

Bölüm 12

AKCİĞER KANSERİNDE PROGNOSTİK VE PREDİKTİF FAKTÖRLER

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GİRİŞ

Akciğer kanserlerinin yaklaşık %95'i küçük hücreli akciğer kanseri ya da küçük hücreli dışı akciğer kanseri olarak sınıflandırılır. Bu ayırım evrelemenin, tedavinin ve prognozun doğru belirlenmesi ve tesbiti için gereklidir (1). Aynı başlık altında da olsa temelde her iki hastalık ayrı ayrı değerlendirilmelidir. Bu gruplar hem evreleme hem prognoz açısından birbirinden tamamen farklı özelliktedirler. Ayrıca moleküler patogeneizde gerçekleşen hızlı gelişmeler ışığında küçük hücre dışı akciğer kanserinin de kendi içinde heterojen bir hastalık grubuna sahip olduğu görülmektedir (2).

Burada prognoz ve prediktif belirteçlerden bahsedilirken akciğer kanserlerinin 2 ana grubu ayrı ayrı ele alınacaktır.

KÜÇÜK HÜCRELİ DIŞI AKCİĞER KANSERİ:

Küçük hücreli dışı akciğer kanseri heterojen bir grup olmasına rağmen erken evre ve lokalize hastalıkta tedavi benzerdir. Metastatik hastalıkta ise tedavi kararı için tümör histolojisi ve tümör dokusunun moleküler analizi önemli rol oynamaktadır.

Günümüzde küçük hücreli dışı akciğer kanserinde bazı özel hedefler ve bunlarla ilgili tedaviler tanımlanmıştır (3). Bunların başlıcaları:

- EGFR (epidermal growth factor receptor) mutasyonu
- BRAF (B-raf protooncogen) mutasyonu
- EML-4-ALK (echinoderm microtubulu associated protein like -4/anaplastic lymphoma kinase) füzyonu

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Sınırlı evre hastalık için iyi prognoz ile ilişkili faktörler olarak; kadın cinsiyet, 70 yaşından küçük olma, normal LDH düzeyleri, evre 1 hastalık bulunurken, yaygın evre hastalığı olanlarda iyi prognozu gösteren faktörler; genç yaş, normal kreatinin düzeyi, normal LDH düzeyi ve tek metastatik bölge olarak belirlenmiştir(38,39).

SONUÇ

Gerek küçük hücreli dışı akciğer kanserinde gerekse küçük hücreli akciğer kanserinde hasta için prognostik ve prediktif önemi olan birçok belirteç tanımlanmıştır. Hastanın tedavi kararını verirken bu belirteçler göz önünde tutulmalıdır.

Anahtar Kelimeler: akciğer kanseri, prediktif belirteçler, prognostik belirteçler

KAYNAKLAR

1. Torre LA, Siegel RL, Jemal A. Lung cancer statistics. *Adv Exp Med Biol* 2016;893:1-19.
2. Travis WD, Brambilla E, et al. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. *J Thorac Oncol* 2015;10:1243-60.
3. Jordan EJ, Kim HR, et al. Prospective comprehensive molecular characterization of lung adenocarcinomas for efficient patient matching to approved and emerging therapies. *Cancer Discov* 2017;7:596-609.
4. Finkelstein DM, Ettinger DS, et al. Long term survivors in metastatic non small cell lung cancer: an eastern cooperative oncology group study. *J Clin Oncol* 1986;4:702-709.
5. Goldstraw P, Chansk K, et al. The IASLC Lung Cancer Staging Project. *J Thor Oncol* 2016; 11: 1612-1614.
6. <https://seer.cancer.gov/statfacts/html/lungb.html>
7. Hoang T, Xu R, Schiller JH, et al. Clinical model to predict survival in chemo-naïve patients with advanced non-small-cell lung cancer treated with third-generation chemotherapy regimens based on eastern cooperative oncology group data. *J Clin Oncol* 2005; 23:175.
8. Lackstock AW, Herndon JE 2nd, Paskett ED, et al. Outcomes among African-American/non-African-American patients with advanced non-small-cell lung carcinoma: report from the Cancer and Leukemia Group B. *J Natl Cancer Inst* 2002; 94:284.
9. Stanley KE. Prognostic factors for survival in patients with inoperable lung cancer. *J Natl Cancer Inst* 1980; 65:25.
10. Feinstein AR. Symptomatic patterns, biologic behavior, and prognosis in cancer of the lung. Practical application of boolean algebra and clinical taxonomy. *Ann Intern Med* 1964; 61:27.
11. Kawaguchi T, Takada M, Kubo A, et al. Performance status and smoking status are independent favorable prognostic factors for survival in non-small cell lung cancer: a comprehensive analysis of 26,957 patients with NSCLC. *J Thorac Oncol* 2010; 5:620.
12. Richards TB, Henley SJ, et al. Lung cancer survival in the United States by race and stage (2001-2009): Findings from the CONCORD-2 study. *Cancer* 2017;123:5079-99.
13. Gail MH, Eagan RT, Feld R, et al. Prognostic factors in patients with resected stage I non-small cell lung cancer. A report from the Lung Cancer Study Group. *Cancer* 1984; 54:1802.
14. Postoperative T1 N0 non-small cell lung cancer. Squamous versus nonsquamous recurrences. The Lung Cancer Study Group. *J Thorac Cardiovasc Surg* 1987; 94:349.
15. Harpole DH Jr, Herndon JE 2nd, Young WG Jr, et al. Stage I non-small cell lung cancer. A multivariate analysis of treatment methods and patterns of recurrence. *Cancer* 1995; 76:787.
16. Pairolero PC, Williams DE, Bergstralh EJ, et al. Postsurgical stage I bronchogenic carcinoma: morbid implications of recurrent disease. *Ann Thorac Surg* 1984; 38:331.

17. Scagliotti G.V ,Parikh P,et al. Phase III Study Comparing Cisplatin Plus Gemcitabine With Cisplatin Plus Pemetrexed in Chemotherapy-Naive Patients With Advanced-Stage Non-Small-Cell Lung Cancer. *J Clin Oncol* ;26:3543-3551.
18. Cagini L, Monacelli M, Giustozzi G, et al. Biological prognostic factors for early stage completely resected non-small cell lung cancer. *J Surg Oncol* 2000; 74:53.
19. Kwiatkowski DJ, Harpole DH Jr, Godleski J, et al. Molecular pathologic substaging in 244 stage I non-small-cell lung cancer patients: clinical implications. *J Clin Oncol* 1998; 16:2468.
20. Shields TW. Prognostic significance of parenchymal lymphatic vessel and blood vessel invasion in carcinoma of the lung. *Surg Gynecol Obstet* 1983; 157:185.
21. Macchiarini P, Fontanini G, Hardin MJ, et al. Blood vessel invasion by tumor cells predicts recurrence in completely resected T1 N0 M0 non-small-cell lung cancer. *J Thorac Cardiovasc Surg* 1993; 106:80.
22. Rusch VW, Hawes D, Decker PA, et al. Occult metastases in lymph nodes predict survival in resectable non-small-cell lung cancer: report of the ACOSOG Z0040 trial. *J Clin Oncol* 2011; 29:4313.
23. Brambilla E, Le Teuff G, Marguet S, et al. Prognostic Effect of Tumor Lymphocytic Infiltration in Resectable Non-Small-Cell Lung Cancer. *J Clin Oncol* 2016; 34:1223.
24. Ruffini E, Asioli S, Filosso PL, et al. Significance of the presence of microscopic vascular invasion after complete resection of Stage I-II pT1-T2N0 non-small cell lung cancer and its relation with T-Size categories: did the 2009 7th edition of the TNM staging system miss something? *J Thorac Oncol* 2011; 6:319.
25. Antonio L, Visbal MD, Brent A, et al. Gender differences in non-small-cell lung cancer survival: an analysis of 4,618 patients diagnosed between 1997 and 2002. (*Ann Thorac Surg* 2004;78:209-15).
26. D'Angelo SP, Janjigian YY, Ahye N, et al. Distinct clinical course of EGFR-mutant resected lung cancers: results of testing of 1118 surgical specimens and effects of adjuvant gefitinib and erlotinib. *J Thorac Oncol* 2012; 7:1815.
27. Miller VA, Riely GJ, et al. Molecular characteristic of bronchoalveolar carcinoma and adenocarcinoma, bronchoalveolar carcinoma subtype, predict response to erlotinib. *J Clin Oncol* 2008;26:1472-78.
28. Hirsch FR, Bunn PA. EGFR testing in lung cancer is ready for prime time. *Lancet Oncol* 2009;10:432-33.
29. Mazieres J, zalcman G, et al. Crizotinib therapy for advanced lung adenocarcinoma and a ROS 1 rearrangement: results from the EUROS1 cohort. *J Clin Oncol* 2015;33:992-999.
30. Kwak EL, Bang YJ, et al. Anaplastic lymphoma kinase inhibition in non small cell lung cancer .*NEJM* 2010;363:1693-1703.
31. Paik PK, Varghese AM, et al. Response to erlotinib in patients with EGFR mutant advanced non small cell lung cancer with a squamous or squamous like component. *Mol Cancer Ther* 2012;11:2535-40.
32. B176. Slebos RJ, Kibbelaar RE, et al. Kras oncogene activation as a prognostic marker in adenocarcinoma of the lung. *N Eng J Med* 1990;323:561-65.
33. Shaw AT, Ou SH, et al. Crizotinib in ROS1 rearrnged non small cell lung cancer. *N Eng J Med* 2014;371:1963-71.
34. Bergethon K, Shaw AT, et al. ROS1 rearrangements define a unique molecular class of lung cancers. *J Clin Oncol* 2012;30:863-70.
35. Takeuchi K, Soda M, et al. RET, ROS 1 and ALK fusions in lung cancer. *Nat Med* 2012;18:378-381.
36. Gautschi O, Milia J, et al. Targeted therapy for patients with BRAF-mutant lung cancer. Result from the European EURAF Cohort. *J Thorac Oncol* 2015;10:1451-1457.
37. B159. Klempner SJ, Borghei A, et al. Intracranial activity of cabozantinib in met exon 14 positive NSCLC with brain metastases. *J Thor Oncol* 2017;12:152-156.
38. Sculier JP, Chansky K, et al. The impact of additional prognostic factors on survival and their relationship with the anatomical extent of disease expressed by the 6Th edition of the TNM clas-

- sification of malignant tumors and the proposal for the 7th edition. *J Thor Oncol* 2008;3:457.
39. Gaspar LE, McNamara EJ, et al. Small cell lung cancer: prognostic factors and changing treatment over 15 years. *Clin Lung Cancer* 2012;13(2):115-22.