

Bölüm 14

MEZOTELYOMA TEDAVİSİNDE İMMÜNOTERAPİNİN YERİ

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GİRİŞ

Malign mezotelyoma, plevra, periton, perikard veya tunika vajinalis'ten gelişebilen, mezotel hücrelerinden köken alan mezotelyal örtünün nadir görülen bir tümördür⁽¹⁾. Tüm dünyada insidansı milyonda 1-2 olup ülkemizde sıklığı yılda 500 vaka civarındadır.

En sık görülen tip plevral mezotelyoma (% 81) olup ayrıca periton (% 8), perikardiyum ve tunica vaginalis testis gibi diğer bölgelerde de görülebilmektedir^(2,3). Mezotelyoma vakalarının çoğunluğu ileri evrelerde karşımıza çıkmakta olup, tedavisi zor olan bir tümördür. Medyan genel sağkalım plevral mezotelyoma hastalarında yaklaşık 1 yıldır ve 5 yıllık genel sağkalım oranları yaklaşık % 10'dur; tedavi ile kür son derece nadirdir⁽⁴⁾.

Mezotelyoma da en önemli risk faktörü asbest maruziyetidir. Asbest maruziyetinden 20-40 yıl sonra ortaya çıkmakta olup, yaşlı erkeklerde daha sıktır. Çoğu mezotelyoma asbest maruziyeti ile bağlantılı olmasına rağmen, araştırmacı raporları iyonize radyasyonun da (Hodgkin lenfoma için mantle radyasyon ile tedavi edilen hastalarda olduğu gibi) mezotelyomaya neden olabileceğini göstermektedir⁽⁵⁾. Ayrıca erionitin (çakıl yollarda bulunabilen bir mineral) mezotelyoma ile ilişkili olduğu gösterilmiştir. Genetik faktörlerde mezotelyoma gelişiminde rol oynayabilir, nadiren familial BRCA1 ile ilişkili protein-1 (BAP1) geninde germline mutasyonu taşırlar. Sigara içmek ise, mezotelyoma için bir risk faktörü değildir^(6,7,8,9).

Mezotelyoma, sarkomatoid, epiteloid ve mikst olmak üzere üç alt histolojik tipte olabilir. Vakaların çoğu epiteloid tipte olup sarkomatoid ve mikst tipten daha iyi prognoza sahiptir⁽¹⁰⁾.

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KAYNAKÇA

1. Robinson BWS, Musk AW, Lake RA. Malignant mesothelioma. *Lancet* 2005; 366: 397-08.
2. Carteni G, Manegold C, Garcia GM, et al. Malignant peritoneal mesothelioma-Results from the International Expanded Access Program using pemetrexed alone or in combination with a platinum agent. *Lung Cancer* 2009;64:211-218.
3. Mirarabshahii P, Pillai K, Chua TC, et al. Diffuse malignant peritoneal mesothelioma--an update on treatment. *Cancer Treat Rev* 2012;38:605-612.
4. Mazurek JM, Syamlal G, Wood JM, et al. Malignant mesothelioma mortality - United States, 1999-2015. *MMWR Morb Mortal Wkly Rep* 2017;66:214-218.
5. Scherpereel A, Astoul P, Baas P, et al. Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for the management of malignant pleural mesothelioma. *Eur Respir J* 2010;35:479-495.
6. Carbone M, Kanodia S, Chao A, et al. Consensus report of the 2015 Weinman International Conference on Mesothelioma. *J Thorac Oncol* 2016;11:1246-1262.
7. Van Gosen BS, Blitz TA, Plumlee GS, et al. Geologic occurrences of erionite in the United States: an emerging national public health concern for respiratory disease. *Environ Geochem Health* 2013;35:419-430.
8. Carbone M, Baris YI, Bertino P, et al. Erionite exposure in North Dakota and Turkish villages with mesothelioma. *Proc Natl Acad Sci U S A* 2011;108:13618-13623.
9. Testa JR, Cheung M, Pei J, et al. Germline BAP1 mutations predispose to malignant mesothelioma. *Nat Genet* 2011;43:1022-1025.
10. 4. Tsao AS, Wistuba I, Roth JA, Kindler HL. Malignant pleural mesothelioma. *J Clin Oncol* 2009;27:2081-2090.
11. Dyer DS, Mohammed TL, Kirsch J, et al. ACR appropriateness Criteria(R) chronic dyspnea: suspected pulmonary origin. *J Thorac Imaging* 2013;28:W64-66. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23846109>.
12. Gadgeel S, Pass H. Malignant mesothelioma. *Commun Oncol* 2006;3:215-224. Available at: 69.
13. Bacchus L, Shah RD, Chung JH, et al. ACR Appropriateness Criteria Review ACR Appropriateness Criteria(R) Occupational Lung Diseases. *J Thorac Imaging* 2016;31:W1-3
13. van Zandwijk N, Clarke C, Henderson D, et al. Guidelines for the diagnosis and treatment of malignant pleural mesothelioma. *J Thorac Dis* 2013;5:E254-307.
14. Husain AN, Colby TV, Ordonez NG, et al. Guidelines for pathologic diagnosis of malignant mesothelioma: 2017 update of the consensus statement from the International Mesothelioma Interest Group. *Arch Pathol Lab Med* 2018;142:89-108.
15. Husain AN, Colby T, Ordonez N, et al. Guidelines for pathologic diagnosis of malignant mesothelioma: 2012 update of the consensus statement from the International Mesothelioma Interest Group. *Arch Pathol Lab Med* 2013;137:647-667.
16. De Paoli L, Quaia E, Poillucci G, et al. Imaging characteristics of pleural tumours. *Insights Imaging* 2015;6:729-740.
17. Grossebner MW, Arifi AA, Goddard M, Ritchie AJ. Mesothelioma--VATS biopsy and lung mobilization improves diagnosis and palliation. *Eur J Cardiothorac Surg* 1999;16:619-623.
18. Bonomi M, De Filippis C, Lopci E, et al. Clinical staging of malignant pleural mesothelioma: current perspectives. *Lung Cancer (Auckl)* 2017;8:127-139.
19. Frick AE, Nackaerts K, Moons J, et al. Combined modality treatment for malignant pleural mesothelioma: a single-centre long-term survival analysis using extrapleural pneumonectomy. *Eur J Cardiothorac Surg* 2018.
20. Sugarbaker DJ, Flores RM, Jaklitsch MT, et al. Resection margins, extrapleural nodal status, and cell type determine postoperative long-term survival in trimodality therapy of malignant pleural mesothelioma: results in 183 patients. *J Thorac Cardiovasc Surg* 1999;117:54-63.
21. Baldini EH. Radiation therapy options for malignant pleural mesothelioma. *Semin Thorac Cardiovasc Surg* 2009;21:159-163.
22. Aelony Y, Yao JF. Prolonged survival after talc poudrage for malignant pleural mesothelioma: case series. *Respirology* 2005;10:649-655.

23. Bolukbas S, Eberlein M, Fisseler-Eckhoff A, Schirren J. Radical pleurectomy and chemoradiation for malignant pleural mesothelioma: the outcome of incomplete resections. *Lung Cancer* 2013;81:241-246.
24. Rice D, Rusch V, Pass H, et al. Recommendations for uniform definitions of surgical techniques for malignant pleural mesothelioma: a consensus report of the international association for the study of lung cancer international staging committee and the international mesothelioma interest group. *J Thorac Oncol* 2011;6:1304-1312.
25. Maziak DE, Gagliardi A, Haynes AE, et al. Surgical management of malignant pleural mesothelioma: a systematic review and evidence summary. *Lung Cancer* 2005;48:157-169.
26. Friedberg JS. The state of the art in the technical performance of lung-sparing operations for malignant pleural mesothelioma. *Semin Thorac Cardiovasc Surg* 2013;25:125-143.
27. Kapeles M, Gensheimer MF, Mart DA, et al. Trimodality treatment of malignant pleural mesothelioma: an institutional review. *Am J Clin Oncol* 2018;41:30-35.
28. Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol* 2003;21:2636-2644.
29. Krug LM. An overview of chemotherapy for mesothelioma. *Hematol Oncol Clin North Am* 2005;19:1117-1136.
30. Zalcman G, Mazieres J, Margery J, et al. Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *Lancet* 2016;387:1405-1414.
31. Katirtzoglou N, Gkiozos I, Makrilia N, et al. Carboplatin plus pemetrexed as first-line treatment of patients with malignant pleural mesothelioma: a phase II study. *Clin Lung Cancer* 2010;11:30-35.
32. van Haarst JMW, Baas P, Manegold C, et al. Multicentre phase II study of gemcitabine and cisplatin in malignant pleural mesothelioma. *Br J Cancer* 2002;86:342-345.
33. Scagliotti GV, Shin D-M, Kindler HL, et al. Phase II study of pemetrexed with and without folic acid and vitamin B12 as front-line therapy in malignant pleural mesothelioma. *J Clin Oncol*.
34. Price A. What is the role of radiotherapy in malignant pleural mesothelioma? *Oncologist* 2011;16:359-365.
35. van Thiel ER, Surmont VF, van Meerbeeck JP. Malignant pleural mesothelioma: when is radiation therapy indicated? *Expert Rev Anticancer Ther* 2011;11:551-560.
36. Ceresoli GL, Zucali PA, Gianoncelli L, et al. Second-line treatment for malignant pleural mesothelioma. *Cancer Treat Rev* 2010;36:24-32.
37. Horn L, Spigel DR, Vokes EE, et al. Nivolumab versus docetaxel in previously treated patients with advanced non small cell lung cancer: two year outcomes from two randomized, open label, phase III trials (CheckMate 017 and CheckMate 057). *J Clin Oncol* 2017;35:3924-3933.
38. Scherpereel A, Mazieres J, Greillier L, et al. Nivolumab or nivolumab plus ipilimumab in patients with relapsed malignant pleural mesothelioma (IFCT-1501 MAPS2): a multicentre, open-label, randomised, non-comparative, phase 2 trial. *Lancet Oncol* 2019;20:239-253.
39. Disselhorst MJ, Quispel-Janssen J, Lalezari F, et al. Ipilimumab and nivolumab in the treatment of recurrent malignant pleural mesothelioma (INITIATE): results of a prospective, single-arm, phase 2 trial. *Lancet Respir Med* 2019;7:260-270.
40. Alley EW, Lopez J, Santoro A, et al. OA13.03 Long-term overall survival for patients with malignant pleural mesothelioma on pembrolizumab enrolled in KEYNOTE-028 [abstract]. *J Thorac Oncol* 2017;12:S294.
41. Kindler HL, Ismaila N, Armato SG, 3rd, et al. Treatment of malignant pleural mesothelioma: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2018;JCO2017766394.
42. Metaxas Y, Rivalland G, Mauti LA, et al. Pembrolizumab as palliative immunotherapy in malignant pleural mesothelioma. *J Thorac Oncol* 2018;13:1784-1791.
43. Tano ZE, Chintala NK, Li X et al. Novel immunotherapy clinical trials in malignant pleural mesothelioma. *Ann Transl Med*. 2017 Jun;5(11):245.