classification for pancreatic neuroendocrine tumors. J Clin Oncol, 2011. **29**(22).
20. Bilimoria, K.Y., et al., Prognostic score predicting survival after resection of pancreatic neuroendocrine tumors: analysis of 3851 patients. Annals of surgery, 2008. **247**(3): p. 490-500.
21. Vinik, A.I., et al., Neuroendocrine tumors: a critical appraisal of management strategies. Pancreas, 2010. **39**(6): p. 801-818.
22. Schernthaner-Reiter, M.H., G. Trivellin, and C.A. Stratakis, MEN1, MEN4, and carney complex: pathology and molecular genetics. Neuroendocrinology, 2016. **103**(1): p. 18-31.
23. Okabayashi, T., et al., Diagnosis and management of insulinoma. World journal of gastroenterology: WJG, 2013. **19**(6): p. 829.
24. Kulke, M.H., et al., NANETS treatment guidelines: well-differentiated neuroendocrine tumors of the stomach and pancreas. Pancreas, 2010. **39**(6): p. 735.
25. Stabile, B.E., D.J. Morrow, and E. Passaro Jr, The gastrinoma triangle: operative implications. The American Journal of Surgery, 1984. **147**(1): p. 25-31.
26. Ito, T., H. Igarashi, and R.T. Jensen, Pancreatic neuroendocrine tumors: clinical features, diagnosis and medical treatment: advances. Best practice & research Clinical gastroenterology, 2012. **26**(6): p. 737-753.
27. Verner, J.V. and A.B. Morrison, Islet cell tumor and a syndrome of refractory watery diarrhea and hypokalemia. The American journal of medicine, 1958. **25**(3): p. 374-380.
28. Williamson, J., et al., Pancreatic and peripancreatic somatostatinomas. The Annals of The Royal College of Surgeons of England, 2011. **93**(5): p. 356-360.
29. Kuo, S.C., et al., Sporadic pancreatic polypeptide secreting tumors (PPomas) of the pancreas. World journal of surgery, 2008. **32**(8): p. 1815-1822.
30. Birnbaum, D.J., et al., Sporadic nonfunctioning pancreatic neuroendocrine tumors: prognostic significance of incidental diagnosis. Surgery, 2014. **155**(1): p. 13-21.
31. Lu, S.-J., et al., Single photon emission computed tomography/computed tomography in the evaluation of neuroendocrine tumours: a review of the literature. Nuclear medicine communications, 2013. **34**(2): p. 98-107.
32. Naswa, N., et al., Diagnostic performance of somatostatin receptor PET/CT using 68 Ga-DOTANOC in gastrinoma patients with negative or equivocal CT findings. Abdominal imaging, 2013. **38**(3): p. 552-560.
33. Treglia, G., et al., A case of insulinoma detected by (68) Ga-DOTANOC PET/CT and missed by (18) F-dihydroxyphenylalanine PET/CT. Clinical nuclear medicine, 2013. **38**(6): p. e267-70.
34. Naswa, N., et al., Gallium-68-DOTA-NOC PET/CT of patients with gastroenteropancreatic neuroendocrine tumors: a prospective single-center study. American Journal of Roentgenology, 2011. **197**(5): p. 1221-1228.
35. Bhate, K., et al., Functional assessment in the multimodality imaging of pancreatic neuro-endocrine tumours. Minerva endocrinologica, 2010. **35**(1): p. 17-25.
36. Bertani, E., et al., Resection of the primary pancreatic neuroendocrine tumor in patients with unresectable liver metastases: possible indications for a multimodal approach. Surgery, 2014. **155**(4): p. 607-614.
37. Zhang, T., et al., Enucleation of pancreatic lesions: indications, outcomes, and risk factors for clinical pancreatic fistula. Journal of Gastrointestinal Surgery, 2013. **17**(12): p. 2099-2104.
38. Giudici, F., et al., Surgical management of insulinomas in multiple endocrine neoplasia type 1. Pancreas, 2012. **41**(4): p. 547-553.
39. Lee, L.C., et al., Small, nonfunctioning, asymptomatic pancreatic neuroendocrine tumors (PNETs): role for nonoperative management. Surgery, 2012. **152**(6): p. 965-974.
40. Libutti, S.K., et al., Clinical and genetic analysis of patients with pancreatic neuroendocrine tumors associated with von Hippel-Lindau disease. Surgery, 2000. **128**(6): p. 1022-1028.

41. Tsutsumi, K., et al., Analysis of lymph node metastasis in pancreatic neuroendocrine tumors (PNETs) based on the tumor size and hormonal production. Journal of gastroenterology, 2012. **47**(6): p. 678-685.
42. Giovinazzo, F., et al., Lymph nodes metastasis and recurrences justify an aggressive treatment of gastrinoma. Updates in surgery, 2013. **65**(1): p. 19-24.
43. Mayo, S.C., et al., Surgical management of hepatic neuroendocrine tumor metastasis: results from an international multi-institutional analysis. Annals of surgical oncology, 2010. **17**(12): p. 3129-3136.
44. Zappa, M., et al., Liver-directed therapies in liver metastases from neuroendocrine tumors of the gastrointestinal tract. Targeted oncology, 2012. **7**(2): p. 107-116.
45. Chan, J. and M. Kulke, Targeting the mTOR signaling pathway in neuroendocrine tumors. Current treatment options in oncology, 2014. **15**(3): p. 365-379.
46. Raymond, E., et al., Sunitinib malate for the treatment of pancreatic neuroendocrine tumors. New England Journal of Medicine, 2011. **364**(6): p. 501-513.
47. Kulke, M.H., et al., Neuroendocrine tumors, version 1.2015. Journal of the National Comprehensive Cancer Network, 2015. **13**(1): p. 78-108.