

Bölüm 17

TEKRARLAYAN GEBELİK KAYIPLARINA YAKLAŞIM

Mustafa TAŞ¹

TANIM

Art arda en az iki defa ya da daha fazla kez klinik olarak tanımlanan yirminci hafta öncesinde gebeliğin sonlanması durumu olarak tanımlanan tekrarlayan gebelik kaybı (TGK) üreme çağındaki kadınların sık karşılaşılan problemlerinden biridir. Bu tanım ektopik, molar ve biyokimyasal gebelikleri kapsamaz. TGK primer ve sekonder olarak iki gruba ayrılır. Tekrarlayan gebelik kaybı canlı doğumu takiben gelişirse sekonder, hiç canlı doğumla sonuçlanan gebelik öyküsü yoksa primer tekrarlayan gebelik kaybı olarak isimlendirilir. Sekonder TGK daha iyi prognoza sahiptir (1).

İNSİDANS

TGK gebelik planlayan kadınların yaklaşık %3-5'ini etkiler. Sporadik gebelik kaybı ultrasonografik ve histopatolojik olarak tanınmış tüm gebeliklerin %15'inde izlenmektedir. Gebelerin yaklaşık %5'inde ardışık iki gebelik kaybı, %1'inde ise üç veya üçten fazla sayıda gebelik kaybı oluşabilir. Tüm gebeliklerde düşük yapma riski % 22 ile % 57 arasında değişmektedir ve bu oran 6-10 haftada % 15, 10.gebelik haftası sonrasında ise % 2-3'e düşmektedir (2,3).

RİSK FAKTÖRLERİ VE ETYOLOJİ

TGK vakalarının %50'sinde bilinen bir etyoloji vardır ve bu grubun tedavisi yapılabilmektedir. Genel olarak yaygın şekilde kabul edilen nedenler anatomik, immünolojik, genetik, endokrin, enfeksiyöz, trombofilik ve çevresel faktörlerdir. Gebelik kaybı riski anne yaşı ve paritesi ile artar, 35 yaşın altındakilerde %19 ve 35 yaşın üzerindeki hastalarda % 47'ye çıkar. Bununla birlikte, TGK riski bir düştükten sonra % 14-21'den % 24-29'a ve üç düştükten sonra % 31-33'e yükselir. TGK öyküsü olan kadınların tanısı için tam bir tıbbi, cerrahi, genetik, aile öyküsü ve

1 Dr. Öğr.Üyesi, Acıbadem Mehmet Ali Aydınlar Üniversitesi, Acıbadem Kayseri Hastanesi, Kadın Hastalıkları ve Doğum Bölümü, drmustafatas@yahoo.com

değerlendirilmesi faydalı olabilir. Bu ekibe kadın doğum uzmanları, tıbbi genetik uzmanları, romatologlar, hematologlar, immünologlar dahil edilmelidir. TGK yönetimi büyük ölçüde TGK'nın altında yatan neden tarafından belirlenir ve şekillenir. Tanı ve tedavinin her aşamasında, çiftlerin sosyal ve psikolojik açıdan desteklenmesi önemlidir.

Anahtar Kelimeler: Gebelik, Abortus, Tekrarlayan gebelik kaybı

KAYNAKLAR

1. Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. *Fertility and sterility*. 2013;99(1):63.
2. James DK, Steer PJ, Weiner CP, et al. *High risk pregnancy e-book: Management options-expert consult*. Elsevier Health Sciences; 2010.
3. Hassold T, Chiu D. Maternal age-specific rates of numerical chromosome abnormalities with special reference to trisomy. *Human genetics*. 1985;70(1):11-17.
4. Warburton D. Cytogenetic abnormalities in spontaneous abortions of recognized conceptions. *Perinatal Genetics Diagnosis and Treatment*. 1986:133-148.
5. Philipp T, Philipp K, Reiner A, et al. Embryoscopic and cytogenetic analysis of 233 missed abortions: factors involved in the pathogenesis of developmental defects of early failed pregnancies. *Human reproduction*. 2003;18(8):1724-1732.
6. Homer HA, Li T-C, Cooke ID. The septate uterus: a review of management and reproductive outcome. *Fertility and sterility*. 2000;73(1):1-14.
7. Grimbizis GF, Camus M, Tarlatzis BC, et al. Clinical implications of uterine malformations and hysteroscopic treatment results. *Human reproduction update*. 2001;7(2):161-174.
8. Jewelewicz R. Incompetent cervix: pathogenesis, diagnosis and treatment. Paper presented at: Seminars in perinatology 1991.
9. Empson M, Lassere M, Craig JC, et al. Recurrent pregnancy loss with antiphospholipid antibody: a systematic review of therapeutic trials. *Obstetrics & Gynecology*. 2002;99(1):135-144.
10. Stagnaro-Green A, Glinoe D. Thyroid autoimmunity and the risk of miscarriage. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2004;18(2):167-181.
11. Christiansen OB, Nielsen HS, Lund M, et al. Mannose-binding lectin-2 genotypes and recurrent late pregnancy losses. *Human Reproduction*. 2008;24(2):291-299.
12. Wegmann TG, Lin H, Guilbert L, et al. Bidirectional cytokine interactions in the maternal-fetal relationship: is successful pregnancy a TH2 phenomenon? *Immunology today*. 1993;14(7):353-356.
13. Rein DT, Schöndorf T, Göhring U-J, et al. Cytokine expression in peripheral blood lymphocytes indicates a switch to Thelper cells in patients with preeclampsia. *Journal of reproductive immunology*. 2002;54(1-2):133-142.
14. King A, Hiby S, Gardner L, et al. Recognition of trophoblast HLA class I molecules by decidual NK cell receptors—a review. *Placenta*. 2000;21:S81-S85.
15. Raghupathy R, Makhseed M, Azizieh F, et al. Th1 and Th2 cytokine profiles in successful pregnancy and unexplained recurrent abortions. In: *Reproductive Immunology*. Springer; 1999 149-158.
16. Yeaman GR, Collins JE, Currie JK, et al. IFN- γ is produced by polymorphonuclear neutrophils in human uterine endometrium and by cultured peripheral blood polymorphonuclear neutrophils. *The Journal of Immunology*. 1998;160(10):5145-5153.
17. Tong S, Marjono B, Brown DA, et al. Serum concentrations of macrophage inhibitory cytokine 1 (MIC 1) as a predictor of miscarriage. *The Lancet*. 2004;363(9403):129-130.
18. Sikora J, Magnucki J, Zietek J, et al. Homocysteine, folic acid and vitamin B12 concentration in patients with recurrent miscarriages. *Neuro endocrinology letters*. 2007;28(4):507-512.

19. Orange JS, Ballas ZK. Natural killer cells in human health and disease. *Clinical immunology*. 2006;118(1):1-10.
20. Quenby S, Nik H, Innes B, et al. Uterine natural killer cells and angiogenesis in recurrent reproductive failure. *Human reproduction*. 2008;24(1):45-54.
21. Quenby S, Kalumbi C, Bates M, et al. Prednisolone reduces preconceptional endometrial natural killer cells in women with recurrent miscarriage. *Fertility and sterility*. 2005;84(4):980-984.
22. Drake PM, Gunn MD, Charo IF, et al. Human placental cytotrophoblasts attract monocytes and CD56bright natural killer cells via the actions of monocyte inflammatory protein 1a. *Journal of Experimental Medicine*. 2001;193(10):1199-1212.
23. Koopman LA, Kopcow HD, Rybalov B, et al. Human decidual natural killer cells are a unique NK cell subset with immunomodulatory potential. *Journal of Experimental Medicine*. 2003;198(8):1201-1212.
24. No G-tG. The investigation and treatment of couples with recurrent first-trimester and second-trimester miscarriage. *April 2011*. 2011.
25. Erden O, Imir A, Guvenal T, et al. Investigation of the effects of heparin and low molecular weight heparin on E-cadherin and laminin expression in rat pregnancy by immunohistochemistry. *Human reproduction*. 2006;21(11):3014-3018.
26. Thum MY, Bhaskaran S, Abdalla HI, et al. Prednisolone suppresses NK cell cytotoxicity in vitro in women with a history of infertility and elevated NK cell cytotoxicity. *American Journal of Reproductive Immunology*. 2008;59(3):259-265.
27. Xu B, Makris A, Thornton C, et al. Glucocorticoids inhibit placental cytokines from cultured normal and preeclamptic placental explants. *Placenta*. 2005;26(8-9):654-660.
28. Coulam CB, Goodman C. Increased pregnancy rates after IVF/ET with intravenous immunoglobulin treatment in women with elevated circulating C56+ cells. *Early pregnancy (Online)*. 2000;4(2):90-98.
29. Stricker RB, Steinleitner A, Bookoff CN, et al. Successful treatment of immunologic abortion with low-dose intravenous immunoglobulin. *Fertility and sterility*. 2000;73(3):536-540.
30. Winger EE, Reed JL. Treatment with tumor necrosis factor inhibitors and intravenous immunoglobulin improves live birth rates in women with recurrent spontaneous abortion. *American journal of reproductive immunology*. 2008;60(1):8-16.
31. Evans KN, Nguyen L, Chan J, et al. Effects of 25-hydroxyvitamin D3 and 1, 25-dihydroxyvitamin D3 on cytokine production by human decidual cells. *Biology of reproduction*. 2006;75(6):816-822.
32. Jerzak M, Kniotek M, Mrozek J, et al. Sildenafil citrate decreased natural killer cell activity and enhanced chance of successful pregnancy in women with a history of recurrent miscarriage. *Fertility and sterility*. 2008;90(5):1848-1853.
33. Rai R, Shlebak A, Cohen H, et al. Factor V Leiden and acquired activated protein C resistance among 1000 women with recurrent miscarriage. *Human Reproduction*. 2001;16(5):961-965.
34. Letsky E. Maternal hemostasis: coagulation problems of pregnancy. *Thrombosis and hemorrhage*. 1994.
35. McColl M, Walker I, Greer I. The role of inherited thrombophilia in venous thromboembolism associated with pregnancy. *British journal of obstetrics and gynaecology*. 1999;106(8):756-766.
36. Jivraj S, Rai R, Underwood J, et al. Genetic thrombophilic mutations among couples with recurrent miscarriage. *Human reproduction*. 2006;21(5):1161-1165.
37. Juul K, Tybjaerg-Hansen A, Schnohr P, et al. Factor V Leiden and the risk for venous thromboembolism in the adult Danish population. *Annals of internal medicine*. 2004;140(5):330.
38. Laude I, Rongieres-Bertrand C, Boyer-Neumann C, et al. Circulating procoagulant microparticles in women with unexplained pregnancy loss: a new insight. *Thrombosis and haemostasis*. 2001;85(01):18-21.
39. Ford HB, Schust DJ. Recurrent pregnancy loss: etiology, diagnosis, and therapy. *Reviews in obstetrics and gynecology*. 2009;2(2):76.

40. Greene MF, Hare JW, Cloherty JP, et al. First-trimester hemoglobin A1 and risk for major malformation and spontaneous abortion in diabetic pregnancy. *Teratology*. 1989;39(3):225-231.
41. Arredondo F, Noble LS. Endocrinology of recurrent pregnancy loss. Paper presented at: Seminars in reproductive medicine 2006.
42. Hirahara F, Andoh N, Sawai K, et al. Hyperprolactinemic recurrent miscarriage and results of randomized bromocriptine treatment trials. *Fertility and sterility*. 1998;70(2):246-252.
43. Kaur R, Gupta K. Endocrine dysfunction and recurrent spontaneous abortion: An overview. *International Journal of Applied and Basic Medical Research*. 2016;6(2):79.
44. Obstetricians ACo, Gynecologists. ACOG practice bulletin. Management of recurrent pregnancy loss. Number 24, February 2001.(Replaces Technical Bulletin Number 212, September 1995). American College of Obstetricians and Gynecologists. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*. 2002;78(2):179.
45. Wallach EE, Hughes EG, Brennan BG. Does cigarette smoking impair natural or assisted fecundity? *Fertility and sterility*. 1996;66(5):679-689.
46. Floyd RL, Decouflé P, Hungerford DW. Alcohol use prior to pregnancy recognition. *American journal of preventive medicine*. 1999;17(2):101-107.
47. Rasch V. Cigarette, alcohol, and caffeine consumption: risk factors for spontaneous abortion. *Acta obstetrica et gynecologica Scandinavica*. 2003;82(2):182-188.
48. Schnorr TM, Grajewski BA, Hornung RW, et al. Video display terminals and the risk of spontaneous abortion. *New England Journal of Medicine*. 1991;324(11):727-733.
49. Brent RL. Utilization of developmental basic science principles in the evaluation of reproductive risks from pre-and postconception environmental radiation exposures. *Teratology*. 1999;59(4):182-204.
50. Bernardini LM, Costa M, Bottazzi C, et al. Sperm aneuploidy and recurrent pregnancy loss. *Reproductive biomedicine online*. 2004;9(3):312-320.
51. Trout SW, Seifer DB. Do women with unexplained recurrent pregnancy loss have higher day 3 serum FSH and estradiol values? *Fertility and sterility*. 2000;74(2):335-337.
52. Tempfer CB, Kurz C, Bentz E-K, et al. A combination treatment of prednisone, aspirin, folate, and progesterone in women with idiopathic recurrent miscarriage: a matched-pair study. *Fertility and sterility*. 2006;86(1):145-148.
53. Wilcox AJ, Weinberg CR, O'Connor JF, et al. Incidence of early loss of pregnancy. *New England Journal of Medicine*. 1988;319(4):189-194.
54. Coulam CB, Roussev R. Chemical pregnancies: immunologic and ultrasonographic studies. *American Journal of Reproductive Immunology*. 2002;48(5):323-328.