Bölüm
11

DESMOİD TÜMÖRLERİN SİSTEMİK TEDAVİSİ

Gülhan İPEK DENİZ[13]

GİRİŞ

Desmoid tümör; aynı zamanda agresif fibromatozis olarak tanımlanan bening, yavaş büyüyen lokal agresif davranış gösteren ve bilinen metastaz/dediferansiyasyon potansiyeli çok düşük olan fibroblastik hücre neoplazmıdır. Desmoid tümör oluşumunda endokrin nedenler öne sürülmüştür. Östrojenin fibroblastların proliferatif aktivitesini artırdığı gösterilmiştir (1). Spesifik olarak, bu tümörler, iyi sınırlı, lokal olarak invaziv ve farklılaşmış fibröz dokunun agresif bir fibroblastik proliferasyonudur. Desmoid tümörler nadir görülür, en sık genç kadın hastaları etkiler ve genellikle ölümcül değildir. Bununla birlikte tümörün yerleşim yerine bağlı olarak yaptığı lokal invazyona bağlı önemli anatomik yapı ve/veya organ disfonksiyonuna yol açarak morbidite (ağrı, hareket kaybı, bağırsak tıkanıklığı ve diğer iç organlarda tutuluma bağlı olarak önemli morbiditeye neden olabilir) ve fetal seyre neden olabilirler. Bu tümörleri sarkom olarak sınıflandırmak için sarkom benzeri histopatolojik özellikler göstermese de, desmoid tümörler eksizyondan sonra lokal olarak nüksetme eğilimleri yüksek olduğu için genellikle düşük dereceli sarkomlar olarak sınıflandırılır.

Her ne kadar desmoid tümörler herhangi bir iskelet kasında ortaya çıkabilse de, en sık karın ön duvarı ve omuz kuşağında gelişir. Retroperitoneal yerleşimli desmoid tümörler, ailesel polipozis koli ve Gardner sendromunda abdominal cerrahi sonrası daha sık görülür (2).

Metastaz yapma potansiyellerinin nadiren olmasından dolayı; geleneksel olarak ana tedaviyi lokal kontrolü sağlamak için cerrahi ve radyoterapi tedavileri oluşturmaktadır. Ancak tam cerrahi rezeksiyona rağmen artmış lokal tekrarlama riski mevcuttur. Bu risk pozitif cerrahi sınırlı olgularda daha yüksektir (3). Tek-

[13] Uzman Doktor, Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi, glhnipek@gmail.com

larının başarısız olduğu desmoid tümörlü hastalarda sistemik tedaviler düşünülmelidir.

Anahtar kelimeler: Desmoid tümör; İnflamasyon; Östrojen; Sistemik tedavi.

KAYNAKLAR

1. Dhingra, K. Antiestrogens—tamoxifen, SERMs and beyond. Invest New Drugs. 1999;17(3):285-311.
2. Raynham, WH, Louw, JH. Desmoid tumours in familial polyposis of the colon. S Afr J Surg. 197;9(3):133-40.
3. Buitendijk ,S, Van de Ven, CP, Dumans, TG, et al. Pediatric aggressive fibromatosis: a retrospective analysis of 13 patients and review of literature. Cancer. 2005;104(5):1090-9.
4. El-Haddad, M, El-Sebaie, M, Ahmad, R, et al. Treatment of aggressive fibromatosis: the experience of a single institution. Clin Oncol (R Coll Radiol). 2009;21(10)775-80.
5. Sparber-Sauer, M, Seitz, G, Von Kalle, T, et al. Systemic therapy of aggressive fibromatosis in children and adolescents: Report of the Cooperative Weichteilsarkom Studiengruppe (CWS). Pediatr Blood Cancer. 2018;65(5):e26943. https://doi.org/10.1002/pbc.26943
6. *Mercier, KA, Al-Jazrawe, M, Poon, R, et al. A Metabolomics Pilot Study on Desmoid Tumors and Novel Drug Candidates. Sci Rep. 2018;8(1):584.*
7. *Oudot, C, Defachelles, AS, Minard-Colin, V, et al. Desmoid tumors in children: current strategy. Bull Cancer. 2013;100(5):518-28.*
8. *Chugh, R, Wathen, JK, Patel, SR, et al. Efficacy of imatinib in aggressive fibromatosis: Results of a phase II multicenter Sarcoma Alliance for Research through Collaboration (SARC) trial. Clin Cancer Res. 2010;16(19):4884-91.*
9. Penel, N, Le Cesne, A, Bui, BN, et al. Imatinib for progressive and recurrent aggressive fibromatosis (desmoid tumors): an FNCLCC/French Sarcoma Group phase II trial with a long-term follow-up. Ann Oncol. 2011;22(2):452-7.
10. Kasper, B, Gruenwald, V, Reichardt, P, et al. Imatinib induces sustained progression arrest in RECIST progressive desmoid tumours: Final results of a phase II study of the German Interdisciplinary Sarcoma Group (GISG). Eur J Cancer. 2017;76:60-67.
11. Gounder, MM, Lefkowitz, RA, Keohan, ML, et al. Activity of Sorafenib against desmoid tumor/deep fibromatosis. Clin Cancer Res. 2011;17:4082- 90.
12. Gounder, MM, Mahoney, MR, Van Tine, BA, et al. Sorafenib for Advanced and Refractory Desmoid Tumors. N Engl J Med. 2018;379(25):2417-28.
13. Szucs, Z, Messiou, C, Wong, HH, et al. Pazopanib, a promising option for the treatment of aggressive fibromatosis. Anticancer Drugs. 2017;28(4):421-6.
14. Bulut, G, Ozluk, A, Erdogan, AP, et al. Pazopanib: a novel treatment option for aggressive fibromatosis. Clin Sarcoma Res. 2016;6:22. http://doi.org/10.1186/s13569-016-0061-3
15. Toulmonde, M, Ray-Coquard, IL, Pulido, M, et al. DESMOPAZ pazopanib (PZ) versus IV methotrexate/vinblastine (MV) in adult patients with progressive desmoid tumors (DT) a randomized phase II study from the French Sarcoma Group (abstract). J Clin Oncol 36, 2018;11501-11501.
16. Tsukada, K, Church, JM, Jagelman, DG, et al. Noncytotoxic drug therapy for intra-abdominal desmoid tumor in patients with familial adenomatous polyposis. Dis Colon Rectum. 1992;35(1):29-33.
17. Waddell, WR, Kirsch, WM. Testolactone, sulindac, warfarin, and vitamin K1 for unresectable desmoid tumors. Am J Surg. 1991;161(4):416-21.

18. Klein, WA, Miller, HH, Anderson M, et al. The use of indomethacin, sulindac, and tamoxifen for the treatment of desmoid tumors associated with familial polyposis. Cancer. 1987;60(12):2863-8.
19. Dominguez-Malagon, HR, Alfeiran-Ruiz, A, Chavarria-Xicotencatl, P, et al. Clinical and cellular effects of colchicine in fibromatosis. Cancer. 1992;69(10):2478-83.
20. Nishida, Y, Tsukushi, S, Shido, Y, et al. Transition of treatment for patients with extra-abdominal desmoid tumors: nagoya university modality. Cancers (Basel). 2012;4(1):88-99.
21. Kinzbrunner, B, Ritter, S, Domingo, J, et al. Remission of rapidly growing desmoid tumors after tamoxifen therapy. Cancer. 1983;52(12):2201-4.
22. Hansmann, A, Adolph, C, Vogel, T, et al. High-dose tamoxifen and sulindac as first-line treatment for desmoid tumors. Cancer. 2004;100(3):612-20.
23. Janinis, J, Patriki, M, Vini, L, et al. The pharmacological treatment of aggressive fibromatosis: a systematic review. Ann Oncol. 2003;14(2):181-90.
24. Sportiello, DJ, Hoogerland, DL. A recurrent pelvic desmoid tumor successfully treated with tamoxifen. Cancer. 1991;67(5):1443-6.
25. Rock, MG, Pritchard, DJ, Reiman, HM, et al. Extra-abdominal desmoid tumors. J Bone Joint Surg Am. 1984;66(9):1369-74.
26. Brooks, MD, Ebbs, SR, Colletta, AA, Desmoid tumours treated with triphenylethylenes. Eur J Cancer. 1992;28A(6-7):1014-8.
27. Fiore, M, Colombo, C, Radaelli, S, et al. Hormonal manipulation with toremifene in sporadic desmoid-type fibromatosis. Eur J Cancer. 2015;51(18):2800-7.
28. Tonelli, F, Ficari, F, Valanzano, R, et al. Treatment of desmoids and mesenteric fibromatosis in familial adenomatous polyposis with raloxifene. Tumori. 2003;89(4):391-6.
29. Wilcken, N, Tattersall, MH. Endocrine therapy for desmoid tumors. Cancer. 1991;68(6):1384-8.
30. Lanari, A. Effect of progesterone on desmoid tumors (aggressive fibromatosis). N Engl J Med. 1983;309(24):1523. http://doi.org/10.1056/NEJM198312153092418
31. Bauernhofer, T, Stöger, H, Schmid, M, et al. Sequential treatment of recurrent mesenteric desmoid tumor. Cancer. 1996;77(6):1061-5.
32. Izes, JK, Zinman, LN, Larsen, CR. Regression of large pelvic desmoid tumor by tamoxifen and sulindac. Urology. 1996;47(5):756-9.
33. Lackner, H, Urban, C, Kerbl, R, et al. Noncytotoxic drug therapy in children with unresectable desmoid tumors. Cancer. 1997;80(2):334-40.
34. Gabbert, HE, Gerharz, CD, Biesalski, HK, et al. Terminal differentiation and growth inhibition of a rat rhabdomyosarcoma cell line (BA- HAN-1C) *in vitro* after exposure to retinoic acid. Cancer Res. 1988; 48: 5264-9.
35. Balkwill, FR, Bokhonko, AI. Differential effects of pure human alpha and gamma interferons on fibroblast cell growth and the cell cycle. Exp Cell Res. 1984;55:190-7.
36. Acker, JC, Bossen, EH, Halperin, EC. The management of desmoid tumours. Int J Radiat Oncol Phys. 1993;26:851-8.
37. Geurs, F, Kok, TC. Regression of a great abdominal desmoid tumor by interferon-α. J Clin Gastrenterol. 1993;16:264-5.
38. Fernberg, JO, Brosjo, O, Larsson, O, et al. Interferon-induced remission in aggressive fibromatosis of the lower extremity. Acta Oncol. 1999;38: 971-2.
39. Leithner, A, Schnack, B, Katterschafka, T, et al. Treatment of extra- abdominal desmoid tumors with interferon-alpha with or without tretinoin. J Surg Oncol. 2000;73:21-5.
40. Patel, SR, Benjamin, RS. Desmoid tumors respond to chemotherapy: defying the dogma in oncology. J Clin Oncol. 2006;24(1):11-2.
41. Stein, R. Chemotherapeutic response in fibromatosis of the neck. J Pediatr. 1977;90:482–3.
42. Goepfert, H, Cangir, A, Ayala, AG, et al. Chemotherapy of locally aggres- sive head and neck tumors in the pediatric age group. Am J Surg. 1982;144:437–44.

43. Raney, B, Evans, A, Granowetter, L, et al. Nonsurgical management of children with recurrent or unresectable fibromatosis. Pediatrics. 1987;79: 394-8.
44. Delepine, N, Delepine, G, Desbois, JC, et al. Objective response of desmoid fibroma to chemotherapy. Biomed Pharmacother. 1987;41:146-8.
45. Gansar, GF, Krementz, ET. Desmoid tumors: experience with new modes of therapy. South Med J. 1988;81:794-6.
46. Tsukada, K, Church, JM, Jagelman, DG, et al. Systemic cytotoxic chemo- therapy and radiation therapy for desmoid in familial adenomatous polyposis. Dis Colon . 1991;34:1090-2.
47. Patel, SR, Evans, HL, Benjamin, RS. Combination chemotherapy in adult desmoid tumors. Cancer. 1993;72:3244-7.
48. Schnitzler, M, Cohen, Z, Blackstein, M, et al. Chemotherapy for desmoid tumours in association with familial adenomatous polyposis. Dis Colon Rectum. 1997;40:798-801.
49. Azzarelli, A, Casali, P, Fissi, S, et al. Effective control of advanced aggressive fibromatosis with chemotherapy. Eight years experience with methotrexate and vinblastine in 27 patients. Proceedings Fourth Annual Meeting Connective Tissue Oncology Society, 1998, Milan, Italy (pp.).
50. Okuno, SH, Edmonson, JH. Combination chemotherapy for desmoid tumors. Cancer. 2003;97(4):1134-5.
51. Weiss, AJ, Horowitz, S, Lackman, RD. Therapy of desmoid tumors and fibromatosis using vinorelbine. Am J Clin Oncol. 1999;22:193-5.
52. Reich, S, Overberg-Schmidt, US, Buhrer, C, et al. Low-dose chemotherapy with vinblastine and methotrexate in childhood desmoid tumors. J Clin Oncol. 1999;17:1086. http://doi.org/10.1200/JCO.1999.17.3.1086
53. Lev-Chelouche, D, Abu-Abeid, Nakache, R, et al. Limb desmoid tumors: a possible role for isolated limb perfusion with tumor necrosis factor-alpha and melphalan. Surgery. 1999;126:963-7.
54. Klaase, JM, Kroon, BB, Benckhuijsen, C, et al. Results of regional isolation perfusion with cytostatics in patients with soft tissue tumors of the extremities. Cancer. 1989;64:616-21.
55. Seiter, K, Kemeny, N. Successful treatment of a desmoid tumor with doxorubicin. Cancer. 1993;71:2242-4.
56. Lynch, HT, Fitzgibbons, R, Chong, S, et al. Use of doxorubicin and dacarbazine for the management of unresectable intra-abdominal desmoid tumors in Gardner's syndrome. Dis Colon Rectum. 1994;37:260-7.
57. Rao, BN, Horowitz, ME, Parham, DM, et al. Challenges in the treatment of childhood fibromatosis. Arch Surg. 1987;122:1296-8.
58. De Camargo, VP, Keohan, ML, D'Adamo, DR, et al. Clinical outcomes of systemic therapy for patients with deep fibromatosis (desmoid tumor). Cancer. 2010;116(9):2258-65.
59. Wehl, G, Rossler, J, Otten, JE, et al. Response of progressive fibromatosis to therapy with liposomal doxorubicin. Onkologie. 2004;27(6):552-6.
60. Constantinidou, A, Jones, RL, Scurr, M, et al. Pegylated liposomal doxorubicin, an effective, well-tolerated treatment for refractory aggressive fibromatosis. Eur J Cancer. 2009;45(17):2930-4.
61. Constantinidou, A, Jones, RL, Scurr, M, Advanced aggressive fibromatosis: Effective palliation with chemotherapy. Acta Oncol. 2011;50(3):455-61.
62. Bertagnolli, MM, Morgan, JA, Fletcher, CD, et al. Multimodality treatment of mesenteric desmoid tumours. Eur J Cancer. 2008;44(16):2404-10.
63. Gega, M, Yanagi, H, Yoshikawa, R, et al. Successful chemotherapeutic modality of doxorubicin plus dacarbazine for the treatment of desmoid tumors in association with familial adenomatous polyposis. J Clin Oncol. 2006;24(1):102-5.
64. Garbay, D, Le Cesne, A, Penel, N, et al. Chemotherapy in patients with desmoid tumors: a study from the French Sarcoma Group (FSG). Ann Oncol. 2012;23(1):182-6.

65. Weiss, AJ, Lackman, RD. Low-dose chemotherapy of desmoid tumors. Cancer. 1989;64(6):1192-4.
66. Azzarelli, A, Gronchi, A, Bertulli, R, et al. Low-dose chemotherapy with methotrexate and vinblastine for patients with advanced aggressive fibromatosis. Cancer. 2001;92(5):1259-64.
67. Skapek, SX, Ferguson, WS, Granowetter, L, et al. Vinblastine and methotrexate for desmoid fibromatosis in children: results of a Pediatric Oncology Group Phase II Trial. J Clin Oncol. 2007;25(5):501-6.
68. Skapek, SX, Hawk, BJ, Hoffer, FA, et al. Combination chemotherapy using vinblastine and methotrexate for the treatment of progressive desmoid tumor in children. J Clin Oncol. 1998;16(9):3021-7.
69. Dileo, P, Sala, P, Piovesan, C, et al. Efficacy of methotrexate + vinblastine in intra-abdominal desmoid (mesenteric aggressive fibromatosis): retrospective analysis of 29 patients from a single institution (abstract). J Clin Oncol. 2008;26;567-9.
70. Palassini, E, Frezza, AM, Mariani, et al. Long-term Efficacy of Methotrexate Plus Vinblastine/Vinorelbine in a Large Series of Patients Affected by Desmoid-Type Fibromatosis. Cancer. J. 2017;23(2):86-91.
71. Sheth, PJ, Del Moral, S, Wilky, BA, et al. Desmoid fibromatosis: MRI features of response to systemic therapy. Skeletal Radiol. 2016;45(10):1365-73.
72. Braschi-Amirfarzan, M, Keraliya, AR, Krajewski, KM, et al. Role of Imaging in Management of Desmoid-type Fibromatosis: A Primer for Radiologists. Radiographics. 2016;36(3):767-82.