

## Bölüm 5

# ENDOKRİN HASTALIKLAR VE JİNEKOLOJİK KANAMA

**Meryem CEYHAN<sup>1</sup>**

## GİRİŞ

Jinekolojik kanamalar kadın genital bölgesinde çoğunlukla vajinal kanama sıkâyeti olarak kendini gösteren abnormal kanamalardır. Genelde kanamanın kaynağı uterus olmakla birlikte kanama üst genital trakt organlarından (korpus uteri, fallop tüpü, overler) ya da alt genital trakt organlarının (serviks, vajina, vulva) birinden kaynaklanabilir (1). Kanamanın kaynağı üretra, mesane, anüs, barsak gibi non-jinekolojik de olabilir. Ayırıcı tanıda bunlar da dikkate alınmalıdır. (Tablo: 1) Jinekolojik kanama nedenleri yaş gruplarına göre farklılık göstermektedir. (Tablo:2) (2)

Anormal uterin kanama terimi normal menstrüasyondan sıklık, düzен, süre ve miktar bakımından tüm farklılıklarını içine alan, ara kanamaların da dahil olduğu genel bir tanımlamadır (3). AUK jinekoloji polikliniklerine başvuran her üç kadından birinin şikayeti olup yaygın bir jinekolojik hastalıktır (4). Anormal uterin kanamalar çok çeşitli lokal ve sistemik hastalıklar veya ilaçlarla ilişkili olabilir. En sık sebepler myoma uteri, endometrial polipler, adenomyozis, sezaryen skar defekti, arterio-venöz malformasyon gibi yapısal bozukluklar, ovulatuar disfonksiyonlar, kanama bozuklukları, neoplaziler (endometrial hiperplazi, endometrium kanseri, uterin sarkomlar), endometrit gibi enfeksiyonlar ya da iyatrojenik (antikoagülanlar, oral kontraseptifler, rahim içi araçlar) olabilir.

<sup>1</sup> Uzman Doktor, Ankara Şehir Hastanesi, meryem.u.ceyhan@gmail.com

## **REFERANSLAR**

1. Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol* 2012; 120:197.
2. APGO educational series on women's health issues. Clinical management of abnormal uterine bleeding. Association of Professors of Gynecology and Obstetrics, May 2002.
3. Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Semin Reprod Med* 2011; 29:383.
4. Spencer CP, Whitehead MI. Endometrial assessment re-visited. *Br J Obstet Gynaecol* 1999; 106:623.
5. Munro MG, Critchley HO, Broder MS, et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011; 113:3.
6. Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol* 2012; 120:197. Reaffirmed 2016.
7. Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011; 113:3. Illustration used with the permission of Elsevier Inc.
8. 2020 UpToDate, Inc. and/or its affiliates Graphic: Causes of ovulatory dysfunction.
9. Gray SH, French A, Emans SJ. Abnormal uterine bleeding in the adolescent. In: Emans, Laufer, Goldstein's Pediatric & Adolescent Gynecology, 7th ed, Emans SJ, Laufer MR, DiVasta AD (Eds), Wolters Kluwer, Philadelphia 2020. p.418.
10. Donnez J. Menometrorrhagia during the premenopause: an overview. *Gynecol Endocrinol* 2011; 27 Suppl 1:1114.
11. Berga SL. Disordered folliculogenesis during the menopausal transition: explaining chaos. *Menopause* 2009; 16:11.
12. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2013; 98:4565.
13. Teede HJ, Misso ML, Costello MF, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertil Steril* 2018; 110:364.
14. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod* 2004; 19:41.
15. Ehrmann DA. Polycystic ovary syndrome. *N Engl J Med* 2005; 352:1223.
16. Azziz R, Woods KS, Reyna R, et al. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab* 2004; 89:2745.
17. Gottschau M, Kjaer SK, Jensen A, et al. Risk of cancer among women with polycystic ovary syndrome: a Danish cohort study. *Gynecol Oncol* 2015; 136:99.
18. Krassas GE, Pontikides N, Kaltsas T, et al. Disturbances of menstruation in hypothyroidism. *Clin Endocrinol (Oxf)* 1999; 50:655.
19. Burrow G. Thyroid diseases. In: Medical complications during pregnancy, 2nd, Burrow GN, Ferri's TF (Eds), WB Saunders, Philadelphia 1982. p. 187.
20. Honbo KS, van Herle AJ, Kelett KA. Serum prolactin levels in untreated primary. Hypothyroidism. *Am J Med* 1978; 64: 782.
21. Lado-Abeal J, Rodriguez-Arnau J, Newell-Price JD, et al. Menstrual abnormalities in women with Cushing's disease are correlated with hypercortisolism rather than raised circulating androgen levels. *J Clin Endocrinol Metab* 1998; 83:3083.
22. Penezić Z, Zarković M, Vujović S, et al. Gonadotropin pulsatility in Cushing's syndrome compared with polycystic ovary syndrome. *Gynecol Endocrinol* 2005; 20:150.

23. Berek JS, Hacker NF. Berek & Hacker's Gynecologic Oncology, 6th edition, Wolters Kluwer, Philadelphia 2015.
24. Zanagnolo V, Pasinetti B, Sartori E. Clinical review of 63 cases of sex cord stromal tumors. *Eur J Gynaecol Oncol* 2004; 25:431.
25. Fassnacht M, Libé R, Kroiss M, Allolio B. Adrenocortical carcinoma: a clinician's update. *Nat Rev Endocrinol* 2011; 7:323.
26. Cundy TF, Butler J, Pope RM, et al. Amenorrhoea in women with non-alcoholic chronic liver disease. *Gut* 1991; 32:202.
27. Burra P, Germani G, Masier A, et al. Sexual dysfunction in chronic liver disease: is liver transplantation an effective cure? *Transplantation* 2010; 89:1425.
28. Santoro N, Filicori M, Crowley WF Jr. Hypogonadotropic disorders in men and women: diagnosis and therapy with pulsatile gonadotropin-releasing hormone. *Endocr Rev* 1986; 7:11.
29. Perkins RB, Hall JE, Martin KA. Neuroendocrine abnormalities in hypothalamic amenorrhea: spectrum, stability, and response to neurotransmitter modulation. *J Clin Endocrinol Metab* 1999; 84:1905.
30. Tyson JE, Hwang P, Guyda H, Friesen HG. Studies of prolactin secretion in human pregnancy. *Am J Obstet Gynecol* 1972; 113:14.
31. Kleinberg DL, Noel GL, Frantz AG. Galactorrhea: a study of 235 cases, including 48 with pituitary tumors. *N Engl J Med* 1977; 296:589.
32. Alexander JM, Biller BM, Bikkal H, et al. Clinically nonfunctioning pituitary tumors are monoclonal in origin. *J Clin Invest* 1990; 86:336.
33. Herman V, Fagin J, Gonsky R, et al. Clonal origin of pituitary adenomas. *J Clin Endocrinol Metab* 1990; 71:1427.
34. Corenblum B, Sirek AM, Horvath E, et al. Human mixed somatotrophic and lactotrophic pituitary adenomas. *J Clin Endocrinol Metab* 1976; 42:857.
35. Mindermann T, Wilson CB. Age-related and gender-related occurrence of pituitary adenomas. *Clin Endocrinol (Oxf)* 1994; 41:359.
36. Prosser PR, Karam JH, Townsend JJ, Forsham PH. Prolactin-secreting pituitary adenomas in multiple endocrine adenomatosis, type I. *Ann Intern Med* 1979; 91:41.
37. Walker JD, Grossman A, Anderson JV, et al. Malignant prolactinoma with extracranial metastases: a report of three cases. *Clin Endocrinol (Oxf)* 1993; 38:411.
38. Petakov MS, Damjanović SS, Nikolić-Durović MM, et al. Pituitary adenomas secreting large amounts of prolactin may give false low values in immunoradiometric assays. The hook effect. *J Endocrinol Invest* 1998; 21:184.
39. St-Jean E, Blain F, Comtois R. High prolactin levels may be missed by immunoradiometric assay in patients with macroadenomas. *Clin Endocrinol (Oxf)* 1996; 44:305.
40. Molitch ME. Drugs and prolactin. *Pituitary* 2008; 11:209.
41. Ajmal A, Joffe H, Nachtigall LB. Psychotropic-induced hyperprolactinemia: a clinical review. *Psychosomatics* 2014; 55:29.
42. Kearns AE, Goff DC, Hayden DL, Daniels GH. Risperidone-associated hyperprolactinemia. *Endocr Pract* 2000; 6:425.
43. Newey PJ, Gorvin CM, Cleland SJ, et al. Mutant prolactin receptor and familial hyperprolactinemia. *N Engl J Med* 2013; 369:2012.
44. Martin TL, Kim M, Malarkey WB. The natural history of idiopathic hyperprolactinemia. *J Clin Endocrinol Metab* 1985; 60:855.
45. Sluijmer AV, Lappöhn RE. Clinical history and outcome of 59 patients with idiopathic hyperprolactinemia. *Fertil Steril* 1992; 58:72.
46. Murdoch FE, Byrne LM, Ariazi EA, et al. Estrogen receptor binding to DNA: affinity for non-palindromic elements from the rat prolactin gene. *Biochemistry* 1995; 34:9144.
47. Malayer JR, Gorski J. The role of estrogen receptor in modulation of chromatin conformation in the 5' flanking region of the rat prolactin gene. *Mol Cell Endocrinol* 1995; 113:145.

48. Honbo KS, van Herle AJ, Kellett KA. Serum prolactin levels in untreated primary hypothyroidism. *Am J Med* 1978; 64:782.
49. Groff TR, Shulkin BL, Utiger RD, Talbert LM. Amenorrhea-galactorrhea, hyperprolactinemia, and suprasellar pituitary enlargement as presenting features of primary hypothyroidism. *Obstet Gynecol* 1984; 63:865.
50. Snyder PJ, Jacobs LS, Utiger RD, Daughaday WH. Thyroid hormone inhibition of the prolactin response to thyrotropin-releasing hormone. *J Clin Invest* 1973; 52:2324.
51. Kavanagh-Wright L, Smith TP, Gibney J, McKenna TJ. Characterization of macroprolactin and assessment of markers of autoimmunity in macroprolactinaemic patients. *Clin Endocrinol (Oxf)* 2009; 70:599.
52. Leslie H, Courtney CH, Bell PM, et al. Laboratory and clinical experience in 55 patients with macroprolactinemia identified by a simple polyethylene glycol precipitation method. *J Clin Endocrinol Metab* 2001; 86:2743.
53. Gibney J, Smith TP, McKenna TJ. Clinical relevance of macroprolactin. *Clin Endocrinol (Oxf)* 2005; 62:633.
54. Sievertsen GD, Lim VS, Nakawatase C, Frohman LA. Metabolic clearance and secretion rates of human prolactin in normal subjects and in patients with chronic renal failure. *J Clin Endocrinol Metab* 1980; 50:846.
55. Lim VS, Kathpalia SC, Frohman LA. Hyperprolactinemia and impaired pituitary response to suppression and stimulation in chronic renal failure: reversal after transplantation. *J Clin Endocrinol Metab* 1979; 48:101.
56. Lo JC, Beck GJ, Kayser GA, et al. Hyperprolactinemia in end-stage renal disease and effects of frequent hemodialysis. *Hemodial Int* 2017; 21:190.
57. Morley JE, Dawson M, Hodgkinson H, Kalk WJ. Galactorrhea and hyperprolactinemia associated with chest wall injury. *J Clin Endocrinol Metab* 1977; 45:931.
58. Gómez F, Reyes FI, Faíman C. Nonpuerperal galactorrhea and hyperprolactinemia. Clinical findings, endocrine features and therapeutic responses in 56 cases. *Am J Med* 1977; 62:648.
59. Bayrak A, Saadat P, Mor E, et al. Pituitary imaging is indicated for the evaluation of hyperprolactinemia. *Fertil Steril* 2005; 84:181.
60. Seppälä M, Ranta T, Hirvonen E. Hyperprolactinaemia and luteal insufficiency. *Lancet* 1976; 1:229.
61. Corenblum B, Pairaudeau N, Shewchuk AB. Prolactin hypersecretion and short luteal phase defects. *Obstet Gynecol* 1976; 47:486.
62. Biller BM, Baum HB, Rosenthal DI, et al. Progressive trabecular osteopenia in women with hyperprolactinemic amenorrhea. *J Clin Endocrinol Metab* 1992; 75:692.
63. Schlechte J, Walkner L, Kathol M. A longitudinal analysis of premenopausal bone loss in healthy women and women with hyperprolactinemia. *J Clin Endocrinol Metab* 1992; 75:698.
64. Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011; 96:273.
65. David SR, Taylor CC, Kinon BJ, Breier A. The effects of olanzapine, risperidone, and haloperidol on plasma prolactin levels in patients with schizophrenia. *Clin Ther* 2000; 22:1085.
66. Vance ML, Evans WS, Thorner MO. Drugs five years later. Bromocriptine. *Ann Intern Med* 1984; 100:78.
67. Wang AT, Mullan RJ, Lane MA, et al. Treatment of hyperprolactinemia: a systematic review and meta-analysis. *Syst Rev* 2012; 1:33.
68. Webster J, Piscitelli G, Polli A, et al. A comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea. Cabergoline Comparative Study Group. *N Engl J Med* 1994; 331:904.
69. Biller BM, Molitch ME, Vance ML, et al. Treatment of prolactin-secreting macroadenomas with the once-weekly dopamine agonist cabergoline. *J Clin Endocrinol Metab* 1996; 81:2338.
70. Schade R, Andersohn F, Suissa S, et al. Dopamine agonists and the risk of cardiac-valve regurgitation. *N Engl J Med* 2007; 356:29.

71. Zanettini R, Antonini A, Gatto G, et al. Valvular heart disease and the use of dopamine agonists for Parkinson's disease. *N Engl J Med* 2007; 356:39.
72. Kleinberg DL, Boyd AE 3rd, Wardlaw S, et al. Pergolide for the treatment of pituitary tumors secreting prolactin or growth hormone. *N Engl J Med* 1983; 309:704.
73. US Food and Drug Administration. FDA announces voluntary withdrawal of pergolide products (March 29, 2007). <http://www.fda.gov/newsevents/newsroom/pressannouncements/2007/ucm108877.htm> (Accessed on August 01, 2012).
74. Di Sarno A, Landi ML, Marzullo P, et al. The effect of quinagolide and cabergoline, two selective dopamine receptor type 2 agonists, in the treatment of prolactinomas. *Clin Endocrinol (Oxf)* 2000; 53:53.
75. Schultz PN, Ginsberg L, McCutcheon IE, et al. Quinagolide in the management of prolactinoma. *Pituitary* 2000; 3:239.
76. Tindall GT, Kovacs K, Horvath E, Thorner MO. Human prolactin-producing adenomas and bromocriptine: a histological, immunocytochemical, ultrastructural, and morphometric study. *J Clin Endocrinol Metab* 1982; 55:1178.
77. Verhelst J, Abs R, Maiter D, et al. Cabergoline in the treatment of hyperprolactinemia: a study in 455 patients. *J Clin Endocrinol Metab* 1999; 84:2518.
78. Molitch ME, Elton RL, Blackwell RE, et al. Bromocriptine as primary therapy for prolactin-secreting macroadenomas: results of a prospective multicenter study. *J Clin Endocrinol Metab* 1985; 60:698.
79. Moster ML, Savino PJ, Schatz NJ, et al. Visual function in prolactinoma patients treated with bromocriptine. *Ophthalmology* 1985; 92:1332.
80. Kletzky OA, Vermesh M. Effectiveness of vaginal bromocriptine in treating women with hyperprolactinemia. *Fertil Steril* 1989; 51:269.
81. Barake M, Evans AE, Stoeckel L, et al. Investigation of impulsivity in patients on dopamine agonist therapy for hyperprolactinemia: a pilot study. *Pituitary* 2014; 17:150.
82. Dogansen SC, Cikirkcili U, Oruk G, et al. Dopamine Agonist-Induced Impulse Control Disorders in Patients With Prolactinoma: A Cross-Sectional Multicenter Study. *J Clin Endocrinol Metab* 2019; 104:2527.
83. Valassi E, Klibanski A, Biller BM. Clinical Review#: Potential cardiac valve effects of dopamine agonists in hyperprolactinemia. *J Clin Endocrinol Metab* 2010; 95:1025.
84. Tan T, Cabrita IZ, Hensman D, et al. Assessment of cardiac valve dysfunction in patients receiving cabergoline treatment for hyperprolactinaemia. *Clin Endocrinol (Oxf)* 2010; 73:369.
85. Devin JK, Lakhani VT, Byrd BF 3rd, Blevins LS Jr. Prevalence of valvular heart disease in a cohort of patients taking cabergoline for management of hyperprolactinemia. *Endocr Pract* 2008; 14:672.
86. Schlechte J, Dolan K, Sherman B, et al. The natural history of untreated hyperprolactinemia: a prospective analysis. *J Clin Endocrinol Metab* 1989; 68:412.
87. Sisam DA, Sheehan JP, Sheeler LR. The natural history of untreated microprolactinomas. *Fertil Steril* 1987; 48:67.
88. Robert E, Musatti L, Piscitelli G, Ferrari CI. Pregnancy outcome after treatment with the ergot derivative, cabergoline. *Reprod Toxicol* 1996; 10:333.
89. Turkalj I, Braun P, Krupp P. Surveillance of bromocriptine in pregnancy. *JAMA* 1982; 247:1589.
90. Ricci E, Parazzini F, Motta T, et al. Pregnancy outcome after cabergoline treatment in early weeks of gestation. *Reprod Toxicol* 2002; 16:791.
91. Faje A, Chunharorith P, Nency J, et al. Dopamine Agonists Can Reduce Cystic Prolactinomas. *J Clin Endocrinol Metab* 2016; 101:3709.
92. Liuzzi A, Dallabonzana D, Oppizzi G, et al. Low doses of dopamine agonists in the long-term treatment of macroprolactinomas. *N Engl J Med* 1985; 313:656.
93. Snyder PJ, Fowble BF, Schatz NJ, et al. Hypopituitarism following radiation therapy of pituitary adenomas. *Am J Med* 1986; 81:457.

94. Feigenbaum SL, Downey DE, Wilson CB, Jaffe RB. Transsphenoidal pituitary resection for pre-operative diagnosis of prolactin-secreting pituitary adenoma in women: long term follow-up. *J Clin Endocrinol Metab* 1996; 81:1711.
95. Randall RV, Laws ER Jr, Abboud CF, et al. Transsphenoidal microsurgical treatment of prolactin-producing pituitary adenomas. Results in 100 patients. *Mayo Clin Proc* 1983; 58:108.
96. Kleinberg DL, Noel GL, Frantz AG. Galactorrhea: a study of 235 cases, including 48 with pituitary tumors. *N Engl J Med* 1977; 296:589.