

## Bölüm 24

# Küçük Hücre Dışı Akciğer Kanserinde İzlenen Paraneoplastik Sendromlar

Sedat Tarık FIRAT<sup>1</sup>

## GİRİŞ

Paraneoplastik sendromlar, doğrudan tümör invazyonu veya metastazları ile ilgisi olmayan, malignite ile ilişkili uzak etkileri ifade eder. Bunlar, kanser teşhisi konmadan önce ortaya çıkabilir ve şiddetli, birincil tümörün evresine göre bağımsız olabilir. Paraneoplastik sendromlar en sık akciğer kanseri ile ilişkilidir ve vakaların yaklaşık %10'unda rapor edilir. Endokrin sendromlar, özellikle uygunsuz ADH sekresyonu sendromu (SIADH) ve malignitenin hümal hiperkalsemisi (HHM), akciğer kanserinde en sık görülen paraneoplastik sendromlardır ve histolojik kanser tipi ile ilişkilidir [1].

## ENDOKRİN SENDROMLAR

### Hiperkalsemi

İlk tanı anında akciğer kanseri hastalarında %2-6 oranında hiperkalsemi bildirilmiştir; hastalık seyri boyunca insidans %8-12'ye yükselir [2]. Kötü прогноз ile ilişkilidir. PTHrP üretimi (paratiroid hormonu ile ilgili protein) ile ilişkilenirildiğinde HHM olarak adlandırılır. HHM, meme, böbrek, multipl miyelom ve akciğer gibi çeşitli malignitelerde gözlenir; akciğer kanserinin skuamöz hücreli alt tipi en sık görülen alt tiptir. Osteolitik metastazlar, malignitede hiperkalseminin bir diğer önemli nedenidir [3-5]. HHM'ye sekonder hiperkalseminin dört mekanizmasından (PTHrP, paratiroid hormonu, 1-25 dihidroksi vitamin D veya granülosit koloni uyarıcı faktör salgılanması), paratiroid hor-

<sup>1</sup> Uzm. Dr., Kayseri Şehir Hastanesi, Tibbi Onkoloji Kliniği tarikfirat18@hotmail.com

da insülin benzeri büyümeye faktörü (IGFR) reseptörlerinde ve fibroblastlarda anormallilikler gözlenmiştir. AN ve işkembe avuç içi tipik olarak altta yatan malignitenin tedavisi ile önemli ölçüde iyileşir ve topikal retinoidler de faydalıdır.

## KAYNAKLAR

1. Heinemann, S., P. Zabel, and H.-P. Hauber, *Paraneoplastic syndromes in lung cancer*. Cancer therapy, 2008. 6(687): p. 98.
2. Spiro, S.G., M.K. Gould, and G.L. Colice, *Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidence-based clinical practice guidelines*. Chest, 2007. 132(3): p. 149S-160S.
3. Clines, G.A., *Mechanisms and treatment of hypercalcemia of malignancy*. Current Opinion in Endocrinology, Diabetes and Obesity, 2011. 18(6): p. 339-346.
4. Mazzone, P.J. and A.C. Arroliga, *Endocrine paraneoplastic syndromes in lung cancer*. Current opinion in pulmonary medicine, 2003. 9(4): p. 313-320.
5. Pelosof, L.C. and D.E. Gerber. *Paraneoplastic syndromes: an approach to diagnosis and treatment*. in *Mayo Clinic Proceedings*. 2010. Elsevier.
6. Yoshimoto, K., et al., *Ectopic production of parathyroid hormone by small cell lung cancer in a patient with hypercalcemia*. The Journal of Clinical Endocrinology & Metabolism, 1989. 68(5): p. 976-981.
7. Hiraki, A., et al., *Hypercalcemia-leukocytosis syndrome associated with lung cancer*. Lung Cancer, 2004. 43(3): p. 301-307.
8. Hanley, D., et al., *Denosumab: mechanism of action and clinical outcomes*. International journal of clinical practice, 2012. 66(12): p. 1139-1146.
9. Moses, A.M. and S.J. Scheinman, *Ectopic secretion of neurohypophyseal peptides in patients with malignancy*. Endocrinology and metabolism clinics of North America, 1991. 20(3): p. 489-506.
10. Kagawa, K., et al., *Syndrome of inappropriate secretion of ADH (SIADH) following cisplatin administration in a pulmonary adenocarcinoma patient with a malignant pleural effusion*. Internal medicine, 2001. 40(10): p. 1020-1023.
11. Hansen, O., P. Sørensen, and K.H. Hansen, *The occurrence of hyponatremia in SCLC and the influence on prognosis: a retrospective study of 453 patients treated in a single institution in a 10-year period*. Lung cancer, 2010. 68(1): p. 111-114.
12. Biswal, S., et al., *Acromegaly caused by ectopic growth hormone: a rare manifestation of a bronchial carcinoid*. The Annals of thoracic surgery, 2008. 85(1): p. 330-332.
13. El Aziz, S., et al., *Pulmonary epidermoid carcinoma in a patient with acromegaly: a rare entity*. Pan African Medical Journal, 2012. 12(1).
14. Gustafsson, B.I., et al., *Bronchopulmonary neuroendocrine tumors*. Cancer, 2008. 113(1): p. 5-21.
15. Thomas, C., J.R. Jett, and J.R. Strosberg, *Lung neuroendocrine (carcinoid) tumors: Epidemiology, risk factors, classification, histology, diagnosis, and staging*.
16. Honnorat, J. and J.-C. Antoine, *Paraneoplastic neurological syndromes*. Orphanet journal of rare diseases, 2007. 2(1): p. 1-8.
17. Yeung, S.-C.J., M.A. Habra, and S.N. Thosani, *Lung cancer-induced paraneoplastic syndromes*. Current opinion in pulmonary medicine, 2011. 17(4): p. 260-268.
18. Graus, F., et al., *Recommended diagnostic criteria for paraneoplastic neurological synd-*

- romes. *Journal of Neurology, Neurosurgery & Psychiatry*, 2004. 75(8): p. 1135-1140.
19. Lee, J.C., H. Yamauchi, and J. HOPPER JR, *The association of cancer and the nephrotic syndrome*. *Annals of Internal Medicine*, 1966. 64(1): p. 41-51.
  20. Lin, F-C., et al., *The association of non-small-cell lung cancer, focal segmental glomerulosclerosis, and platelet dysfunction*. *The American journal of the medical sciences*, 2002. 324(3): p. 161-165.
  21. Eagen, J.W. and E.J. Lewis, *Glomerulopathies of neoplasia*. *Kidney international*, 1977. 11(5): p. 297-306.
  22. Burstein, D.M., S.M. Korbet, and M.M. Schwartz, *Membranous glomerulonephritis and malignancy*. *American journal of kidney diseases*, 1993. 22(1): p. 5-10.
  23. Chew, H.K., et al., *The incidence of venous thromboembolism among patients with primary lung cancer*. *Journal of Thrombosis and Haemostasis*, 2008. 6(4): p. 601-608.
  24. Blom, J., S. Osanto, and F. Rosendaal, *The risk of a venous thrombotic event in lung cancer patients: higher risk for adenocarcinoma than squamous cell carcinoma*. *Journal of Thrombosis and Haemostasis*, 2004. 2(10): p. 1760-1765.
  25. Goldin-Lang, P., et al., *Tissue factor expression pattern in human non-small cell lung cancer tissues indicate increased blood thrombogenicity and tumor metastasis*. *Oncology reports*, 2008. 20(1): p. 123-128.
  26. Raskob, G.E., et al., *Edoxaban for the treatment of cancer-associated venous thromboembolism*. *New England Journal of Medicine*, 2018. 378(7): p. 615-624.
  27. Streiff, M.B., et al., *NCCN guidelines insights: cancer-associated venous thromboembolic disease, version 2.2018*. *Journal of the National Comprehensive Cancer Network*, 2018. 16(11): p. 1289-1303.
  28. Young, A.M., et al., *Comparison of an oral factor Xa inhibitor with low molecular weight heparin in patients with cancer with venous thromboembolism: results of a randomized trial (SELECT-D)*. *J Clin Oncol*, 2018.
  29. Khorana, A.A., et al., *Rivaroxaban for preventing venous thromboembolism in high-risk ambulatory patients with cancer: rationale and design of the CASSINI trial*. *Thrombosis and haemostasis*, 2017. 117(11): p. 2135-2145.
  30. Martinez-Lavin, M., *Hypertrophic osteoarthropathy: consensus on its definition, classification, assessment and diagnostic criteria*. *J Rheumatol*, 1993. 20: p. 1386-1387.
  31. King, M.M. and D.A. Nelson, *Hypertrophic osteoarthropathy effectively treated with zoledronic acid*. *Clinical lung cancer*, 2008. 9(3): p. 179-182.
  32. Ito, T., et al., *Hypertrophic pulmonary osteoarthropathy as a paraneoplastic manifestation of lung cancer*. *Journal of thoracic oncology*, 2010. 5(7): p. 976-980.
  33. Yao, Q., R.D. Altman, and E. Brahn. *Periostitis and hypertrophic pulmonary osteoarthropathy: report of 2 cases and review of the literature*. in *Seminars in arthritis and rheumatism*. 2009. Elsevier.
  34. Davis, M.C. and V. Sherry, *Hypertrophic osteoarthropathy as a clinical manifestation of lung cancer*. *Clinical journal of oncology nursing*, 2011. 15(5).
  35. Santini, D., et al., *Pamidronate induces modifications of circulating angiogenetic factors in cancer patients*. *Clinical Cancer Research*, 2002. 8(5): p. 1080-1084.
  36. Hayashi, M., et al., *Successful treatment of hypertrophic osteoarthropathy by gefitinib in a case with lung adenocarcinoma*. *Anticancer research*, 2005. 25(3C): p. 2435-2438.
  37. Bohan, A. and J.B. Peter, *Polymyositis and Dermatomyositis: (First of Two Parts)*. *New England Journal of Medicine*, 1975. 292(7): p. 344-347.
  38. Zhang, W., S.-P. Jiang, and L. Huang, *Dermatomyositis and malignancy: a retrospective study of 115 cases*. *Eur Rev Med Pharmacol Sci*, 2009. 13(2): p. 77-80.
  39. Chen, Y-J., et al., *Cancer risks of dermatomyositis and polymyositis: a nationwide co-*

- hort study in Taiwan. *Arthritis research & therapy*, 2010. 12(2): p. 1-7.
- 40. Fujita, J., et al., *Primary lung cancer associated with polymyositis/dermatomyositis, with a review of the literature*. *Rheumatology international*, 2001. 20(2): p. 81-84.
  - 41. Kannenberg, S., et al., *A patient with leonine facies and occult lung disease*. *Respiration*, 2010. 79(3): p. 250.
  - 42. Mukherjee, S., et al., *A case of squamous cell carcinoma of lung presenting with paraneoplastic type of acanthosis nigricans*. *Lung India: Official Organ of Indian Chest Society*, 2011. 28(1): p. 62.