

# Bölüm 64

## ENDOMETRİOZİS

Özlem ERTEN<sup>1</sup>

### GİRİŞ

Endometriozis hormonlara duyarlı endometrial gland ve stromanın uterin kavite ve kas dokusu dışında olması durumu olarak tanımlanmaktadır (1).

Endometriozis estrojen bağımlı, inflamatuvar süreçlerin baskın olduğu bir durumdur. Reprodüktif dönemde daha belirgin olmakla birlikte premenarşial ve postmenopozal dönemde de görülmektedir. Benign bir hastalık olarak kabul edilmekle birlikte implantasyon, proliferasyon ve neovaskülarizasyon gibi malign hastalıklardaki davranışa benzer bir patoloji sergilemektedir. Asemptomatik bir hal ile akut batın durumu arasında geniş bir semptom çeşitliliğinin görülebildiği ciddi bir jinekolojik patolojidir.

Pelvis dışı dokularda da görülmekle birlikte en sık yerleşimi pelvistedir. Sıklık sırasına göre en sık overler, anterior ve posterior kul de sak, posterior broad ligamentler, uterus, tubalar, sigmoid kolon, apendiks ve round ligamentlarda görülmektedir. Pelvisteki yerleşim gösteren lezyonlar büyüklük ve mikroskopik incelemeye göre 3 alt grupta sınıflandırılmaktadır. Bu patolojiler ayrı ayrı olabileceği gibi tümü birlikte de bulunabilmektedir (1).

1. Yüzeysel peritoneal implantlar; ektopik endometrial doku stroma ve gland dışında fibröz doku, kan ve kistik komponentler de içerebildiğinden eritrosit yıkımına bağlı inflamatuvar sürece bağlı pigmente histiosit ve hemosiderin yüklü makrofajlar olduğu gösterilmiştir. Bu da yüzeysel perito-

neal implantlarda mavi mor ve eskidikçe kahverengi renk değişikliklerine neden olmaktadır (2).

2. Ovarian kistik oluşumlar (endometrioma); ektopik endometrial dokunun overde yerleşmesi durumudur. dublike ovarian parankim ile çevrili olduğundan kanama olduğunda ovarian hematoma neden olur. Olguların üçte ikisi bilateraldir. Fizyolojik hemorajik ovarian kistlerin aksine endometriomalar tipik olarak fibrotik kist duvarı ve yüzeysel adezyonlar da barındırır. İçeriği çikolata renkli sıvıyla dolu olduğundan çikolata kisti olarak da adlandırılmaktadır. Adezyonların varlığı ve çikolata renkli sıvıdaki hemosiderin yüklü makrofajların olması histolojik olarak endometriozisi göstermektedir (2).

3. Derin infiltratif endometriozis (DİE); solid endometrial dokunun peritonun 5mm den fazal derininde yerleşmesi olarak tanımlanmaktadır. Mesane, üreterler, uterosakral ligament, douglasın kısmi ya da tamamen obliterasyonu, rektovajinal septum tutlumunu da içeren şiddetli bir formudur. anatomik yapıların infiltrasyonu nedeniyle organ fonksiyonlarının kaybına ve hayat kalitesini etkileyen ciddi ağrıya neden olabilmektedir (3).

### TARİHÇE

Bugün için endometriozis olarak tanımlanan peritoneal lezyonlar, tıp literatüründe ilk olarak yaklaşık 300 yıl önce 17-18. yüzyıllarda Knapp tarafından tanımlanmıştır. Endometriozis hakkındaki en eski yayın ise 1690 yılında Alman hekim Daniel

yeklinikleri.com/article/tr-turkiye-endometriyozis-tani-ve-yonetim-kilavuzu-74863.html).

**Anahtar Kelimeler:** Endometriozis, medikal tedavi, cerrahi tedavi

### KAYNAKÇA

- Nisolle M, Donnez J. Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. *Fertil Steril* 1997;68:585-96.
- Montanari E, Dauser B, Keckstein J, Kirchner E, Nemeth Z, Hudelist G. Association between disease extent and pain symptoms in patients with deep infiltrating endometriosis. *Reprod Biomed Online*. 2019 Jun 19. pii: S1472-6483(19)30593-0. doi: 10.1016/j.rbmo.2019.06.006).
- Brosens IA, Puttemans PJ, Deprest J. The endoscopic localization of endometrial implants in the ovarian chocolate cyst. *Fertil Steril* 1994; 61:1034.
- Benagiano G, Brosens I. Who identified endometriosis? *Fertility and Sterility* 2011;95(1): 13-16.
- Suwandinata F.S. Endometriosis-associated Pain Social Impact and Information through Internet Survey. Ed; Suwandinata F.S, 1st edition. Vvb Lauferweiler Verlag. Germany. 2006; 1-90.
- Santanam N, Kavtaradze N, Murphy A, Dominguez C, Parthasarathy S. Antioxidant supplementation reduces endometriosis related pelvic pain in humans. *Translational Research* 2012; 1-7.
- Cramer DW, Missmer SA. The epidemiology of endometriosis. *Ann N Y Acad Sci* 2002; 955: 11-22.
- Chatman DL, Ward AB. Endometriosis in adolescents. *J Reprod Med* 1982; 27:156.
- Goldstein DP, deCholnoky C, Emans SJ, Leventhal JM. Laparoscopy in the diagnosis and management of pelvic pain in adolescents. *J Reprod Med* 1980; 24:251.
- Reese KA, Reddy S, Rock JA. Endometriosis in an adolescent population: the Emory experience. *J Pediatr Adolesc Gynecol* 1996; 9:125.
- Laufer MR, Goitein L, Bush M, et al. Prevalence of endometriosis in adolescent girls with chronic pelvic pain not responding to conventional therapy. *J Pediatr Adolesc Gynecol* 1997; 10:199.
- Giudice LC. Clinical practice. Endometriosis. *N Engl J Med* 2010; 362:2389.
- Harris HR, Wieser F, Vitonis AF, et al. Early life abuse and risk of endometriosis. *Hum Reprod* 2018; 33:1657.
- Missmer SA, Hankinson SE, Spiegelman D, et al. Incidence of laparoscopically confirmed endometriosis by demographic, anthropometric, and lifestyle factors. *Am J Epidemiol* 2004; 160:784.
- Parazzini F, Cipriani S, Bianchi S, et al. Risk factors for deep endometriosis: a comparison with pelvic and ovarian endometriosis. *Fertil Steril* 2008; 90:174.
- Kavoussi SK, Odenwald KC, As-Sanie S, Lebovic DI. Incidence of ovarian endometrioma among women with peritoneal endometriosis with and without a history of hormonal contraceptive use. *Eur J Obstet Gynecol Reprod Biol* 2017; 215:220.
- Sampson JA. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obst Gynecol* 1927; 14: 442- 469.
- Bergqvist A, Ferno M, Skoog L. Quantitative enzyme immunoassay and semiquantitative immunohistochemistry of oestrogen and progesterone receptors in endometriotic tissue and endometrium. *J Clin Pathol* 1997; 50: 496-500.
- Blumenkrantz MJ, Gallagher N, Bashore RA, Tenckhoff H. Retrograde menstruation in women undergoing chronic peritoneal dialysis. *Obstet Gynecol* 1981; 57: 667-670.
- Simpson JL, Elias S, Malinak LR, Buttram VC, Jr. Heritable aspects of endometriosis. I. Genetic studies. *Am J Obstet Gynecol* 1980; 137: 327-331.
- Stefansson H, Geirsson RT, Steinthorsdottir V, Jonsson H, Manolescu A, Kong A, Ingadottir G, Gulcher J, Stefansson K. Genetic factors contribute to the risk of developing endometriosis. *Hum Reprod* 2002; 17: 555-559.
- Berkkanoglu M, Arici A. Immunology and endometriosis. *Am J Reprod Immunol* 2003; 50: 48-59.
- Ulukus M, Arici A. Immunology of endometriosis. *Minerva Ginecol* 2005; 57: 237- 248.
- Liu DTY, Hitchcock A. Endometriosis: its association with retrograde menstruation, dysmenorrhea, and tubal pathology. *BrJ Obst Gynaecol* 1986; 93: 859.
- Blumenkrantz MJ, Gallagher N, Bashore RA, Tenckhoff H. Retrograde menstruation in women undergoing chronic peritoneal dialysis. *Obstet Gynecol* 1981; 57: 667-670.
- Olive DL, Henderson DY. Endometriosis and mullerian anomalies. *Obstet Gynecol* 1987; 69: 412.
- Darrow SL, Vena JE, Batt RE, Zielezny MA, Michalek AM, Selman S. Menstrual cycle characteristics and the risk of endometriosis. *Epidemiology* 1993; 4: 135.
- Suginami H. A reappraisal of the coelomic metaplasia theory by reviewing endometriosis occurring in unusual sites and instances. *Am J Obstet Gynecol* 1991; 165: 214.
- Foster DC, Stern JL, Buscema J, Rock JA, Woodruff JD. Pleural and parenchymal pulmonary endometriosis. *Obstet Gynecol* 1981; 58: 552.
- Ueki M. Histologic study of endometriosis and examination of lymphatic drainage in and from the uterus. *Am J Obstet Gynecol* 1991; 165: 201.
- Mathur S, Garza DE, Smith LF. Endometrial autoantigens eliciting immunoglobulin IgG, IgA, and IgM responses in endometriosis. *Fertil Steril* 1990;54(1):56-63.
- Badawy SZ, Cuenca V, Stitzel A, Jacobs RD, Tomar RH. Autoimmune phenomena in infertile patients with endometriosis. *Obstet Gynecol* 1984;63(3):271-5.
- Gleicher N, el-Roeiy A, Confino E, Friberg J. Is endometriosis an autoimmune disease? *Obstet Gynecol* 1987;70(1):115-22.
- Marquardt RM, Kim TH, Shin JH, Jeong JW. Progesterone and Estrogen Signaling in the Endometrium: What Goes Wrong in Endometriosis? *Int J Mol Sci*. 2019 Aug 5;20(15). pii: E3822. doi: 10.3390/ijms20153822.
- Rier SE, Martin DC, Bowman RE, Dmowski WP, Becker JL. Endometriosis in rhesus monkeys (*Macaca mulatta*) following chronic exposure to 2,3,7,8-tetrachlorodibenzo p-dioxin. *Fundam Appl Toxicol* 1993; 21: 433-41.

36. Whitlock JP, Jr. Genetic and molecular aspects of 2,3,7,8-tetrachlorodibenzo-pdioxin action. *Annu Rev Pharmacol Toxicol* 1990 ; 30: 251-77.
37. Hadfield RM, Manek S, Weeks DE, Mardon HJ, Barlow DH, Kennedy SH. Linkage and association studies of the relationship between endometriosis and genes encoding the detoxification enzymes GSTM1, GSTT1 and CYP1A1. *Mol Hum Reprod* 2001; 7: 1073-8.
38. Coxhead D, Thomas EJ. Familial inheritance of endometriosis in a British population: a case control study. *J Obstet Gynecol* 1993; 13: 42-46.
39. Ayranci H, Dogan H, Ceylaner S, Dilbaz B, Goktolga U, Karasu Y. Are Endothelial Nitric Oxide Synthase Gene -894 G>T and 786 T>C polymorphisms risk factors for endometriosis? XX. FIGO World Congress of Gynecology and Obstetrics. Roma, Italya, 7-12 Ekim 2012.
40. Vercellini P, Parazzini F, Bolis G, Carinelli S, Dindelli M, Vendola N, Luchini L, Endometriosis and ovarian cancer. *Am J Obst Gyn* 1993; 169: 181-2.
41. Brinten LA, Gridley G, Persson I, Baron J, Cancer risk after a hospital discharge diagnosis of endometriosis. *Am J Obst Gyn* 1997; 176: 572-9.
42. Goumenou AG, arvanitis DA, Matalliotakis IM, Koumantakis EE, Spandidos DA, Microsatellite DNA assays reveal an allelic imbalance in p 16 (Ink4), GALT, p53, and APOA2 loci in patients with endometriosis. *Fertil Steril* 2001; 75: 160-5.
43. Sain e la Cuesta R, Izquierdo M, Canamero M, Granizo JJ, Manzarbeitia , Increased prevalence of p53 overexpression from typical endometriosis to atypical endometriosis and ovarian cancer associated with endometriosis. *Eur J Obstet Gyn Reprod Biol* 2004; 13: 87-93.
44. Jiang X, Hitchcock A, Bryan EJ, Watson RH; Englefield P, Thomas EJ, Microsatellite analysis of endometriosis reveals loss of heterozygosity at candidate ovarian tumor suppressor gene loci. *Cancer Res* 1996; 56: 3534-9.
45. Jimbo H, Oshikawa H, Onda T, Yasugi T, Sakamoto A, Taketani Y, Prevalence of ovarian endometriosis in epithelial ovarian cancer *Int J Gyn Obstet* 1997;59: 245-50.
46. Obata K, Morland SJ, Watson RH, Hitchcock A, Chevenix G, Thomas EJ, Campbell IG, Frequent PTEN/MMAC mutations in endometrioid but not serous or mucinous epithelial ovarian tumors. *Cancer Res* 1998; 58: 2095-7.
47. Serafini M, Del Rio D. Understanding the association between dietary antioxidants, redox status and disease: is the total antioxidant capacity the right tool?. *Redox Report* 2004; 9: 145-154.
48. Van Langendonck A, Casanas-Roux F, Donnez J. Oxidative stress and peritoneal endometriosis. *Fertil Steril* 2002;77: 861-70.
49. Agarwal A, Sharma RK, Nallella KP, Thomas AJ Jr, Alvarez JG, Sikka SC. Reactive oxygen species as an independent marker of male factor infertility. *Fertility and Sterility* 2006; 86: 878-885.
50. Erten OU, Ensari TA, Dilbaz B, Cakiroglu H, Altinbas SK, Çaydere M, Goktolga U. Vitamin C is effective for the prevention and regression of endometriotic implants in an experimentally induced rat model of endometriosis. *Taiwan J Obstet Gynecol*. 2016 Apr;55(2):251-7. doi: 10.1016/j.tjog.2015.07.004.
51. Hickey M, Ballard K, Farquhar C. Endometriosis. *BMJ* 2014; 348:g1752.
52. Sinaii N, Plumb K, Cotton L, et al. Differences in characteristics among 1,000 women with endometriosis based on extent of disease. *Fertil Steril* 2008; 89:538.
53. Givens V, Mitchell GE, Harraway-Smith C, et al. Diagnosis and management of adnexal masses. *Am Fam Physician* 2009; 80:815.
54. Hansen KE, Kesmodel US, Baldursson EB, et al. Visceral syndrome in endometriosis patients. *Eur J Obstet Gynecol Reprod Biol* 2014; 179:198.
55. Wang S, Li XC, Lang JH. Cervical endometriosis: clinical character and management experience in a 27-year span. *Am J Obstet Gynecol* 2011; 205:452.e1.
56. Berlanda N, Vercellini P, Carmignani L, et al. Ureteral and vesical endometriosis. Two different clinical entities sharing the same pathogenesis. *Obstet Gynecol Surv* 2009; 64:830.
57. Koninckx PR, Meuleman C, Demeyere S, et al. Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain. *Fertil Steril* 1991; 55:759.
58. Horton JD, Dezee KJ, Ahnfeldt EP, Wagner M. Abdominal wall endometriosis: a surgeon's perspective and review of 445 cases. *Am J Surg* 2008; 196:207.
59. Hwang SM, Lee CW, Lee BS, Park JH. Clinical features of thoracic endometriosis: A single center analysis. *Obstet Gynecol Sci* 2015; 58:223.
60. Vercellini P, Trespidi L, De Giorgi O, et al. Endometriosis and pelvic pain: relation to disease stage and localization. *Fertil Steril* 1996; 65:299.
61. Stegmann BJ, Sinaii N, Liu S, et al. Using location, color, size, and depth to characterize and identify endometriosis lesions in a cohort of 133 women. *Fertil Steril* 2008; 89:1632.
62. Wykes CB, Clark TJ, Khan KS. Accuracy of laparoscopy in the diagnosis of endometriosis: a systematic quantitative review. *BJOG* 2004; 111:1204.
63. Husby GK, Haugen RS, Moen MH. Diagnostic delay in women with pain and endometriosis. *Acta Obstet Gynecol Scand* 2003; 82:649.
64. Staal AH, van der Zanden M, Nap AW. Diagnostic Delay of Endometriosis in the Netherlands. *Gynecol Obstet Invest* 2016; 81:321.
65. Arıcı A, Örnek T, Ulukuş M. Endometriosis. *Reprodükatif Endokrinoloji ve İnfertilite*. Ed; Çolgar U. Birinci baskı, İstanbul Medikal Yayıncılık, İstanbul. 2006;109-129.
66. Ozakşit G, Çağlar T, Çiçek N, Kuşçu E, Batioğlu S, Gökmen O. Serum CA 125 levels before, during and after treatment for endometriosis. *Int J Gynaecol Obstet*. 1995;50(3): 269- 73.
67. Stratton P, Winkel C, Premkumar A, Chow C, Wilson J, Hearn-Stokes R, Heo S, Merino M, Nieman LK. Diagnostic accuracy of laparoscopy, magnetic resonance imaging, and histopathologic examination for the detection of endometriosis. *Fertil Steril* 2003; 79: 1078.
68. Dunselman GA, Vermeulen N, Becker C, Calhaz-Jorge C, D'Hooghe T, De Bie B, et al; European Society of Human Reproduction and Embryology. ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014;29(3):400-12.
69. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. *Fertil Steril* 2002;77(6):1148-55.

70. Sallam HN, Garcia-Velasco JA, Dias S, Arici A. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. *Cochrane Database Syst Rev* 2006;(1):CD004635.
71. Martin DC, Ahmic R, El-Zeky FA, et al. Increased histologic confirmation of endometriosis. *J Gynecologic Surg* 1990; 6:275.
72. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril*. 1997; 67(5): 817- 21.
73. Roman H. Guidelines for the management of painful endometriosis. *J Gynecol Obstet Biol Reprod (Paris)*. 2007;36(2):141-50.
74. Vural B (Çeviri). Endometriosis. *Klinik Jinekolojik Endokrinoloji ve İnfertilite*. Ed; Speroff L, Fritz M.A. Çeviri Ed; Erk A, Günalp S. Yedinci baskı, Güneş Tıp Kitabevleri Öncü Basımevi; Ankara. 2007; 1103-1124.
75. Adamson GD, Pasta DJ. Surgical treatment of endometriosis- associated with infertility: meta-analysis compared with survival analysis. *Am J Obstet Gynecol* 1994; 171: 1488.
76. D'Hooghe TM, Hill JA. Endometriosis. In Berek & Novak's *Gynecology*. Ed; Berek JS. 14th ed. Lippincot Williams and Wilkins Inc. Philadelphia USA. 2007; 29: 1161-1170.
77. Guo SW. The Epigenetics of Endometriosis. *Tollefsbol T, ed. Epigenetics of Human Disease, 1 st edition*. USA: Elsevier Inc; 2012; 443-469.
78. Dunselman GA, Vermeulen N, Becker C, Calhaz- Jorge C, D'Hooghe T, De Bie B, et al; European Society of Human Reproduction and Embryology. ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014;29(3):400-12.
79. Cheong YC, Smotra G, Willimas AC. Non-surgical interventions for the management of chronic pelvic pain. *Cochrane Database Syst Rev* 2014;(3):CD008797.
80. Xu XW, Zhang YW, He FF, Wang LD, Guan YT, Sun J, Lin M, Hu Y. Evaluation of levonorgestrel-releasing intrauterine system in treatment of recurrent endometriosis after conservative surgery. *Zhonghua Fu Chan Ke Za Zhi* 2011; 46(4):250-4.
81. Bayoglu Tekin Y, Dilbaz B, Altinbas SK, Dilbaz S. Postoperative medical treatment of chronic pelvic pain related to severe endometriosis: levonorgestrel-releasing intrauterine system versus gonadotropin-releasing hormone analogue. *Fertil Steril*. 2011; 95(2):492-6.
82. Cosson M, Querleu D, Donnez J, Madelenat P, Konincks P, Audebert A, Manhes H. Dienogest is as effective as triptorelin in the treatment of endometriosis after laparoscopic surgery; results of a prospective, multicenter, randomized study. *Fertil Steril* 2002; 77(4): 684-692.
83. Strowitzki T, Marr J, Gerlinger C, Faustmann T, Seitz C. Detailed analysis of a randomized, multicenter, comparative trial of dienogest versus leuprolide acetate in endometriosis. *Int J Gynaecol Obstet*. 2012;117(3):228-33.
84. Dawood MY, Ramos J, Khan-Dawood FS. Depot leuprolide acetate versus danazol for treatment of pelvic endometriosis: changes in vertebral bone mass and serum estradiol and calcitonin. *Fertil Steril* 1995; 63: 1177.
85. Revilla R, Revilla M, Hernandez ER, Villa LF, Varela L, Rico H. Evidence that the loss of bone mass induced by GnRH agonists is not totally recovered. *Maturitas* 1995; 22: 145.
86. Ripps BA, VanGilder K, Minhas B, Welford M, Mamish Z. Alendronate for the prevention of bone mineral loss during GnRH agonist therapy. *J Reprod Med* 2003; 48: 761.
87. Palomba S, Orio F, Morelli M, Russo T, Pellicano M, Zupi E, Lombardi G, Nappi C, Panici PL, Zullo F. Raloxifene administration in premenopausal woman with uterine leiomyomas: a pilot study. *J Clin Endocrinol Metab* 2002; 87: 3603.
88. Batzer FR. GnRH analogs: options for endometriosis-associated pain treatment. *J Minim Invasive Gynecol*. 2006 Nov-Dec;13(6):539-45.
89. Küpker W, Felberbaum RE, Krapp M, Schill T, Malik E, Diedrich K. Use of GnRH antagonists in the treatment of endometriosis. *Reprod Biomed Online*. 2002; 5(1):12-6.
90. Vignali M, Infantino M, Matrone R, Chiodo I, Somigliana E, Busacca M, Viganò P. Endometriosis: novel etiopathogenetic concepts and clinical perspectives. *Fertil Steril*. 2002 Oct; 78(4): 665-78.
91. Ebert AD, Bartley J, David M. Aromatase inhibitors and cyclooxygenase-2 (COX- 2) inhibitors in endometriosis: new questions--old answers? *Eur J Obstet Gynecol Reprod Biol*. 2005 Oct 1;122(2):144-50.
92. Ferrero S, Gillott DJ, Venturini PL, Remorgida V. Use of aromatase inhibitors to treat endometriosis-related pain symptoms: a systematic review. *Reprod Biol Endocrinol* 2011;9:89.