



ONKOLOJİK TEDAVİYE BAĞLI DİĞER KARDİYOVASKÜLER KOMPLİKASYONLAR

Mustafa AĞCA¹

Günümüzde kanser ve kanser tedavisine bağlı olarak görülen kardiyovasküler komplikasyonlar, hastaların morbidite ve mortalitesini etkileyen önemli nedenler arasında yer almaktadır. Bu nedenle kanser hastalarının takipleri sırasında bu komplikasyonların tanı ve tedavisi, прогноз açısından oldukça önemlidir. Perikarditler, perikardiyal efüzyon, plevral efüzyon ve otonomik disfonksiyona bağlı görülen komplikasyonlar, kanser tedavisi alan hastalarda sıkılıkla görülmektedir.

1. Perikard Hastalıkları

Perikard hastalıkları, kanser tedavisi sırasında izlenebileceği gibi kanserin kendisine bağlı olarak da görülebilmektedir. Akciğer kanseri, meme kanseri, lenfoma, malign melanom ve lösemilerin birçoğunda perikardit, perikardiyal efüzyon ve buna bağlı olarak tamponad bulguları izlenebilmektedir. Ancak kanser hastalarının yaklaşık üçte ikisisinde perikardiyal hastalıkların görülmeye nedeni malignite dışı nedenlere (radyoterapi, kemoterapi ve fırsatçı enfeksiyonlar vb.) bağlı olarak izlenmektedir.^(1,2,3)

1.1. Perikardit

Perikarditler, perikardiyal hastalıkların en sık görülen formudur. Özellikle genç ve orta yaş erişkinlerde sıkılıkla görülmekte ve acil serviste izlenen non-iskemik göğüs ağrısı nedenlerinin yaklaşık %5'ini oluşturmaktadır. Elektrokardiyografide (EKG) yaygın ST elevasyonu ve PR segmentinde depresyon izlenebilir. Kardiyak enzimler normal olmakla beraber eşlik eden miyokardit varlığında artış gözlenebilir.^(4,5)

¹ Uzm. Dr. Bartın Devlet Hastanesi, Kardiyoloji Kliniği agca87@hotmail.com.

larının otonomik fonksiyonu artırarak, semptomları azalttığı gösterilmiştir.⁽⁶²⁾ Yine otonomik disfonksiyonun ciddi semptomatik olduğu seçilmiş vakalarda vagal sinir stimulasyonu ve karotis baroreseptör stimülasyonu gibi girişimsel işlemler de tedavide kullanılmaktadır.⁽⁶³⁾

KAYNAKLAR

1. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC). Adler Y, Charron P, Imazio M, Badano L, et al. *European Heart Journal* (2015) 36, 2921–2964. doi: 10.1093/eurheartj/ehv318.
2. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). Zamorano JL, Lancellotti P, Muñoz DR, Aboyans V, et al. *European Heart Journal*, Volume 37, Issue 36, 21 September 2016, Pages 2768–2801. <https://doi.org/10.1093/eurheartj/ehw211>.
3. Imazio M, Demichelis B, Parrini I, Favro E, Beqaraj F, Cecchi E, Pomari F, Demarie D, Ghisio A, Belli R, Bobbio M, Trinchero R. Relation of acute pericardial disease to malignancy. *Am J Cardiol* 2005; 95:1393–1394.
4. Ghosh AK, Crake T, Manisty C, Westwood M. Pericardial Disease in Cancer Patients. *Curr Treat Options Cardio Med* (2018) 20: 60. doi:10.1007/s11936-018-0654-7
5. Mody P, Bikdeli B, Wang Y, ImazioM, KrumholzHM. Trends in acute pericarditis hospitalizations and outcomes among the elderly in the United States, 1999– 2012. *EurHearth JQual Care Clin Outcomes*. 2017;4:98–105. <https://doi.org/10.1093/ejhjccq/qcx040>.
6. Hardenbergh PH, Munley MT, Bentel GC, Kedem R, Borges-Neto S, Hollis D, et al. Cardiac perfusion changes in patients treated for breast cancer with radiation therapy and doxorubicin: preliminary results. *Int J Radiat Oncol Biol Phys*. 2001;49:1023–8.
7. Darby SC, Ewertz M, McGale P, Bennet AM, Blom- Goldman U, Brønnum D, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. *N Engl J Med*. 2013;368:987–98.
8. Gagliardi G, Constine LS, Moiseenko V, Correa C, Pierce LJ, Allen AM, et al. Radiation dose-volume effects in the heart. *Int J Radiat Oncol Biol Phys*. 2010;76:S77–85.
9. Wang K, Eblan MJ, Deal AM, Lipner M, Zagar TM, Wang Y, et al. Cardiac toxicity after radiotherapy for stage III non-small-cell lung cancer: pooled analysis of dose-escalation trials delivering 70 to 90 Gy. *J Clin Oncol*. 2017;35:1387–94.
10. Walker C, Saldaña A, Gladish G, Dicks D, Kicska G, Mitsumori L, Reddy GP. Cardiac complications of oncologic therapy. *RadioGraphics* 2013; 33:1801–1815. doi:10.1148/radio.336125005/-DC1.
11. Laham RJ, Cohen DJ, Kuntz RE, Baim DS, Lorell BH, Simons M. Pericardial effusion in patients with cancer: outcome with contemporary management strategies. *Heart*. 1996;75:67–71.
12. Bristow MR, Thompson PD, Martin RP, Mason JW, Billingham ME, Harrison DC. Early anthracycline cardiotoxicity. *Am J Med*. 1978;65:823–32.
13. Gottdiener JS, AppelbaumFR, Ferrans VJ, Deisseroth A, Ziegler J. Cardiotoxicity associated with high-dose cyclophosphamide therapy. *Arch Intern Med*. 1981;141:758–63.
14. Appelbaum F, Strauchen JA, Graw RG, Savage DD, Kent KM, Ferrans VJ, et al. Acute lethal carditis caused by high-dose combination chemotherapy: a unique clinical and pathological entity. *Lancet (London, England)*. 1976;1:58–62.
15. van Rijssel RH, Wegman J, Oud ME, Pals ST, van Oers MHJ. A case of ATRA-induced isolated myocarditis in the absence of circulating malignant cells: demonstration of the

- t(15;17) translocation in the inflammatory infiltrate by in situ hybridisation. Leuk Res. 2010;34:e142–4.
- 16. De Santis GC, Madeira MIA, de Oliveira LCO, Falcao RP, Rego EM. Cardiac stunning as a manifestation of ATRA differentiation syndrome in acute promyelocytic leukemia. Med Oncol. 2012;29:248–50.
 - 17. Işık P, Çetin I, Tavil B, Azik F, Kara A, Yarali N, et al. Alltransretinoic acid (ATRA) treatment-related pancarditis and severe pulmonary edema in a child with acute promyelocytic leukemia. J Pediatr Hematol Oncol. 2010;32:e346–8.
 - 18. Morandi P, Ruffini PA, Benvenuto GM, Raimondi R, Fosser V. Cardiac toxicity of high-dose chemotherapy. Bone Marrow Transplant. 2005;35:323–34.
 - 19. Yamamoto R, Kanda Y, Matsuyama T, Oshima K, Nannya Y, Suguro M, et al. Myopericarditis caused by cyclophosphamide used to mobilize peripheral blood stem cells in a myeloma patient with renal failure. Bone Marrow Transplant. 2000;26:685–8.
 - 20. Cham WC, Freiman AH, Carstens PH, Chu FC. Radiation therapy of cardiac and pericardial metastases. Radiology. 1975;114:701–4.
 - 21. Posner MR, Cohen GI, Skarin AT. Pericardial disease in patients with cancer. The differentiation of malignant from idiopathic and radiation-induced pericarditis. Am J Med. 1981;71:407–13.
 - 22. Buck M, Ingle JN, Giuliani ER, Gordon JR, Therneau TM. Pericardial effusion in women with breast cancer. Cancer. 1987;60:263–9.
 - 23. Lee PJ, Mallik R. Cardiovascular effects of radiation therapy: practical approach to radiation therapy-induced heart disease. Cardiol Rev 2005;13(2):80–86.
 - 24. Yusuf SW, Sami S, Daher IN. Radiation-induced heart disease: a clinical update. Cardiol Res Pract 2011;2011:317659.
 - 25. Wang ZJ, Reddy GP, Gotway MB, Yeh BM, Hetts SW, Higgins CB. CT and MR imaging of pericardial disease. RadioGraphics 2003;23(Spec No): S167–S180.
 - 26. Çelik S, Lestuzzi C, Cervesato E, Dequanter D, Piotti P, De Biasio M, et al. Systemic chemotherapy in combination with pericardial window has better outcomes in malignant pericardial effusions. J Thorac Cardiovasc Surg. 2014;148:2288–93.
 - 27. Patel N, Rafique AM, Eshaghian S, Mendoza F, Biner S, Cersek B, et al. Retrospective comparison of outcomes, diagnostic value, and complications of percutaneous prolonged drainage versus surgical pericardiectomy of pericardial effusion associated with malignancy. Am J Cardiol. 2013;112:1235–9.
 - 28. Saltzman AJ, Paz YE, Rene AG, Green P, Hassanin A, Argenziano MG, et al. Comparison of surgical pericardial drainage with percutaneous catheter drainage for pericardial effusion. J Invasive Cardiol. 2012;24:590–3.
 - 29. El Haddad D, Iliescu C, Yusuf SW, William WN, Khair TH, Song J, et al. Outcomes of cancer patients undergoing percutaneous pericardiocentesis for pericardial effusion. J Am Coll Cardiol. 2015;66:1119–28.
 - 30. Virk SA, Chandrakumar D, Villanueva C, Wolfenden H, Liou K, Cao C. Systematic review of percutaneous interventions for malignant pericardial effusion. Heart. 2015;101:1619–26.
 - 31. Gagliardi G, Constine LS, Moiseenko V, Correa C, Pierce LJ, Allen AM, Marks LB. Radiation dose-volume effects in the heart. Int J Radiat Oncol Biol Phys 2010;76: S77–85.
 - 32. Wang ZJ, Reddy GP, Gotway MB, Yeh BM, Hetts SW, Higgins CB. CT and MR imaging of pericardial disease. RadioGraphics 2003;23(Spec No): S167–S180.
 - 33. Masui T, Finck S, Higgins CB. Constrictive pericarditis and restrictive cardiomyopathy: evaluation with MR imaging. Radiology 1992;182(2):369–373.
 - 34. Parakh N, Mehrotra S, Seth S, Ramakrishnan S, Kothari S, Bhargava B, Bahl VK. *NT pro B type natriuretic peptide levels in constrictive pericarditis and restrictive cardiomyopathy*. Indian Heart J. 2015 Jan-Feb; 67(1): 40–44. doi: 10.1016/j.ihj.2015.02.008
 - 35. Khandaker M, Espinosa R, Nishimura R, Sinak L, Hayes S, Melduni R, Oh JK. “Pericardial Disease: Diagnosis and Management”. Mayo Clinic Proceedings. 85 (6): 572–593. doi:10.4065/mcp.2010.0046.

36. Lee PJ, Mallik R. Cardiovascular effects of radiation therapy: practical approach to radiation therapy-induced heart disease. *Cardiol Rev* 2005;13(2):80–86.
37. Ling LH, Oh JK, Schaff HV, Danielson GK, Mahoney DW, Seward JB, et al. Constrictive pericarditis in the modern era: evolving clinical spectrum and impact on outcome after pericardectomy. *Circulation*. 1999;100:1380–6.
38. Murashita T, Schaff HV, Daly RC, Oh JK, Dearani JA, Stulak JM, et al. Experience with pericardectomy for constrictive pericarditis over eight decades. *Ann Thorac Surg*. 2017;104:742–50.
39. Shannon V, Nates J, Price K. Cancer Treatment-Related Lung Injury. *Oncologic Critical Care*. 2019 Jul 9 : 531–556. doi: 10.1007/978-3-319-74588-6_52
40. Chen MH, Kerkela R, Force T. Mechanisms of cardiac dysfunction associated with tyrosine kinase inhibitor cancer therapeutics. *Circulation* 2008; 118:84–95.
41. Huggins JT, Sahn SA. Drug-induced pleural disease. *Clin Chest Med*. 2004; 25:141–53.
42. Wohlrbab J, Liu M, Anderson E, Kia Noury D. Docetaxel induced pleural effusions [abstract]. *Chest*. 2002;122:94S–5S.
43. Zhao J, Day R, Jin J, Quint L, Williams H, et al. Thoracic radiation-induced pleural effusion and risk factors in patients with lung cancer. *Oncotarget*. 2017 Nov 14; 8(57): 97623–97632. doi: 10.18632/oncotarget.18824
44. Cornelissen R, Senan S, Antonisse IE, Liem H, Tan YK, Rudolphus A, Aerts JG. Bronchiolitis obliterans organizing pneumonia (BOOP) after thoracic radiotherapy for breast carcinoma. *Radiat Oncol*. 2007;2:1–5.
45. Schweitzer V, Juillard G, Bajada C. Radiation recall dermatitis and pneumonitis in a patient treated with paclitaxel. *Cancer*. 1995;76:1069–72.
46. Cottin V, Frogner R, Monnot H, Levy A, DeVuyst P, Cordier JF, Pulmonaires. GdEedRsl-MO. Chronic eosinophilic pneumonia after radiation therapy for breast cancer. *Eur Respir J*. 2004;23:9–13.
47. Coumbe BGT, Groarke JD. Cardiovascular Autonomic Dysfunction in Patients with Cancer. *Current Cardiology Reports* (2018) 20:69. <https://doi.org/10.1007/s11886-018-1010-y>
48. Walsh D, Nelson KA. Autonomic nervous system dysfunction in advanced cancer. *Support Care Cancer*. 2002;10:523–8.
49. Fadul N, Strasser F, Palmer JL, Yusuf SW, Guo Y, Li Z, et al. The association between autonomic dysfunction and survival in male patients with advanced cancer: a preliminary report. *J Pain Symptom Manag*. 2010;39:283–90.
50. Lakoski SG, Jones LW, Krone RJ, Stein PK, Scott JM. Autonomic dysfunction in early breast cancer: incidence, clinical importance, and underlying mechanisms. *Am Heart J*. 2015;170:231–41.
51. Park SB, Goldstein D, Krishnan AV, Lin CS, Friedlander ML, Cassidy J, et al. Chemotherapy-induced peripheral neurotoxicity: a critical analysis. *CA Cancer J Clin*. 2013;63:419–37.
52. Richardson P, Cantwell BM. Autonomic neuropathy after cisplatin based chemotherapy. *BMJ*. 1990;300:1466–7.
53. Nazir HF, AlFutaisi A, Zacharia M, Elshinawy M, Nevada ST, Alrawas A, Khater D, Jaju D and Wali Y. Vincristine-induced neuropathy in pediatric patients with acute lymphoblastic leukemia in Oman: frequent autonomic and more severe cranial nerve involvement. *Pediatr Blood Cancer* 2017;64.
54. Dermitzakis EV, Kimiskidis VK, Lazaridis G, Alexopoulou Z, Timotheadou E, Papanikolaou A, et al. The impact of paclitaxel and carboplatin chemotherapy on the autonomous nervous system of patients with ovarian cancer. *BMC Neurol*. 2016;16:190.
55. Ekholm E, Rantanen V, Bergman M, Vesalainen R, Antila K, Salminen E. Docetaxel and autonomic cardiovascular control in anthracycline treated breast cancer patients. *Anticancer Res*. 2000;20:2045–8.
56. Stratogianni A, Tosch M, Schlemmer H, Weis J, Katona I, Isenmann S, et al. Bortezomib-induced severe autonomic neuropathy. *Clin Auton Res*. 2012;22:199–202.

57. Hoca A, Yildiz M, Ozyigit G. Evaluation of the effects of mediastinal radiation therapy on autonomic nervous system. *Med Oncol* (2012) 29:3581–3586. doi:10.1007/s12032-012-0237-5.
58. Sharabi Y, Dendi R, Holmes C, Goldstein DS. Baroreflex failure as a late sequela of neck irradiation. *Hypertension*. 2003;42:110–6.
59. Adams MJ, Lipsitz SR, Colan SD, Tarbell NJ, Treves ST, Diller L, et al. Cardiovascular status in long-term survivors of Hodgkin's disease treated with chest radiotherapy. *J Clin Oncol*. 2004;22: 3139–48.
60. Ness KK, Armstrong GT. Screening for cardiac autonomic dysfunction among Hodgkin lymphoma survivors treated with thoracic radiation. *J Am Coll Cardiol* 2015;65:584–585.
61. Wolf S, Barton D, Kottschade L, Grothey A, Loprinzi C. Chemotherapy-induced peripheral neuropathy: prevention and treatment strategies. *Eur J Cancer*. 2008;44:1507–15.
62. Scott JM, Jones LW, Hornsby WE, Koelwyn GJ, Khouri MG, Joy AA, et al. Cancer therapy-induced autonomic dysfunction in early breast cancer: implications for aerobic exercise training. *Int J Cardiol*. 2014;171:e50–1.
63. Chatterjee NA, Singh JP. Novel interventional therapies to modulate the autonomic tone in heart failure. *JACC Heart Fail*. 2015;3: 786–802.