

BÖLÜM 52

SERVİKSİN SİTOLOJİK HÜCRE ANORMALLİKLERİNİN TANI VE TEDAVİSİ

İlyas TURAN¹

Giriş

Serviks kanseri, kadın kanserleri içerisinde meme ve akciğerden sonra üçüncü sırada bulunmaktadır. Ayrıca kadınlarda kansere bağlı ölümler içerisinde ikinci sırada yer almaktadır. Günümüzde sitolojik hücre anormallikleri tanı ve tedavisinin standartize edilmesi kanser gelişiminin önlenmesi açısından önem arz etmektedir. Servikal kanser öncüllerini tarayan servikal sitoloji tarama testi olan pap-smear, 1950'den beri servikal malignite insidansını %79, mortalitesini ise %70 oranında azaltmıştır (1). Kanser öncül lezyonların çoğu regrese olsa da eşlik eden hpv enfeksiyonu olduğunda progrese olabilir. Bu servikal sitolojik anormalliklerin histolojik olarak displazi zemininden geliştiği ve ilk defa 1968 yılında servikal intraepitelyal neoplazi (CIN) terimi ile literatüre girmeye başlamıştır. Serviks epitelindeki displazinin derecesine bağlı olarak CIN kendi içinde CIN 1 (hafif displazi), CIN 2 (orta displazi), CIN 3 (şiddetli displazi) olmak üzere 3'e ayrılmıştır. Serviks epitel hücre tabakasının tamamının kaybı ile birlikte aşırı mitoz ve immatür hücrenin bulunması ise karsinoma in situ olarak ifade edilir. CIN genelde skuamokolumnar

bileşkenin geçiş bölgesindeki (transformasyon zon) metaplazik alandan gelişir. CIN 1 ve CIN 2 lezyonları büyük ihtimalle regrese olabilen kanser öncül lezyonlardır. CIN lezyonlarının yaklaşık olarak %90'ında HPV'nin rolü mevcuttur (2).

Premalign squamöz lezyonlar ise kendi içinde 3 alt gruba klasifiye edilmiştir.

- 1) Atipik squamöz hücreler (ASC). ASC hücrelerde, kendi içinde önemi bilinmeyen (ASC-US) ve yüksek dereceli lezyondan ayırt edilemeyen (ASC-H) olmak üzere 2 alt gruba ayrılır.
- 2) Düşük dereceli squamöz intraepitelyal lezyonlar (LSIL): CIN1 ve koilositik atipi olarak adlandırılan HPV değişimlerini içerir.
- 3) Yüksek dereceli squamöz intraepitelyal lezyonlar (HSIL).

Bu sınıflama ile beraber LSIL, CIN 1'e teka-bül ederken, HSIL ise CIN 2, CIN 3 ve karsinoma in-situya (CIS) karşılık gelmektedir. CIN 1 ilk 2 yıllık takipte yaklaşık % 60-80 oranlarında regrese olabilmektedir. Fakat CIN 3 tedavi edilmediği takdirde invaziv kansere ilerlemektedir.

¹ Op. Dr. İlyas TURAN, Süleyman Demirel Üniversitesi Araştırma ve Uygulama Hastanesi, Kadın Hastalıkları Ve Doğum Bölümü ilyasturan04@gmail. com



- mavirus infection of the cervix: relative risk associations of 15 common anogenital types. *Obstet Gynecol* 1992;79:328–337.
3. ASCCP Guideline Data, 2012 (ASCCP Journal of Lower Genital Tract Disease, V17, N5, S 1-27, 2013)
 4. Cibas, E. S. (2014). Cervical and Vaginal Cytology. In E. S. Cibas, B. S. Ducatman (Eds.) *Cytology : diagnostic principles and clinical correlates* (4th ed., pp. 1-58). China:Elsevier.
 5. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. *Am J Epidemiol* 1995;141:680–689.
 6. Mitchell MF, Schottenfeld D, Tortolero-Luna G, et al. Colposcopy for the diagnosis of squamous intraepithelial lesions: a meta-analysis. *Obstet Gynecol* 1998;91:626–631.
 7. Nanda K, McCrory DC, Myers ER, et al. Accuracy of the Papanicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic review. *Ann Intern Med* 2000;132:810–819.
 8. Birdsong, G. C., Davey, D. D. (2014). Specimen Adequacy. In R. Nayar, D. C. Wilbur. *The bethesda system for reporting cervical cytology* (3rd ed. pp. 1-28). Switzerland:Spiringer.
 9. National Cancer Institute Workshop. The 1988 Bethesda System for reporting cervical/vaginal cytological diagnoses. *JAMA* 1989;262:931–934.
 10. Nayar, R., Wilbur, D. C. (2015). The bethesda system for reporting cervical cytology. In M. Biblo, D. C. Wilbur (Eds.), *Comprehensive Cytopathology* (4th ed., pp. 70-81). China:Elsevier.
 11. Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA* 2002;287:2114–2119.
 12. Nasiell K, Roger V, Nasiell M. Behavior of mild cervical dysplasia during long-term follow-up. *Obstet Gynecol* 1986;67:665–669.
 13. Wang, Z., Stephen C. P (2015). HPV Detection Techniques. In M. Biblo, D. C. Wilbur (Eds.), *Comprehensive Cytopathology* (4th ed., pp. 926-932). China:Elsevier.
 14. Polman NJ, Snijders PJF, Kenter GG, et. al. HPV-based cervical screening: rationale, expectations and future perspectives of the new dutch screening programme. *Prev Med*, 119, 108-117. doi: 10. 1016/j. ypm. 2018. 12. 021.
 15. Henry, M. R., Russell, D. K., Luff R. D. (2014). Epithelial cell abnormalities:Squamous. In R. Nayar, D. C. Wilbur. *The bethesda system for reporting cervical cytology* (3rd ed. pp. 135-192). Switzerland:Spiringer.
 16. The GlaxoSmithKline Vaccine HPV-007 Study Group. Sustained efficacy and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine: analysis of a randomised placebo-controlled trial up to 6. 4 years. *Lancet* 2009;374:1975–1985.
 17. McCrory DC, Matchar DB, Bastian L, et al. Evaluation of cervical cytology. Evidence Report/Technology Assessment No. 5. (Prepared by Duke University under Contract No. 290-97-0014.) AHCPR Publication No. 99-E010. Rockville, MD: Agency for Health Care Policy and Research. February 1999.
 18. Hatch KD. Handbook of colposcopy: diagnosis and treatment of lower genital tract neoplasia and HPV infections. Boston, MA: Little Brown, 1989.
 19. Smith, P. A., Gray, W. (2010). Cervical intraepithelial neoplasia and squamous cell carcinoma of the cervix. In W. Gray, G. Kocjan. (Eds.), *Diagnostic cytopathology* (3rd ed., pp. 609-645). China:Elsevier.
 20. Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis*, 121(4), 829-846. doi: 10. 1097/AOG. 0b013e3182883a34.
 21. Andersen ES, Thorup K, Larsen G. The results of cryosurgery for cervical intraepithelial neoplasia. *Gynecol Oncol* 1988;30:21–25.
 22. Ostergard DR. Cryosurgical treatment of cervical intraepithelial neoplasia. *Obstet Gynecol* 1980;56:231–233.
 23. Creasman WT, Weed JC, Curry SL, et al. Efficacy of cryosurgical treatment of severe cervical intraepithelial neoplasia. *Obstet Gynecol* 1973;41:501–506.
 24. Benedet JL, Miller DM, Nickerson KG, et al. The results of cryosurgical treatment of cervical intraepithelial neoplasia at one, five, and ten years. *Am J Obstet Gynecol* 1987;157:268–273.
 25. Townsend DE. Cryosurgery for CIN. *Obstet Gynecol Surv* 1979;34:828.
 26. Burke L. The use of the carbon dioxide laser in the therapy of cervical intraepithelial neoplasia. *Am J Obstet Gynecol* 1982;144:337–340.
 27. Wright VC, Riopelle MA, Rubinstein E, et al. CO2 laser and cervical intraepithelial neoplasia. *Acta Obstet Gynecol Scand Suppl* 1984;125:1–36.
 28. Rylander E, Isberg A, Joelsson I. Laser vaporization of cervical intraepithelial neoplasia: a five-year follow-up. *Acta Obstet Gynecol Scand Suppl* 1984;125:33–36.
 29. Jordan JA, Mylotte MJ, Williams DR. The treatment of cervical intraepithelial neoplasia by laser vaporization. *Br J Obstet Gynaecol* 1985;92:394–398.
 30. Benedet JL, Miller DM, Nickerson KG. Results of conservative management of cervical intraepithelial neoplasia. *Obstet Gynecol* 1992;79:105–110.
 31. Baggish MS, Dorsey JH, Adelson M. A ten-year experience treating cervical intraepithelial neoplasia with the CO2 laser. *Am J Obstet Gynecol* 1989;161:60–68.
 32. Baggish MS. A comparison between laser excisional conization and laser vaporization for the treatment of cervical intraepithelial neoplasia. *Am J Obstet Gynecol* 1986;155:39–44.
 33. Larsson G, Gullberg B, Grundsell H. A comparison of complications of laser and cold knife conization. *Obstet Gynecol* 1983;62:213–217.
 34. Bjerre B, Eliasson G, Linell F, et al. Conization as only treatment of carcinoma in situ of the uterine cervix. *Am J Obstet Gynecol* 1976;125:143–152.
 35. Luesley DM, McCrum A, Terry PB, et al. Complications of cone biopsy related to the dimensions of the cone and the influence of prior colposcopic assessment. *Br J Obstet Gynaecol* 1985;92:158–164.
 36. Mathevet P, Chemali E, Roy M, et al. Long-term outcome of a randomized study comparing three techniques of conization: cold knife, laser, and LEEP. *Eur J Obstet*



- Gynecol Reprod Biol 2003;106:214–218.
37. Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D; 2006 American Society for Colposcopy and Cervical Pathology-sponsored Consensus Conference. 2006 consensus guidelines for the management of women with cervical intraepithelial neoplasia or adenocarcinoma in situ. *J Low Genit Tract Dis.* 2007; 11(4):223-39.
 38. Bansal N, Wright JD, Cohen CJ, Herzog TJ. Natural history of established low grade cervical intraepithelial (CIN 1) lesions. *Anticancer Res* 2008;28(3B):1763-6.
 39. Barbara S. Apgar, MD, MS; Anne L. Kittendorf, MD; Catherine M. Bettcher, MD; Jean Wong, MD; and Amanda J. Kaufman, MD, *University of Michigan Medical Center, Ann Arbor, Michigan* Update on ASCCP Consensus Guidelines for Abnormal Cervical Screening Tests and Cervical Histology
 40. Ana Claudia Guedes¹, Luis Carlos Zeferino², Kari Juhan SYRJÄNEN³ and Sylvia Michelina Fernandes Brenna¹ Short-term Outcome of Cervical Intraepithelial Neoplasia Grade 2: Considerations for Management Strategies and Reproducibility of Diagnosis, *Anticancer Research* June 2010 vol. 30 no. 6 2319-2323
 41. Castle PE, Schiffman M, Wheeler CM, Solomon D. Evidence for frequent regression of cervical intraepithelial neoplasia-grade 2. *Obstet Gynecol* 2009;113(1):18-25.
 42. Chan JK, Monk BJ, Brewer C, Keefe KA, Osann K, McMeekin S, et al. HPV infection and number of lifetime sexual partners are strong predictors for 'natural' regression of CIN 2 and 3. *Br J Cancer* 2003;89(6):1062-6.
 43. McCredie MR, Sharples KJ, Paul C, Baranyai J, Medley G, Jones RW, et al. Natural history of cervical neoplasia and risk of invasive cancer in women with cervical intraepithelial neoplasia 3: a retrospective cohort study. *Lancet Oncol* 2008;9(5):425-34.
 44. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin number 66, September 2005. Management of abnormal cervical cytology and histology. *Obstet Gynecol* 2005;106(3):645-64.
 45. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2013;17(5 Suppl 1):S1-S27.
 46. Brent Tierney, ¹ Shannon N. Westin, ² Matthew P. Schlumbrecht, ² and Pedro T. Ramirez^{2,*} Early Cervical Neoplasia: Advances in Screening and Treatment Modalities, *Clin Adv Hematol Oncol.* 2010 Aug; 8(8): 547–555.
 47. Committee on Practice Bulletins-Gynecology. ACOG Practice Bulletin Number 131: Screening for cervical cancer. *Obstet Gynecol* 2012;120(5): 1222-38.
 48. Carla Vitola Gonçalves^I; Geraldo Duarte^{II}; Juvenal Soares Dias da Costa^{III}; Alessandra Cristina Marcolin^{IV}; Mônia Steigleder Bianchi^V; Daison Dias^{VI}; Luis Cláudio de Velleca e Lima^{VI}. Diagnosis and treatment of cervical cancer during pregnancy, *Sao Paulo Med. J.* vol. 127 no. 6 São Paulo Nov. 2009.
 49. Soutter WP, Haidopoulos D, Gornall RJ, et al. Is conservative treatment for adenocarcinoma in situ of the cervix safe? *BJOG.* 2001;108:1184-9.
 50. Berek JS. (2012). *Intraepithelial Diseases of the Cervix, Vagina and Vulva.* Francisco Garcia, Kenneth D. Hatch, Jonathan S. (Ed.), Berek Berek&Novak's Gynecology (Fifteenth Edition) (p. 1049-1100). Philadelphia: Lippincott Williams&Wilkins, a Wolters Kluwer business.