

# BÖLÜM 31

## UTERUS SARKOMLARI

Özgecan DÜLGAR<sup>1</sup>

### GİRİŞ

Uterus sarkomları, tüm uterin malignitelerinin %8'inden azını oluşturan nadir görülen malign mezenkimal tümörlerdir(1). En sık görülen alt tipleri leiomyosarkom(%63)(LMS) ve endometrial stromal sarkom (%21)(ESS) iken, undiferansiye uterin sarkomlar(%6)(UUS) daha nadir görülür(2). Adenosarkom, rabdomyosarkom ve Pecoma da çok nadiren uterusta görülebilen sarkom alttiplerindedir(2,3). ESS ve LMS saf mezenkimal tümörler olarak sınıflandırılır. Adenosarkom ve karsinosarkom epitelyal ve mezenkimal hücreler içeren heterolog alt tiplerdir. Karsinosarkom, yeni sınıflamalarda endometrial karsinom gibi evrelendirilmekte ve tedavi edilmektedir(2). Sarkom vakalarının çoğunluğu sporadiktir ve özel bir etyolojiye sahip değildirler(4). Fakat uterin sarkomlarda alt tipe özel çok sayıda kromozomal translokasyon tanımlanmıştır(4). Özellikle ESS sitogenetik analiz ile de ayrılabilir.

Uterus sarkomlarının etyolojisi az bilinmekle beraber pelvik bölgeye radyoterapi sonrası gelişen LMS ve karsinosarkom olguları mevcuttur(5). Radyoterapi sonrası, sarkomlar ortalama 17 yılda (3-30 yıl) gelişmekte olup kötü prognoza sahiptir (5). Tamoksifen kullanımı sonrası 1000 kadından 0,17'sinde uterus sarkomu gelişmektedir. Tamoksifen sonrası karsinosarkom baskın histoloji olup ileri evrede tanı alırken adenosarkomlar erken evrede tanı almaktadır(6,7).

### Evreleme

Uterus sarkomları 2009 FIGO evreleme sistemine göre evrelendirilmektedir. Evreleme, LMS'ler/endometriyal stromal sarkomlar (ESS'ler) ve adenosarkomlarda farklıdır. Tablo 1'de özetlenmiştir(8).

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## Adenosarkom

Uterin adenosarkomlar iyi huylu bir epitelyal bileşene sahipken, stromal bileşen tipik olarak düşük dereceli bir sarkomdur. Vakaların çoğunda sarkomatöz bileşen ESS benzeridir ve vakaların ek %9'unda ESS benzeri hücreler ve fibrosarkom karışımı heterolog olarak mevcuttur(37). Bir çalışmada, uterin adenosarkomun sarkomatöz bileşeni, 20 hastanın 18'inde (%90) östrojen veya progesteronu eksprese ettiği gösterilmiştir(38). Tümör biyolojisindeki benzerlik göz önüne alındığında, tedavi seçenekleri ESS'ye benzer. Sarkomatöz aşırı büyümeye sahip uterin adenosarkom, hormona duyarlı olması muhtemel olmayan agresif bir antitedir.

## SONUÇ

Uterin sarkomlar nadirdir ve preoperatif tanı sıklıkla bilinmemektedir. Histerektomi, erken evre uterin leiomyosarkom ve ESS için tedavinin temel taşıdır. Her iki antite için de herhangi bir adjuvan tedavinin (yani radyoterapi, kemoterapi veya hormonoterapi) kanıtlanmış bir faydası yoktur. Hormon reseptörleri, tekrarlayan uterin leiomyosarkomların bir alt grubu için olduğu gibi, metastatik ESS için de en önemli hedeflerdir.

## KAYNAKLAR

1. Hosh M, Antar S, Nazzal A, et al. Uterine Sarcoma: Analysis of 13,089 Cases Based on Surveillance, Epidemiology, and End Results Database. *International journal of gynecological cancer*. 2016 Jul;26(6):1098-104. doi: 10.1097/IGC.000.000.0000000720.
2. Tropé CG, Abeler VM, Kristensen GB. Diagnosis and treatment of sarcoma of the uterus. A review. *Acta oncologica*. 2012 Jul;51(6):694-705. doi: 10.3109/0284186X.2012.689111.
3. Novetsky AP, Powell MA. Management of sarcomas of the uterus. *Current opinion in oncology*. 2013 Sep;25(5):546-52. doi: 10.1097/CCO.0b013e328363e0ef.
4. Helman LJ, Meltzer P. Mechanisms of sarcoma development. *Nature reviews Cancer*. 2003 Sep;3(9):685-94. doi: 10.1038/nrc1168.
5. Mark RJ, Poen J, Tran LM et al. Postirradiation sarcoma of the gynecologic tract. A report of 13 cases and a discussion of the risk of radiation-induced gynecologic malignancies. *American journal of clinical oncology*. 1996 Feb;19(1):59-64. doi: 10.1097/00000.421.199602000-00013.
6. Wysowski DK, Honig SF, Beitz J. Uterine sarcoma associated with tamoxifen use. *The New England journal of medicine*. 2002 Jun 6;346(23):1832-3. doi: 10.1056/NEJM200.206.063462319.
7. Gottlieb S. Tamoxifen may increase risk of uterine sarcoma. *BMJ : British medical journal*. 2002 Jul 6;325(7354):7. doi: 10.1136/bmj.325.7354.7/a.
8. Prat J. FIGO staging for uterine sarcomas. *International journal of gynaecology and obstetrics*. 2009 Mar;104(3):177-8. doi: 10.1016/j.ijgo.2008.12.008. Epub 2009 Jan 9. Erratum in: *Int J Gynaecol Obstet*. 2009 Sep;106(3):277.
9. Bell SW, Kempson RL, Hendrickson MR. Problematic uterine smooth muscle neoplasms. A clinicopathologic study of 213 cases. *The American journal of surgical pathology*. 1994 Jun;18(6):535-58.
10. Cho YL, Bae S, Koo MS, et al. Array comparative genomic hybridization analysis of uterine leiomyosarcoma. *Gynecologic oncology*. 2005 Dec;99(3):545-51. doi: 10.1016/j.ygyno.2005.07.017.
11. Nielsen TO, West RB, Linn SC, et al. Molecular characterisation of soft tissue tumours: a gene

## Uterus Sarkomları

- expression study. *Lancet*. 2002 Apr 13;359(9314):1301-7. doi: 10.1016/S0140-6736(02)08270-3.
12. Yang J, Du X, Chen K, et al. Genetic aberrations in soft tissue leiomyosarcoma. *Cancer Letters*. 2009 Mar 8;275(1):1-8. doi: 10.1016/j.canlet.2008.06.013.
  13. Leitao MM, Soslow RA, Nonaka D, et al. Tissue microarray immunohistochemical expression of estrogen, progesterone, and androgen receptors in uterine leiomyomata and leiomyosarcoma. *Cancer*. 2004 Sep 15;101(6):1455-62. doi: 10.1002/cncr.20521.
  14. Amant F, Vloeberghs V, Woestenborghs H, et al. ERBB-2 gene overexpression and amplification in uterine sarcomas. *Gynecologic oncology*. 2004 Dec;95(3):583-7. doi: 10.1016/j.ygy-no.2004.07.041.
  15. Gadducci A, Cosio S, Romanini A, et al. The management of patients with uterine sarcoma: a debated clinical challenge. *Critical reviews in oncology/hematology*. 2008 Feb;65(2):129-42. doi: 10.1016/j.critrevonc.2007.06.011.
  16. Bogani G, Cliby WA, Aletti GD. Impact of morcellation on survival outcomes of patients with unexpected uterine leiomyosarcoma: a systematic review and meta-analysis. *Gynecologic oncology*. 2015 Apr;137(1):167-72. doi: 10.1016/j.ygyno.2014.11.011.
  17. Amant F, Coosemans A, Debiec-Rychter M, Timmerman D, Vergote I. Clinical management of uterine sarcomas. *The Lancet Oncology*. 2009 Dec;10(12):1188-98. doi: 10.1016/S1470-2045(09)70226-8.
  18. ESMO / European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology: official journal of the European Society for Medical Oncology / ESMO*. 2012 Oct;23 Suppl 7:vii92-9. doi: 10.1093/annonc/mds253.
  19. Reed NS, Mangioni C, Malmström H, et al; European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group. Phase III randomised study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcomas stages I and II: an European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874). *European journal of cancer*. 2008 Apr;44(6):808-18. doi: 10.1016/j.ejca.2008.01.019.
  20. Omura GA, Blessing JA, Major F, et al. A randomized clinical trial of adjuvant adriamycin in uterine sarcomas: a Gynecologic Oncology Group Study. *Journal of clinical oncology*. 1985 Sep;3(9):1240-5. doi: 10.1200/JCO.1985.3.9.1240.
  21. Hensley ML, Ishill N, Soslow R, et al. Adjuvant gemcitabine plus docetaxel for completely resected stages I-IV high grade uterine leiomyosarcoma: Results of a prospective study. *Gynecologic oncology*. 2009 Mar;112(3):563-7. doi: 10.1016/j.ygyno.2008.11.027.
  22. Hensley ML, Wathen JK, Maki RG, et al Adjuvant therapy for high-grade, uterus-limited leiomyosarcoma: results of a phase 2 trial (SARC 005). *Cancer*. 2013 Apr 15;119(8):1555-61. doi: 10.1002/cncr.27942.
  23. Karavasilis V, Seddon BM, Ashley S, et al. Significant clinical benefit of first-line palliative chemotherapy in advanced soft-tissue sarcoma: retrospective analysis and identification of prognostic factors in 488 patients. *Cancer*. 2008 Apr 1;112(7):1585-91. doi: 10.1002/cncr.23332.
  24. Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel compared with gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002 [corrected]. *Journal of clinical oncology*. 2007 Jul 1;25(19):2755-63. doi: 10.1200/JCO.2006.10.4117. Erratum in: *J Clin Oncol*. 2007 Aug 20;25(24):3790.
  25. Judson I, Verweij J, Gelderblom H, et al; European Organisation and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomised controlled phase 3 trial. *The Lancet Oncology*. 2014 Apr;15(4):415-23. doi: 10.1016/S1470-2045(14)70063-4.
  26. Van der Graaf WT, Blay JY, Chawla SP, et al; EORTC Soft Tissue and Bone Sarcoma Group; PALETTE study group. Pazopanib for metastatic soft-tissue sarcoma (PALETTE): a randomised,

- double-blind, placebo-controlled phase 3 trial. *Lancet*. 2012 May 19;379(9829):1879-86. doi: 10.1016/S0140-6736(12)60651-5.
27. Hensley ML, Patel SR, von Mehren M, et al. Efficacy and safety of trabectedin or dacarbazine in patients with advanced uterine leiomyosarcoma after failure of anthracycline-based chemotherapy: Subgroup analysis of a phase 3, randomized clinical trial *Gynecologic oncology*. 2017 Sep;146(3):531-537. doi: 10.1016/j.ygyno.2017.06.018.
  28. George S, Feng Y, Manola J, et al. Phase 2 trial of aromatase inhibition with letrozole in patients with uterine leiomyosarcomas expressing estrogen and/or progesterone receptors. *Cancer*. 2014 Mar 1;120(5):738-43. doi: 10.1002/cncr.28476.
  29. Oliva E, Clement PB, Young RH. Endometrial stromal tumors: an update on a group of tumors with a protean phenotype. *Advances in anatomic pathology*. 2000 Sep;7(5):257-81. doi: 10.1097/00125.480.200007050-00001.
  30. Huang HY, Ladanyi M, Soslow RA. Molecular detection of JAZF1-JJAZ1 gene fusion in endometrial stromal neoplasms with classic and variant histology: evidence for genetic heterogeneity. *The American journal of surgical pathology*. 2004 Feb;28(2):224-32. doi: 10.1097/00000.478.200402000-00010.
  31. Lee CH, Mariño-Enriquez A, Ou W, et al. The clinicopathologic features of YWHAE-FAM22 endometrial stromal sarcomas: a histologically high-grade and clinically aggressive tumor. *The American journal of surgical pathology*. 2012 May;36(5):641-53. doi: 10.1097/PAS.0b013e-31824a7b1a.
  32. Tavassoli, F.A. and Devilee, P., Eds. (2003) World Health Organization Classification of Tumors. *Pathology & Genetics of Tumours of the Breast and Female Genital Organs*. IARC (International Agency for Research on Cancer) Press, Lyon, 153-158.
  33. Chan JK, Kawar NM, Shin JY, et al. Endometrial stromal sarcoma: a population-based analysis. *British journal of cancer*. 2008 Oct 21;99(8):1210-5. doi: 10.1038/sj.bjc.6604527.
  34. Chu MC, Mor G, Lim C, et al. Low-grade endometrial stromal sarcoma: hormonal aspects. *Gynecologic oncology*. 2003 Jul;90(1):170-6. doi: 10.1016/s0090-8258(03)00258-0.
  35. Amant F, De Knijf A, Van Calster B, et al. Clinical study investigating the role of lymphadenectomy, surgical castration and adjuvant hormonal treatment in endometrial stromal sarcoma. *British journal of cancer*. 2007 Nov 5;97(9):1194-9. doi: 10.1038/sj.bjc.6603986. Epub 2007 Sep 25.
  36. Maluf FC, Sabbatini P, Schwartz L, et al. Endometrial stromal sarcoma: objective response to letrozole. *Gynecologic oncology*. 2001 Aug;82(2):384-8. doi: 10.1006/gy.2001.6238.
  37. Clement PB, Scully RE. Mullerian adenosarcoma of the uterus: a clinicopathologic analysis of 100 cases with a review of the literature. *Human pathology*. 1990 Apr;21(4):363-81. doi: 10.1016/0046-8177(90)90198-e.
  38. Amant F, Schurmans K, Steenkiste E, et al. Immunohistochemical determination of estrogen and progesterone receptor positivity in uterine adenosarcoma. *Gynecologic oncology*. 2004 Jun;93(3):680-5. doi: 10.1016/j.ygyno.2004.03.021.