

Bölüm 6

KONJENİTAL UTERİN ANOMALİLER

Fatma Nurgül TAŞGÖZ¹

Konjenital uterin anomaliler reproduktif dönemde adet düzensizliği, infertilite, obstetrik sorunlar ile karşımıza çıkabileceği gibi çocukluk ve adölesan dönemde de tanı alabilen, eşlik edebilen diğer sistem anomalileri ile birlikte multidisipliner yaklaşım gerektiren genital sistem gelişim anomalileridir. Anomalilerin tanı, tedavi ve takibini yönetebilmek için embriyolojik kökeni ile ilgili bilgi sahibi olmakta fayda vardır.

EMBRİYOLOJİK GELİŞİM

Cinsel farklılaşmanın olmadığı ilk 6 haftada hem dişi hem erkek embriyoda iç genital organların gelişimini sağlayacak 2 çift genital kanal bulunur (1). Y kromozomun kısa kolunda bulunan SRY geni (Yp11.3) farklılaşmamış gonaddan testis gelişimine neden olur. Testiste bulunan sertoli hücrelerinden salınan MIF-AMH (Mülleryan inhibe edici faktör veya Anti Mülleryan Hormon) ve leydig hücrelerinden salınan testosteron mezonefrik (Wolffian) kanal gelişimine sebep olurken, AMH ve testosteron yokluğunda paramezonefrik (Mülleryan) kanal gelişir. 12.gebelik haftasında iki mülleryan kanal füzyona uğrar, internal kanalizasyonun ardından arada oluşan septumun rezorpsiyonu 20.gebelik haftası civarında gerçekleşir (2). Tüm bu gelişim 3 basamakta tamamlanır. İlk basamakta her bir mülleryan kanalın üst kısımları fallop tüplerine dönüşürken her iki kanalın kaudal kısımlarından sol ve sağ uterus, serviks ve vajinanın üst 2/3'ü gelişir. Mülleryan kanaldan bağımsız olarak, vajinanın alt 1/3'ü ürogenital sinüsten, overler gonadlardan gelişir. İkinci aşamada, ayrı sol ve sağ uterus, serviks ve üst vajinanın orta hat füzyonu gerçekleşir. Gelişimin üçüncü aşamasında, uterus, serviks ve üst vajinadaki orta hat kaynaşmış segmentlerin rezorpsiyonu ile tek bir uterus boşluğu ve tek servikal ve vajinal kanallarla sonuçlanır (3,4).

Bu gelişim basamakları herhangi bir seviyede kesintiye uğradığında mülleryan anomaliler olarak karşımıza çıkar.

¹ Dr., Bursa Yüksek İhtisas Eğitim Araştırma Hastanesi. fnurgulaktas@gmail.com.

KAYNAKÇA

1. Sajjad Y. Development of the genital ducts and external genitalia in the early human embryo. *J Obstet Gynaecol Res.* 2010; 36:929–937 DOI: 10.1111/j.1447-0756.2010.01272.x
2. Embrey MP. A case of uterus didelphys with unilateral gynatresia. *Brit Med J.* 1950;1:820. DOI: 10.1136/bmj.1.4657.820
3. Deutch TD, Abuhamad AZ. The role of 3-dimensional ultrasonography and magnetic resonance imaging in the diagnosis of Mullerian duct anomalies: a review of the literature. *J Ultrasound Med* 2008;27:413–423 DOI: 10.7863/jum.2008.27.3.413
4. Speroff L, Glass RH, Kase NG. Development of the Mullerian system. In: Mitchell C, editor. *Clinical gynecologic endocrinology and infertility*, 6th ed. Baltimore: Lippincott, Williams & Wilkins, 1998
5. Oppelt P, von Have M, Paulsen M, et al. Female genital malformations and their associated abnormalities. *Fertil Steril* 2007;87:335 DOI: 10.1016/j.fertnstert.2006.07.1501
6. Larsen WJ. Development of the urogenital system. In: *Human embryology*. New York, NY: Churchill Livingstone, 1993; 235–279.
7. Moore KL, Persaud TV. The urogenital system: the development of the genital system. In: *The developing human: clinically oriented embryology*. 6th ed. Philadelphia, Pa: Saunders, 1998; 303.
8. Raga F, Bauset C, Remohi J, et al. Reproductive impact of congenital mullerian anomalies. *Hum Reprod* 1997;12: 2277–81. DOI: 10.1093/humrep/12.10.2277
9. Buttram VC. Mullerian anomalies and their management. *Fertil Steril* 1983; 40:159–63. DOI: 10.1016/s0015-0282(16)47230-4
10. Edwards JA, Gale RP. Camptobrachydactyly: a new autosomal dominant trait with two probable homozygotes. *Am J Hum Genet* 1972; 24:464–474.
11. Sarto GE, Simpson JL. Abnormalities of the mullerian and wolffian duct systems. *Birth Defects Orig Artic Ser* 1978; 14:37–54.
12. Jacquinet A, Millar D, Lehman A. Etiologies of uterine malformations. *Am J Med Genet A.* 2016;170:2141–2172. DOI: 10.1002/ajmg.a.37775
13. Golan A, Langer R, Bukovsky I. et al. Congenital anomalies of the mullerian system. *Fertil Steril* 1989; 51:747–755. DOI: 10.1016/s0015-0282(16)60660-x
14. Robert N, Troiano, Shirley M. Mullerian Duct Anomalies: Imaging and Clinical Issues *Radio-logy* 2004; 233:19–34 DOI: 10.1148/radiol.2331020777
15. Chan YY, Jayaprakasan K, Zamora J. et al. The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review. *Hum Reprod Update* 2011;17:761–71. DOI: 10.1093/humupd/dmr028
16. Grimbizis GF, Camus M, Tarlatzis BC. et al. Clinical implications of uterine malformations and hysteroscopic treatment results. *Hum Reprod Update.* 2001;7(2):161–74 DOI: 10.1093/humupd/7.2.161
17. American Fertility Society. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, mullerian anomalies and intrauterine adhesions. *Fertil Steril* 1988;49:944–55. DOI: 10.1016/s0015-0282(16)59942-7
18. Grimbizis GF, Gordts S, di Spiezio Sardo A, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod* 2013;28:2032–44. DOI: 10.1093/humrep/det098
19. Ludwin A, Ludwin I. Comparison of the ESHRE-ESGE and ASRM classifications of mullerian duct anomalies in everyday practice. *Hum Reprod* 2015;30:569–80. DOI: 10.1093/humrep/deu344
20. Grimbizis GF, Gordts S, di Spiezio Sardo A, et al. Reply: are the ESHRE/ESGE criteria of female genital anomalies for diagnosis of septate uterus appropriate? *Hum Reprod* 2014;29:868–9. DOI: 10.1093/humrep/deu002

Güncel Kadın Hastalıkları ve Doğum Çalışmaları

21. Mazouni C, Girard G, Deter R, et al. Diagnosis of Mullerian anomalies in adults:evaluation of practice. *Fertil Steril* 2008;89:219. DOI: 10.1016/j.fertnstert.2007.02.044
22. Rackow BW, Arici A. Reproductive performance of women with mullerian anomalies. *Curr Opin Obstet Gynecol* 2007; 19: 229–237. DOI: 10.1097/GCO.0b013e32814b0649
23. Tomazevic T, Ban-Franjez H, Ribic-Pucelj M,et al. Small uterine septum is an important risk variable for preterm birth. *Eur J Obstet Gynecol Reprod Biol* 2007; 135: 154–157. DOI: 10.1016/j.ejogrb.2006.12.001.
24. Rock JA, Schlaff WD. The obstetric consequences of uterovaginal anomalies. *Fertil Steril* 1985; 43: 681–692. DOI: 10.1016/s0015-0282(16)48548-1
25. Stein AL, March CM. Pregnancy outcome in women with mullerian duct anomalies. *J Reprod Med* 1990; 35: 411–414.
26. Valdes C, Malini S, Malinak LR. Ultrasound evaluation of female genital tract anomalies: a review of 64 cases. *Am J Obstet Gynecol* 1984;149:285. DOI: 10.1016/0002-9378(84)90228-x
27. Raga F, Bonilla-Musoles F, Blanes J. Congenital Mullerian anomalies:diagnostic accuracy of three- dimensional ultrasound. *Fertil Steril* 1996;65:523 DOI: 10.1016/s0015-0282(16)58147-3
28. Carrington BM, Hricak H, Nuruddin RN,et al. Mullerian duct anomalies: MR imaging evaluation. *Radiology* 1990; 176:715–720. DOI: 10.1148/radiology.176.3.2202012
29. Pellerito JS, McCarthy SM, Doyle MB,et al. Diagnosis of uterine anomalies: relative accuracy of MR imaging, endovaginal ultrasound, and hysterosalpingography. *Radiology* 1992; 183:795–800. DOI: 10.1148/radiology.183.3.1584936
30. Reuter KL, Daly DC, Cohen SM. Septate versus bicornuate uteri: errors in imaging diagnosis. *Radiology* 1989; 172:749–752. DOI: 10.1148/radiology.172.3.2528160
31. Devi Wold AS, Pham N, Arici A. Anatomic factors in recurrent pregnancy loss. *Semin Reprod Med.* 2006; 24:25–32. DOI: 10.1055/s-2006-931798
32. Practice Committee of the American Society for Reproductive Medicine. Uterine septum: a guideline. *Fertil Steril* 2016;106:530–40. DOI: 10.1016/j.fertnstert.2016.05.014
33. Ludwin A, Ludwin I, Banas T, Knafel A, Miedzyblocki M, Basta A. Diagnostic accuracy of sonohysterography, hysterosalpingography and diagnostic hysteroscopy in diagnosis of arcuate, septate and bicornuate uterus. *J Obstet Gynaecol Res* 2011;37:178–86. DOI: 10.1111/j.1447-0756.2010.01304.x
34. Ludwin A, Pitynski K, Ludwin I, Banas T, Knafel A. Two- and threedimensional ultrasonography and sonohysterography versus hysteroscopy with laparoscopy in the differential diagnosis of septate, bicornuate, and arcuate uteri. *J Minim Invasive Gynecol* 2013;20:90–9. DOI: 10.1016/j.jmig.2012.09.011
35. Groszmann YS, Benacerraf BR. Complete evaluation of anatomy and morphology of the infertile patient in a single visit: the modern infertility pelvic ultrasound examination. *Fertil Steril* 2016;105:1281–93. DOI: 10.1016/j.fertnstert.2016.03.026
36. Wu MH, Hsu CC, Huang KE. Detection of congenital mullerian duct anomalies using three-dimensional ultrasound. *J Clin Ultrasound* 1997; 25:487–492 DOI: 10.1002/(sici)1097-0096(199711/12)25:9<487::aid-jcu4>3.0.co;2-j
37. Kupesic S, Kurjak A. Ultrasound and Doppler assessment of uterine anomalies. In: Kupesic S, de Ziegler D, eds. *Ultrasound and infertility*. Pearl River, NY: Parthenon, 2000; 147–153
38. Economy KE, Barnewolt C, Laufer MR. A comparison of MRI and laparoscopy in detecting pelvic structures in cases of vaginal agenesis. *J Pediatr Adolesc Gynecol* 2002;15:101. DOI: 10.1016/s1083-3188(02)00136-5
39. A. Di Spiezo Sardo, M. Spinelli , C. Nappi. (2015) Current Work-Up for Screening and Diagnosing Female Genital Malformations. In: Grigoris F. Grimbizis (Ed) *Female Genital Tract Congenital Malformations*. (p:121-130) London: Springer
40. Stanheiser J, Attaran M. (2016) Müllerian Agenesis: Diagnosis, Treatment, and Future Fertility. In: S.M. Pfeifer (ed.), *Congenital Müllerian Anomalies* (p:65-78) New York: Springer

41. Brody JM, Koelliker SL, Frishman GN. Unicornuate uterus: imaging appearance, associated anomalies, and clinical implications. *AJR Am J Roentgenol.*1998;171(5):1341–7 DOI: 10.2214/ajr.171.5.9798876
42. Fedele L, Bianchi S, Agnoli B, Tozzi L, Vignali M. Urinary tract anomalies associated with unicornuate uterus. *J Urol* 1996; 155:847–848.
43. Acien P. Incidence of Mullerian defects in fertile and infertile women. *Hum Reprod* 1997;12:1372 DOI: 10.1093/oxfordjournals.humrep.a019588
44. Jayasinghe Y, Rane A, Stalewski H, Grover S. The presentation and early diagnosis of the rudimentary uterine horn. *Obstet Gynecol* 2005;105(6):1456e67 DOI: 10.1097/01.AOG.0000161321.94364.56
45. Falcone T, Gidwani G, Paraiso M, et al. Anatomical variation in the rudimentary horns of a unicornuate uterus: implications for laparoscopic surgery. *Hum Reprod* 1997;12(2):263e5. DOI: 10.1093/humrep/12.2.263
46. Heinonen PK, Saarikoski S, Pystynen P. Reproductive performance of women with uterine anomalies. Anevaluation of 182 cases. *Acta Obstet Gynecol Scand.* 1982;61(2):157–62. DOI: 10.3109/00016348209156548
47. Humphries PD, Simpson JC, Creighton SM, Hall- Craggs MA. MRI in the assessment of congenital vaginal anomalies. *Clin Radiol.* 2008;63(4):442–8. DOI: 10.1016/j.crad.2007.04.025
48. Venetis CA, Papadopoulos SP, Campo R, et al. Clinical implications of congenital uterine anomalies: a meta-analysis of comparative studies. *Reprod Biomed Online* 2014;29:665. DOI: 10.1016/j.rbmo.2014.09.006
49. Musich JR, Behrman SJ. Obstetric outcome before and after metroplasty in women with uterine anomalies. *Obstet Gynecol* 1978;52:63
50. Ghi T, Casadio P, Kuleva M, Perrone AM, Savelli L, Giunchi S, et al. Accuracy of three-dimensional ultrasound in diagnosis and classification of congenital uterine anomalies. *Fertil Steril.* 2009;92:808–13. DOI: 10.1016/j.fertnstert.2008
51. Letterie G. Surgery, assisted reproductive technology and infertility: diagnosis and management of problems in gynecologic reproductive medicine. 2nd ed. Boca Raton: CRC; 2007. p. 149–80.
52. Strassman EO. Fertility and unification of double uterus. *Fertil Steril* 1966;17:165e76. DOI: 10.1016/s0015-0282(16)35882-4
53. Lolis DE, Paschopoulos M, Makrydimas G, et al. Reproductive outcome after Strassman metroplasty in women with a bicornuate uterus. *J Reprod Med* 2005;50(5):297e301.
54. Sinha R, Mahajan C, Hegde A. Laparoscopic metroplasty for bicornuate uterus. *J Minim Invasive Gynecol* 2006;13(1):70e3. DOI: 10.1016/j.jmig.2005.11.004
55. Haddad B, Louis-Sylvestre C, Poitout P, Paniel BJ. Longitudinal vaginal septum: a retrospective study of 202 cases. *Eur J Obstet Gynecol Reprod Biol.*1997;74:197–9. DOI: 10.1016/s0301-2115(97)00105-x
56. Rikken J. F. W , C. R. Kowalik CR, Emanuel MH, et al. The randomised uterine septum transection trial (TRUST): design and protocol *BMC Women's Health* 2018;18:163 DOI:10.1186/s12905-018-0637-6
57. Fedele L, Bianchi S, Marchini M, et al. Ultrastructural aspects of endometrium in infertile women with septate uterus. *Fertility & Sterility.* 1996;65(4):750–2.
58. Dabirashrafi H, Bahadori M, Mohammad K, et al. Septate uterus: new idea on the histologic features of the septum in this abnormal uterus. *American Journal of Obstetrics & Gynecology.* 1995;172(1 Pt 1):105–7. DOI: 10.1016/0002-9378(95)90093-4
59. Du H, Taylor HS. Molecular regulation of mullerian development by Hox genes. *Ann N Y Acad Sci.*2004;1034:152–65. DOI: 10.1196/annals.1335.018.
60. Braun P, Grau FV, Pons RM, Enguix DP. Is hysterosalpingography able to diagnose all uterine malformations correctly? A retrospective study. *Eur J Radiol* 2005;53:274–9. DOI: 10.1016/j.ejrad.2004.04.004

61. Bermejo C, Martínez Ten P, Cantarero R, et al. Three-dimensional ultrasound in the diagnosis of Mullerian duct anomalies and concordance with magnetic resonance imaging. *Ultrasound Obstet Gynecol* 2010;35:593–601. DOI: 10.1002/uog.7551
62. Mollo A, De Franciscis P, Colacurci N, et al. Hysteroscopic resection of the septum improves the pregnancy rate of women with unexplained infertility: a prospective controlled trial. *Fertil Steril* 2009;91(6):2628e31. DOI: 10.1016/j.fertnstert.2008.04.011
63. Gergolet M, Campo R, Verdenik I, et al. No clinical relevance of the height of fundal indentation in subseptate or arcuate uterus: a prospective study. *Reprod Biomed Online* 2012;24:576e82. DOI: 10.1016/j.rbmo.2012.01.025
64. Tomažević T, Ban-Frangež H, Virant-Klun I, et al. Septate, subseptate and arcuate uterus decrease pregnancy and live birth rates in IVF/ICSI. *Reprod Biomed Online*. 2010;21(5):700–5. DOI: 10.1016/j.rbmo.2010.06.028
65. Valle RF, Ekpo GE. Hysteroscopic metroplasty for the septate uterus: review and meta-analysis. *J Minim Invasive Gynecol*. 2013;20:22–42 DOI: 10.1016/j.jmig.2012.09.010
66. Paradisi R, Barzanti R, Fabbri R. The techniques and outcomes of hysteroscopic metroplasty. *Curr Opin Obstet Gynecol*. 2014;26(4):295–301. DOI:10.1097/GCO.0000000000000077
67. Ubeda B, Paraira M, Alert E. Hysterosalpingography: spectrum of normal variants and non-pathologic findings. *AJR* 2001; **177**: 131–135. DOI: 10.2214/ajr.177.1.1770131
68. Lin PC, Bhatnagar KP, Nettleton GS et al. Female genital anomalies affecting reproduction. *Fertil Steril* 2002;78:899–915 DOI: 10.1016/s0015-0282(02)03368-x
69. Di Spiezio Sardo A, Florio P, Nazzaro G, et al. Hysteroscopic outpatient metroplasty to expand dysmorphic uteri (HOME-DU technique): a pilot study. *Reprod Biomed Online* 2015; 30: 166–174. DOI: 10.1016/j.rbmo.2014.10.016.
70. Fernandez H, Garbin O, Castaigne V, et al. Surgical approach to and reproductive outcome after surgical correction of a T-shaped uterus. *Hum Reprod* 2011; 26: 1730–1734. DOI:10.1093/humrep/der056
71. Ahmadi F, Zafarani F, Shahrzad GS. Hysterosalpingographic Appearances of Female Genital Tract Tuberculosis: Part II: Uterus. *Int J Fertil Steril* 2014; 8: 13–20.
72. Puente JM, Fabris A, Patel J et al. Adenomyosis in infertile women: prevalence and the role of 3D ultrasound as a marker of severity of the disease. *Reprod Biol Endocrinol* 2016; 14: 60. DOI: 10.1186/s12958-016-0185-6.
73. Ludwin A, Coelho Neto M.A, Ludwin I. et al Congenital Uterine Malformation by Experts (CUME): diagnostic criteria for T-shaped uterus *Ultrasound Obstet Gynecol* 2020; 55: 815–829. DOI: 10.1002/uog.20845
74. Goldberg JM, Falcone T. Effect of diethylstilbestrol on reproductive function. *Fertil Steril*. 1999;72:1-7. DOI: 10.1016/s0015-0282(99)00153-3.
75. Meier R, De Bruyn C, Mestdagh G, et al. Reproductive outcomes after hysteroscopic management of dysmorphic uterus: report of 100 cases. Selected abstract ESGE 23rd annual congress, Brussels. 2014.