

Bölüm 24

OVARİAN SEX CORD-STROMAL TÜMÖRLERE GÜNCEL YAKLAŞIM

Yasin DURMUŞ¹

Malign ovarian sex cord-stromal tümörler tüm over malignitelerinin % 5-8'ini oluşturmaktadır. Sex cord-stromal tümör alt grubu ovarian stroma ve sex cordlar- dan köken alan bir tümör grubunu oluştursa da, histolojik alıtımları kendi içerisinde farklı biyolojik davranış, klinik prezentasyon ve прогноз gösterir. En sık karşılaşılan histolojik tip granuloza hücreli tümörlerdir(1). Tablo 1'de WHO(World Health Organization)'nun ovarian sex cord-stromal tümörler için önerdiği güncel sınıflama sistemi verilmiştir (2).

Tablo 1. Ovarian Sex Cord-Stromal Tümörler İçin WHO 2014 Sınıflandırması

Ovarian Sex Cord-Stromal Tümörler

Saf Stromal Tümörler

- Fibroma
- Selüler fibroma
- Tekoma
- Luteinize tekoma (Sklerozan peritonit ile ilişkili)
- Fibrosarkom
- Sklerozan stromal tümör
- Signet-ring stromal tümör
- Mikrokistik stromal tümör
- Leydig hücreli tümör
- Steroid hücreli tümör
- Steroid hücreli tümör, malign

Saf Sex Cord Tümörler

- Erişkin granuloza hücreli tümör
- Juvenil granuloza hücreli tümör
- Sertoli hücreli tümör
- Anuler tüberller ile birlikte olan sex cord tümör

Mixed Sex Cord-Stromal Tümörler

- Sertoli-leydig hücreli tümörler
- Sex cord-stromal tümörler, başka türlü sınıflandırılamayan

¹ Dr. Yasin Durmuş Etlik Zübeyde Hanım Kadın Hastalıkları Eğitim ve Araştırma Hastanesi
E-posta: dr_yasindurmus@hotmail.com

hastalarda tüm metastatik hastalığın çıkarılmasına yönelik bir cerrahi efor önerilmektedir(1, 18, 35, 45). Brown ve arkadaşları sertoli-leydig hücreli tümörü olan 31 hasta bildirmişler ve 5 hastada lenf nodu diseksiyonu yapmışlardır. Lenf nodu diseksiyonu yapılan bu 5 hastada metastatik lenf nodu izlenmemiştir. Takipte 9 hastada rekürrens olmuş ve bu 9 hastanın hiçbirinde lenf nodlarında rekürren hastalık izlenmemiştir. Yazarlar lenf nodu metastazının nadir olduğunu ve lenfadenektominin bu hastalarda ihmali edilebileceğini bildirmiştir(19). Sonrasında cerrahi evreleme sırasında lenfadenektominin ihmali edilebileceği görüşü başka yayın ve yazarlar tarafından da desteklenmiştir(1, 18).

Sertoli-leydig hücreli tümörlerde adjuvant kemoterapi konusunda bilgiler kısıtlıdır ve retrospektif olgu sunumları ya da küçük hasta serilerine dayanmaktadır. Mevcut veriler doğrultusunda evre 1'de kötü differansiyel tümörlerde veya heterolog eleman varlığında ve evre 2-4'de adjuvant tedavi önerilir(18, 43, 45). Schneider ve arkadaşları 44 hastalık bir sertoli-leydig hücreli tümör serisi yayınlamışlardır. 17 hasta evre 1C'dir. 6 hastada preoperatif rüptür ya da malign asit, 11 hastada intraoperatif rüptür bildirmiştir. İtraoperatif rüptür olan hastaların beşinde rekürrens meydana gelmiş, üçü ölümle sonuçlanmıştır. Preoperatif rüptür olan hastalardan 1 tanesinde rekürrens ve takibinde ölüm meydana gelmiştir. Bu nedenle yazarlar istatistiksel bir kanıt olmamasına rağmen hem intraoperatif rüptür hem preoperatif rüptürü olan hastalar için adjuvant kemoterapi önermişlerdir(37). Postoperatif adjuvant kemoterapide ve rekürren hastalıkta kemoterapi rejimi olarak BEP rejimi önerilmektedir(1, 18, 43).

Young ve Scully'nin 207 hastalık tarihi çalışmásında iyi diferansiyel tümörlerin hiçbirinde klinik malign seyir bildirilmez iken, orta diferansiyel tümörlü hastaların %11'inin, kötü diferansiyel tümörlü hastaların %59'unun ve histolojisinde heterolog eleman içeren hastaların %19'unun klinik olarak malign seyir izlediğini bildirmiştir(38). Sigismundi ve arkadaşlarının 21 hastalık serisinde 5 yıllık sağkalım iyi diferansiyel hastalar için %100, orta ve kötü diferansiyel hastalar için %77.8 , evre 1 hastalar için 92.3% , evre>1 hastalar için ise %33.3 olarak bildirilmiştir.

Referanslar

1. Boussios S, Zarkavelis G, Seraj E, Zerde I, Tatsi K, Pentheroudakis G. Non-epithelial Ovarian Cancer: Elucidating Uncommon Gynaecological Malignancies. Anticancer research. 2016;36(10):5031-42.
2. Horta M, Cunha TM. Sex cord-stromal tumors of the ovary: a comprehensive review and update for radiologists. Diagnostic and interventional radiology (Ankara, Turkey). 2015;21(4):277-86.
3. Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2003;21(6):1180-9.
4. Gittleman AM, Price AP, Coren C, Akhtar M, Donovan V, Katz DS. Juvenile granulosa cell tumor. Clinical imaging. 2003;27(4):221-4.

5. Young RH. Ovarian sex cord-stromal tumours and their mimics. *Pathology*. 2018;50(1):5-15.
6. Jamieson S, Fuller PJ. Management of granulosa cell tumour of the ovary. *Current opinion in oncology*. 2008;20(5):560-4.
7. Shah SP, Kobel M, Senz J, Morin RD, Clarke BA, Wiegand KC, et al. Mutation of FOXL2 in granulosa-cell tumors of the ovary. *The New England journal of medicine*. 2009;360(26):2719-29.
8. Bryk S, Farkkila A, Butzow R, Leminen A, Tapper J, Heikinheimo M, et al. Characteristics and outcome of recurrence in molecularly defined adult-type ovarian granulosa cell tumors. *Gynecologic oncology*. 2016;143(3):571-7.
9. Farkkila A, Haltia UM, Tapper J, McConechy MK, Huntsman DG, Heikinheimo M. Pathogenesis and treatment of adult-type granulosa cell tumor of the ovary. *Annals of medicine*. 2017;49(5):435-47.
10. Kim JA, Chun YK, Moon MH, Lee YH, Cho HC, Lee MS, et al. High-resolution sonographic findings of ovarian granulosa cell tumors: correlation with pathologic findings. *Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine*. 2010;29(2):187-93.
11. van Meurs HS, Bleeker MC, van der Velden J, Overbeek LI, Kenter GG, Buist MR. The incidence of endometrial hyperplasia and cancer in 1031 patients with a granulosa cell tumor of the ovary: long-term follow-up in a population-based cohort study. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2013;23(8):1417-22.
12. Mangili G, Ottolina J, Gadducci A, Giorda G, Breda E, Savarese A, et al. Long-term follow-up is crucial after treatment for granulosa cell tumors of the ovary. *British journal of cancer*. 2013;109(1):29-34.
13. Rey RA, Lhomme C, Marcillac I, Lah lou N, Duvillard P, Josso N, et al. Antimullerian hormone as a serum marker of granulosa cell tumors of the ovary: comparative study with serum alpha-inhibin and estradiol. *American journal of obstetrics and gynecology*. 1996;174(3):958-65.
14. Lappohn RE, Burger HG, Bouma J, Bangah M, Krans M, de Brujin HW. Inhibin as a marker for granulosa-cell tumors. *The New England journal of medicine*. 1989;321(12):790-3.
15. Hildebrandt RH, Rouse RV, Longacre TA. Value of inhibin in the identification of granulosa cell tumors of the ovary. *Human pathology*. 1997;28(12):1387-95.
16. Mom CH, Engelen MJ, Willemse PH, Gietema JA, ten Hoor KA, de Vries EG, et al. Granulosa cell tumors of the ovary: the clinical value of serum inhibin A and B levels in a large single center cohort. *Gynecologic oncology*. 2007;105(2):365-72.
17. Geerts I, Vergote I, Neven P, Billen J. The role of inhibins B and antimullerian hormone for diagnosis and follow-up of granulosa cell tumors. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2009;19(5):847-55.
18. Colombo N, Peiretti M, Garbi A, Carinelli S, Marini C, Sessa C. Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology : official journal of the European Society for Medical Oncology*. 2012;23 Suppl 7:vii20-6.
19. Brown J, Sood AK, Deavers MT, Milojevic L, Gershenson DM. Patterns of metastasis in sex cord-stromal tumors of the ovary: can routine staging lymphadenectomy be omitted? *Gynecologic oncology*. 2009;113(1):86-90.
20. Thrall MM, Paley P, Pizer E, Garcia R, Goff BA. Patterns of spread and recurrence of sex cord-stromal tumors of the ovary. *Gynecologic oncology*. 2011;122(2):242-5.
21. Homesley HD, Bundy BN, Hurteau JA, Roth LM. Bleomycin, etoposide, and cisplatin combination therapy of ovarian granulosa cell tumors and other stromal malignancies: A Gynecologic Oncology Group study. *Gynecologic oncology*. 1999;72(2):131-7.
22. Uygun K, Aydiner A, Saip P, Kocak Z, Basaran M, Dincer M, et al. Clinical parameters and treatment results in recurrent granulosa cell tumor of the ovary. *Gynecologic oncology*. 2003;88(3):400-3.
23. Al-Badawi IA, Brasher PM, Ghatage P, Nation JG, Schepansky A, Stuart GC. Postoperative chemotherapy in advanced ovarian granulosa cell tumors. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2002;12(1):119-23.

24. Wilson MK, Fong P, Mesnage S, Chrystal K, Shelling A, Payne K, et al. Stage I granulosa cell tumours: A management conundrum? Results of long-term follow up. *Gynecologic oncology*. 2015;138(2):285-91.
25. van Meurs HS, Buist MR, Westermann AM, Sonke GS, Kenter GG, van der Velden J. Effectiveness of chemotherapy in measurable granulosa cell tumors: a retrospective study and review of literature. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2014;24(3):496-505.
26. Abu-Rustum NR, Restivo A, Ivy J, Soslow R, Sabbatini P, Sonoda Y, et al. Retroperitoneal nodal metastasis in primary and recurrent granulosa cell tumors of the ovary. *Gynecologic oncology*. 2006;103(1):31-4.
27. Chua TC, Iyer NG, Soo KC. Prolonged survival following maximal cytoreductive effort for peritoneal metastases from recurrent granulosa cell tumor of the ovary. *Journal of gynecologic oncology*. 2011;22(3):214-7.
28. Lee YK, Park NH, Kim JW, Song YS, Kang SB, Lee HP. Characteristics of recurrence in adult-type granulosa cell tumor. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2008;18(4):642-7.
29. Wolf JK, Mullen J, Eifel PJ, Burke TW, Levenback C, Gershenson DM. Radiation treatment of advanced or recurrent granulosa cell tumor of the ovary. *Gynecologic oncology*. 1999;73(1):35-41.
30. Savage P, Constenla D, Fisher C, Shepherd JH, Barton DP, Blake P, et al. Granulosa cell tumours of the ovary: demographics, survival and the management of advanced disease. *Clinical oncology (Royal College of Radiologists (Great Britain))*. 1998;10(4):242-5.
31. Hauspy J, Beiner ME, Harley I, Rosen B, Murphy J, Chapman W, et al. Role of adjuvant radiotherapy in granulosa cell tumors of the ovary. *International journal of radiation oncology, biology, physics*. 2011;79(3):770-4.
32. E C, Samant R, Fung MF, Le T, Hopkins L, Senterman M. Palliative radiotherapy for recurrent granulosa cell tumor of the ovary: a report of 3 cases with radiological evidence of response. *Gynecologic oncology*. 2006;102(2):406-10.
33. van Meurs HS, van Lonkhuijzen LR, Limpens J, van der Velden J, Buist MR. Hormone therapy in ovarian granulosa cell tumors: a systematic review. *Gynecologic oncology*. 2014;134(1):196-205.
34. van Meurs HS, van der Velden J, Buist MR, van Driel WJ, Kenter GG, van Lonkhuijzen LR. Evaluation of response to hormone therapy in patients with measurable adult granulosa cell tumors of the ovary. *Acta obstetricia et gynecologica Scandinavica*. 2015;94(11):1269-75.
35. Colombo N, Parma G, Zanagnolo V, Insinga A. Management of ovarian stromal cell tumors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2007;25(20):2944-51.
36. Melero Cortes LM, Martinez Maestre MA, Vieites Perez-Quintela MB, Gambadauro P. Ovarian Sertoli-Leydig cell tumours: How typical is their typical presentation? *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*. 2017;37(5):655-9.
37. Schneider DT, Orbach D, Cecchetto G, Stachowicz-Stencel T, Brummel B, Brecht IB, et al. Ovarian Sertoli Leydig cell tumours in children and adolescents: an analysis of the European Cooperative Study Group on Pediatric Rare Tumors (EXPeRT). *European journal of cancer (Oxford, England : 1990)*. 2015;51(4):543-50.
38. Young RH, Scully RE. Ovarian Sertoli-Leydig cell tumors. A clinicopathological analysis of 207 cases. *The American journal of surgical pathology*. 1985;9(8):543-69.
39. Stacher E, Pristauz G, Scholz HS, Moinfar F. Bilateral ovarian well-differentiated Sertoli-Leydig cell tumors with heterologous elements associated with unilateral serous cystadenoma--a case report. *International journal of gynecological pathology : official journal of the International Society of Gynecological Pathologists*. 2010;29(5):419-22.
40. Lou W, Cao D, Yang J, Guo L, Shen K. Retiform Sertoli-Leydig cell tumor of ovary in a 9-year-old girl: case report and review of the literature. *International journal of clinical oncology*. 2011;16(6):705-8.

41. Akman L, Ertas IE, Gokcu M, Terek MC, Sanci M, Sanli UA, et al. Ovarian sertoli-leydig cell tumors: A multicenter long-term clinicopathological analysis of 27 patients. *Journal of cancer research and therapeutics.* 2016;12(1):290-4.
42. Schultz KAP, Harris AK, Finch M, Dehner LP, Brown JB, Gershenson DM, et al. DICER1-related Sertoli-Leydig cell tumor and gynandroblastoma: Clinical and genetic findings from the International Ovarian and Testicular Stromal Tumor Registry. *Gynecologic oncology.* 2017;147(3):521-7.
43. Gui T, Cao D, Shen K, Yang J, Zhang Y, Yu Q, et al. A clinicopathological analysis of 40 cases of ovarian Sertoli-Leydig cell tumors. *Gynecologic oncology.* 2012;127(2):384-9.
44. Weng CS, Chen MY, Wang TY, Tsai HW, Hung YC, Yu KJ, et al. Sertoli-Leydig cell tumors of the ovary: a Taiwanese Gynecologic Oncology Group study. *Taiwanese journal of obstetrics & gynecology.* 2013;52(1):66-70.
45. Sigismundi C, Gadducci A, Lorusso D, Candiani M, Breda E, Raspagliesi F, et al. Ovarian Sertoli-Leydig cell tumors. a retrospective MITO study. *Gynecologic oncology.* 2012;125(3):673-6.
46. Kato N, Kusumi T, Kamataki A, Tsunoda R, Fukase M, Kurose A. DICER1 hotspot mutations in ovarian Sertoli-Leydig cell tumors: a potential association with androgenic effects. *Human pathology.* 2017;59:41-7.
47. Kim MS, Lee SH, Yoo NJ, Lee SH. DICER1 exons 25 and 26 mutations are rare in common human tumours besides Sertoli-Leydig cell tumour. *Histopathology.* 2013;63(3):436-8.
48. de Kock L, Terzic T, McCluggage WG, Stewart CJR, Shaw P, Foulkes WD, et al. DICER1 Mutations Are Consistently Present in Moderately and Poorly Differentiated Sertoli-Leydig Cell Tumors. *The American journal of surgical pathology.* 2017;41(9):1178-87.
49. Pastorelli LM, Wells S, Fray M, Smith A, Hough T, Harfe BD, et al. Genetic analyses reveal a requirement for Dicer1 in the mouse urogenital tract. *Mammalian genome : official journal of the International Mammalian Genome Society.* 2009;20(3):140-51.
50. Durmus Y, Kilic C, Cakir C, Yuksel D, Boran N, Karalok A, et al. Sertoli-Leydig cell tumor of the ovary: Analysis of a single institution database and review of the literature. *The journal of obstetrics and gynaecology research.* 2019;45(7):1311-8.
51. Xiao H, Li B, Zuo J, Feng X, Li X, Zhang R, et al. Ovarian Sertoli-Leydig cell tumor: a report of seven cases and a review of the literature. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology.* 2013;29(3):192-5.
52. Bhat RA, Lim YK, Chia YN, Yam KL. Sertoli-Leydig cell tumor of the ovary: analysis of a single institution database. *The journal of obstetrics and gynaecology research.* 2013;39(1):305-10.
53. Nam SM, Kim JW, Eoh KJ, Kim HM, Lee JY, Nam EJ, et al. A novel clinicopathological analysis of early stage ovarian Sertoli-Leydig cell tumors at a single institution. *Obstetrics & gynecology science.* 2017;60(1):39-45.
54. Zhang HY, Zhu JE, Huang W, Zhu J. Clinicopathologic features of ovarian Sertoli-Leydig cell tumors. *International journal of clinical and experimental pathology.* 2014;7(10):6956-64.
55. Demidov VN, Lipatenkova J, Vikhareva O, Van Holsbeke C, Timmerman D, Valentin L. Imaging of gynecological disease (2): clinical and ultrasound characteristics of Sertoli cell tumors, Sertoli-Leydig cell tumors and Leydig cell tumors. *Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 2008;31(1):85-91.