

GERM HÜCRELİ OVER TÜMÖRLERİNDE SİSTEMİK TEDAVİ

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GİRİŞ

Germ hücreli over tümörleri (GHOT) primordiyal germ hücrelerinden köken alan benign veya malign karakter gösterebilen over tümörleridir. Bu neoplazmlar over kaynaklı tümörlerin yaklaşık % 20-25 ini oluşturmakla beraber malign over tümörlerinin sadece yaklaşık yüzde beşlik kısmı germ hücre kökenli malign over tümörüdür (1-3). GHOT 10 ve 30 yaş arası genç bayanlarda görülür ve bu yaş grubundaki over kaynaklı tümörlerin yüzde 70 inden sorumludur (4).

Histopatoloji : GHOT yaygın olarak embriyo benzeri dokulardan köken alan neoplazmlar (teratoma ve alttipleri ile disgerminom) ve ekstra embriyonik fötal dokulardan (plesenta benzeri) köken alan tümörler ile bu iki dokunun karışımından oluşan mikst tip neoplazmlar olmak üzere kabaca üç sınıftan oluşmaktadır.

Teratomlar : dermoid kist olarak da adlandırılan benign kistik matür teratom en yaygın görülen GHOT olmakla beraber immatür teratom daha az görülen ve malign karakterli teratom alt grubudur.

Disgerminom : erkeklerde görülen seminomların bayanlardaki karşılığıdır ve immatür germ hücrelerinden oluşur.

Yolk sak tümörü: primitif plesentadan köken alan epitelyal karakterli malign neoplazmdir.

Mikst germ hücreli tümör : teratom ile yolk sak , disgerminom ve/veya embriyonel karsinomun kombinasyonundan oluşurlar.

Nadir GHOT : pür embriyonel karsinom , nongestasyonel koryokarsinom ve pür poliembriyomlar bu sınıfa dahildir.

Malign GHOT nin yaklaşık yüzde 90 lık kısmını teratom , disgerminom , yolk sak tümörü ve mikst tip germ hücreli over tümörleri oluşturmaktadır (2,3). Pür

etoposid uygulandığında lösemi oranı % 5 civarına kadar yükseldiği belirlenmiştir (45,46).

Küçük serilere dayanan analizler sonucunda GHOT nedeni ile tanı alıp tedavi görmüş hastalarda hipertansiyon , hipercolesterolemİ ve saç dökülmesinde artışlar olduğu tespit edilmiştir.

KAYNAKLAR

1. Sagae S, Kudo R. Surgery for germ cell tumors. Semin Surg Oncol 2000; 19:76.
2. Talerman A. Germ cell tumours of the ovary. In: Blaustein's Pathology of the Female Genital Tract, Kurman RJ (Ed), Springer Verlag, New York 1994. p.849.
3. Tewari K, Cappuccini F, Disaia PJ, et al. Malignant germ cell tumors of the ovary. Obstet Gynecol 2000; 95:128.
4. Zalel Y, Piura B, Elchalal U, et al. Diagnosis and management of malignant germ cell ovarian tumors in young females. Int J Gynaecol Obstet 1996; 55:1.
5. Smith HO, Berwick M, Verschraegen CF, et al. Incidence and survival rates for female malignant germ cell tumors. Obstet Gynecol 2006; 107:1075.
6. Pectasides D, Pectasides E, Kassanos D. Germ cell tumors of the ovary. Cancer Treat Rev 2008; 34:427.
7. Ihara T, Ohama K, Satoh H, et al. Histologic grade and karyotype of immature teratoma of the ovary. Cancer 1984; 54:2988.
8. Mann JR, Raafat F, Robinson K, et al. The United Kingdom Children's Cancer Study Group's second germ cell tumor study: carboplatin, etoposide, and bleomycin are effective treatment for children with malignant extracranial germ cell tumors, with acceptable toxicity. J Clin Oncol 2000; 18:3809.
9. Kumar S, Shah JP, Bryant CS, et al. The prevalence and prognostic impact of lymph node metastasis in malignant germ cell tumors of the ovary. Gynecol Oncol 2008; 110:125.
10. Slaton RE, Park RC, Silverberg SG, et al. Vincristine, dactinomycin, and cyclophosphamide in the treatment of malignant germ cell tumors of the ovary. A Gynecologic Oncology Group Study (a final report). Cancer 1985; 56:243.
11. Williams SD, Blessing JA, Moore DH, et al. Cisplatin, vinblastine, and bleomycin in advanced and recurrent ovarian germ-cell tumors. A trial of the Gynecologic Oncology Group. Ann Intern Med 1989; 111:22.
12. Bafna UD, Umadevi K, Kumaran C, et al. Germ cell tumors of the ovary: is there a role for aggressive cytoreductive surgery for nondysgerminomatous tumors? Int J Gynecol Cancer 2001; 11:300.
13. Gershenson DM, Morris M, Cangir A, et al. Treatment of malignant germ cell tumors of the ovary with bleomycin, etoposide, and cisplatin. J Clin Oncol 1990; 8:715.
14. Dimopoulos MA, Papadopoulou M, Andreopoulou E, et al. Favorable outcome of ovarian germ cell malignancies treated with cisplatin or carboplatin-based chemotherapy: a Hellenic Cooperative Oncology Group study. Gynecol Oncol 1998; 70:70.
15. Mann JR, Raafat F, Robinson K, et al. The United Kingdom Children's Cancer Study Group's second germ cell tumor study: carboplatin, etoposide, and bleomycin are effective treatment for children with malignant extracranial germ cell tumors, with acceptable toxicity. J Clin Oncol 2000; 18:3809.
16. Williams SD. Ovarian germ cell tumors: an update. Semin Oncol 1998; 25:407.
17. Segelov E, Campbell J, Ng M, et al. Cisplatin-based chemotherapy for ovarian germ cell malignancies: the Australian experience. J Clin Oncol 1994; 12:378.
18. Rescorla F, Billmire D, Vinocur C, et al. The effect of neoadjuvant chemotherapy and surgery in children with malignant germ cell tumors of the genital region: a pediatric intergroup trial. J Pediatr Surg 2003; 38:910.

19. Talukdar S, Kumar S, Bhatla N, et al. Neo-adjuvant chemotherapy in the treatment of advanced malignant germ cell tumors of ovary. *Gynecol Oncol* 2014; 132:28.
20. Williams S, Blessing JA, Liao SY, et al. Adjuvant therapy of ovarian germ cell tumors with cisplatin, etoposide, and bleomycin: a trial of the Gynecologic Oncology Group. *J Clin Oncol* 1994; 12:701.
21. Culin S, Lhomme C, Kattan J, et al. Cisplatin-based chemotherapy in the management of germ cell tumors of the ovary: The Institut Gustave Roussy Experience. *Gynecol Oncol* 1997; 64:160.
22. Gershenson DM, Kavanagh JJ, Copeland LJ, et al. Treatment of malignant nondysgerminomatous germ cell tumors of the ovary with vinblastine, bleomycin, and cisplatin. *Cancer* 1986; 57:1731.
23. Carlson RW, Sikic BI, Turbow MM, Ballon SC. Combination cisplatin, vinblastine, and bleomycin chemotherapy (PVB) for malignant germ-cell tumors of the ovary. *J Clin Oncol* 1983; 1:645.
24. Taylor MH, Depetris AD, Turner AR. Vinblastine, bleomycin, and cisplatin in malignant germ cell tumors of the ovary. *Cancer* 1985; 56:1341.
25. Mayordomo JL, Paz-Ares L, Rivera F, et al. Ovarian and extragonadal malignant germ-cell tumors in females: a single-institution experience with 43 patients. *Ann Oncol* 1994; 5:225.
26. Tewari K, Cappuccini F, Disaia PJ, et al. Malignant germ cell tumors of the ovary. *Obstet Gynecol* 2000; 95:128.
27. Murugaesu N, Schmid P, Dancey G, et al. Malignant ovarian germ cell tumors: identification of novel prognostic markers and long-term outcome after multimodality treatment. *J Clin Oncol* 2006; 24:4862.
28. Rogers PC, Olson TA, Cullen JW, et al. Treatment of children and adolescents with stage II testicular and stages I and II ovarian malignant germ cell tumors: A Pediatric Intergroup Study--Pediatric Oncology Group 9048 and Children's Cancer Group 8891. *J Clin Oncol* 2004; 22:3563.
29. Culin S, Lhomme C, Kattan J, et al. Cisplatin-based chemotherapy in dysgerminoma of the ovary: thirteen-year experience at the Institut Gustave Roussy. *Gynecol Oncol* 1995; 58:344.
30. Williams SD, Kauderer J, Burnett AF, et al. Adjuvant therapy of completely resected dysgerminoma with carboplatin and etoposide: a trial of the Gynecologic Oncology Group. *Gynecol Oncol* 2004; 95:496.
31. Brewer M, Gershenson DM, Herzog CE, et al. Outcome and reproductive function after chemotherapy for ovarian dysgerminoma. *J Clin Oncol* 1999; 17:2670.
32. Park JY, Kim DY, Suh DS, et al. Outcomes of Surgery Alone and Surveillance Strategy in Young Women With Stage I Malignant Ovarian Germ Cell Tumors. *Int J Gynecol Cancer* 2016; 26:859.
33. Stambaugh MD. Ovary. In: Principles and Practice of Radiation Oncology, 4th, Perez CA, Brady LW, Halperin CA, Schmidt-Ullrich RK (Eds), Lippincott, Williams and Wilkins, Philadelphia 1997. p.1948.
34. Gershenson DM, Del Junco G, Copeland LJ, Rutledge FN. Mixed germ cell tumors of the ovary. *Obstet Gynecol* 1984; 64:200.
35. Gershenson DM, Del Junco G, Herson J, Rutledge FN. Endodermal sinus tumor of the ovary: the M. D. Anderson experience. *Obstet Gynecol* 1983; 61:194.
36. Abdul Razak AR, Li L, Bryant A, Diaz-Padilla I. Chemotherapy for malignant germ cell ovarian cancer in adult patients with early stage, advanced and recurrent disease. *Cochrane Database Syst Rev* 2011; :CD007584.
37. Mandanas RA, Saez RA, Epstein RB, et al. Long-term results of autologous marrow transplantation for relapsed or refractory male or female germ cell tumors. *Bone Marrow Transplant* 1998; 21:569.
38. Theodore C, Chevreau C, Yataqhene Y, et al. A phase II multicenter study of oxaliplatin in combination with paclitaxel in poor prognosis patients who failed cisplatin-based chemotherapy for germ-cell tumors. *Ann Oncol* 2008; 19:1465.
39. Li J, Yang W, Wu X. Prognostic factors and role of salvage surgery in chemorefractory ovarian germ cell malignancies: a study in Chinese patients. *Gynecol Oncol* 2007; 105:769.

40. Maltaris T, Boehm D, Dittrich R, et al. Reproduction beyond cancer: a message of hope for young women. *Gynecol Oncol* 2006; 103:1109.
41. Gershenson DM, Miller AM, Champion VL, et al. Reproductive and sexual function after platinum-based chemotherapy in long-term ovarian germ cell tumor survivors: a Gynecologic Oncology Group Study. *J Clin Oncol* 2007; 25:2792.
42. Gordon A, Lipton D, Woodruff JD. Dysgerminoma: a review of 158 cases from the Emil Novak Ovarian Tumor Registry. *Obstet Gynecol* 1981; 58:497.
43. Byrne J, Fears TR, Gail MH, et al. Early menopause in long-term survivors of cancer during adolescence. *Am J Obstet Gynecol* 1992; 166:788.
44. Sklar CA, Mertens AC, Mitby P, et al. Premature menopause in survivors of childhood cancer: a report from the childhood cancer survivor study. *J Natl Cancer Inst* 2006; 98:890.
45. Travis LB, Andersson M, Gospodarowicz M, et al. Treatment-associated leukemia following testicular cancer. *J Natl Cancer Inst* 2000; 92:1165.
46. Pedersen-Bjergaard J, Daugaard G, Hansen SW, et al. Increased risk of myelodysplasia and leukaemia after etoposide, cisplatin, and bleomycin for germ-cell tumours. *Lancet* 1991; 338:359.