Bölüm
14

FEOKROMASİTOMAYA BAĞLI HİPERTANSİYON

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GİRİŞ

Feokromasitoma, adrenal medullanın kromaffin hücrelerinden köken alan ve katekolamin salgılayan nadir görülen bir nöroendokrin tümörüdür. Kromaffin hücrelerden köken olan nöroendokrin tümörlerin % 80-85'ini feokromasitomalar, % 10-15'ini paragangliomalar oluşturur. Tüm katekolamin sekrete eden tümörlerin % 85-90'u intrabdominal, % 10-15'i ekstradrenal yerleşim gösterir. Sempatik ve parasempatik ganglionlardaki kromaffin hücrelerden köken alan ekstraadrenal nöroendokrin tümörlere paraganglioma adı verilir (1,2). Her iki tümör de benzer klinik prezentasyonlar gösterip benzer şekilde tedavi edildikleri için bir çok klinisyen tarafından feokromasitoma ve paraganglioma için ortak bir terminoloji olan 'feokromasitoma' ifadesi kullanılır. İki tümör arasındaki ayırt edici tanımlama eşlik eden diğer neoplazmlar, malignite riski ve genetik araştırma açısından önem taşımaktadır. Her iki tümörden de çoğunlukla adrenalin, noradrenalin, dopamin gibi katekolaminlerden bir veya daha fazlası sekrete edilir. Ancak, boyun ve kafa tabanındaki glossofaringeal ve vagal sinirler boyunca uzanan parasempatik ganglionlardan köken alan paragangliomalarda katekolamin sekresyonu gerçekleşmez. Feokromasitomada katekolaminler dışında PTH ilişkili peptid, IL-6, kromogranin, ACTH, seratonin, eritropoetin ve daha başka bir çok peptid sekrete edilebilir (3).

Feokromasitomaların çoğu sporodik olup, yaklaşık % 40'ında genetik mutasyonlar bulunur ve kalıtsal sendromlarla birliktelik gösterir. Sporodik olgular unilateral görülürken, kalıtsal olanlar genellikle bilateraldir. Hastalık her yaşta olmakla birlikte en sık dört ve beşinci dekatta görülür. Kalıtsal formlar sporo-

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masitoma mutlaka akla gelmeli ve hastalar bu konuda tecrübeli merkezlere yönlendirilmelidir.

KAYNAKLAR

1. Martucci VL, Pacak K. Pheochromocytoma and paraganglioma: Diagnosis, genetics, management, and treatment. Curr Probl Cancer. 2014;38,7–41.
2. Pacak K. Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab. 2007;92,4069–4079.
3. DeLellis RA, Lloyd RV, Heitz PU, et al. Pathology and Genetics of Tumours of Endocrine Organs (IARC WHO Classification of Tumours). Lyon, France: World Health Organization; 2004.
4. Dahia PL. Pheochromocytoma and paraganglioma pathogenesis: Learning from genetic heterogeneity. Nat Rev Cancer. 2014;14:108–109.
5. Guerrero MA, Schreinemakers JM, Vriens MR, et al. Clinical spectrum of pheochromocytoma. J Am Coll Surg. 2009;209(6):727-732.
6. Anderson GH Jr, Blakeman N, Streeten DH. The effect of age on prevalence of secondary forms of hypertension in 4429 consecutively referred patients. J Hypertens. 1994;12:609–615.
7. Ariton M, Juan CS, Av Ruskin TW. Pheochromocytoma: clinical observations from a Brooklyn tertiary hospital. Endocr Pract. 2000;6:249–252.
8. Omura M, Saito J, Yamaguchi K, et al. Prospective study on the prevalence of secondar hypertension among hypertensive patients visiting a general outpatient clinic in Japan. Hypertens Res. 2004;27:193–202.
9. Mantero F, Terzolo M, Arnaldi G, et al. A survey on adrenal incidentaloma in Italy. Study Group on Adrenal Tumors of the Italian Society of Endocrinology. J Clin Endocrinol Metab. 2000;85: 637–644.
10. Mansmann G, Lau J, Balk E, et al. The clinically inapparent adrenal mass: update in diagnosis and management. Endocr Rev. 2004;25:309–340.
11. Greenleaf CE, Griffin LA, Shake JG, et al. Hypertensive crisis secondary to pheochromocytoma. Proc (Bayl Univ Med Cent). 2017;30(3): 314–315.
12. Manger VM. Diagnosis and management of pheochromocytoma-recent advances and current concepts. Kidney International. 2006;70, S30–S35. doi:10.1038/sj.ki.5001974
13. Goldstein RE, O'Neill JA Jr, Holcomb GW, et al. Clinical experience over 48 years with pheochromocytoma. Ann Surg. 1999;229(6):755.
14. Hamidi O, Young WF Jr, Iñiguez-Ariza NM, et al. Malignant Pheochromocytoma and Paraganglioma: 272 Patients Over 55 Years. J Clin Endocrinol Metab. 2017;102(9):3296.
15. Bravo EL. Pheochromocytoma: new concepts and future trends.Kidney Int. 1991;40(3):544-56.
16. Lo CY, Lam KY, Wat MS, et al. Adrenal pheochromocytoma remains a frequently overlooked diagnosis. Am J Surg. 2000;179: 212–215.
17. Zelinka T, Petrák O, Turková H, et al. High incidence of cardiovascular complications in pheochromocytoma. Horm Metab Res. 2012;44:379–384.
18. Stolk RF, Bakx C, Mulder J, et al. Is the excess cardiovascular morbidity in pheochromocytoma related to blood pressure ortocatecholamines? J Clin Endocrinol Metab. 2013;98:1100–1106.
19. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/ AHA/ AAPA/ ACPM/ AGS/ APhA/ ASPC/ NMA/ PCNA. Guideline for Prevention, Detection, Evaluation, and Management of high Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018;71,1269-1324.
20. Manger WM. The Protean Manifestations of Pheochromocytoma. Horm Metab Res. 2009;41(09): 658–663.
21. Zelinka T, Eisenhofer G, Pacak K. Pheochromocytoma as a catecholamine producing tumor: Implications for clinical practice. Stress: The International Journal on the Biology of Stress. 2007; 10(2):195–203.

22. O'Rourke MF, Staessen JA, Vlachopoulos C, et al. Clinical applications of arterial stiffness; definitions and reference values. Am J Hypertens. 2002;15(5):426–444.
23. Manger, W., Gifford, RW. (1996). Clinical and Experimental Pheochromocytoma (Second Edition). Blackwell Science: Cambridge.
24. Ionescu CN, Sakharova OV, Harwood MD, et al. Cyclic Rapid Fluctuation of Hypertension and Hypotension in Pheochromocytoma. The Journal of Clinical Hypertension. 2008;10(12):936–940.
25. Kobal SL, Paran E, Jamali A, et al. Pheochromocytoma: cyclic attacks of hypertension alternating with hypotension. Nat Clin Pract Cardiovasc Med. 2008 5(1):53–57.
26. Bravo E, Tarazi R, Fouad F, et al. Blood pressure regulation in pheochromocytoma. Hypertension. 1982;4(3):193–199. 1982.
27. Engleman K, Zelis R, Waldmann T, et al. Mechanism of orthostatic hypotension in pheochromocytoma. Circulation. 1968;38(Suppl. 6):VI–72.
28. Streeten DHP, Anderson GH. Mechanisms of orthostatic hypotension and tachycardia in patients with pheochromocytoma. American Journal of Hypertension. 1996;9(8):760–769.
29. Mantero F, Albiger N. A comprehensive approach to adrenal incidentalomas. Arquivos Brasileiros de Endocrinologia&Metabologia. 2004;48:583–591.
30. Erickson D, Kudva YC, Ebersold MJ, et al. Benign Paragangliomas: Clinical Presentation and Treatment Outcomes in 236 Patients. J Clin Endocrinol Metab. 2001;86(11):5210– 5216.
31. Eisenhofer G, Goldstein DS, Sullivan P, et al. Biochemical and Clinical Manifestations of Dopamine-Producing Paragangliomas: Utility of Plasma Methoxytyramine. J Clin Endocrinol Metab. 2005;90(4):2068–2075.
32. Ariton M, Juan CS, Av Ruskin TW. Pheochromocytoma: Clinical observations from a brooklyn tertiary hospital. Endocrine Practice. 2000;6(3):249–252.
33. Londe S. Causes of hypertension in the young. Pediatr Clin North Am. 1978;25(1):55–65.
34. Ross JH. Pheochromocytoma: Special Considerations in Children. Urologic Clinics of North America. 2000;27(3):393–402.
35. Oliva R, Angelos P, Kaplan E, et al. Pheochromocytoma in Pregnancy: A Case Series and Review. Hypertension. 2010;55(3):600–606.
36. Dugas G, Fuller J, Singh S, et al. Pheochromocytoma and pregnancy: a case report and review of anesthetic management. Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2004; 51(2):134–138.
37. George J, Tan JYL. Pheochromocytoma in pregnancy: a case report andr eview of literature. Obstet Med. 2010;3(2):83–85.
38. Pacak K, Eisenhofer G, Ahlman H, et al. Pheochromocytoma: recommendations for clinical practice from the First International Symposium. Nat Clin Pract End Met. 2007;3(2):92–102.
39. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99:1915–1942. doi: 10.1210/jc.2014-1498.
40. Hoffman, BB. (2001). Catecholamines, sympathomimetic drugs and adrenergic receptor antagonists. In Hardman JG, Limbird LE, eds. Goodman&Gillman's The Pharmacological Basis of Therapeutics (215–268). Philadelphia; McGraw-Hill.
41. Weingarten TN, Cata JP, O'Hara JF, et al. Comparison of two preoperative medical management strategies for laparoscopic resection of pheochromocytoma. Urology. 2010;76:508.e6-11. doi: 10.1016/j.urology.2010.03.032
42. Pacak K. Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab. 2007; 92:4069–4079.
43. Proye C, Thevenin D, Cecat P, et al. Exclusive use of calcium channel blockers in preoperative and intraoperative control of pheochromocytomas: hemodynamics and free catecholamine assays in ten consecutive patients. Surgery. 1989;106:1149–1154.
44. Takahashi S, Nakai T, Fujiwara R, et al. Effectiveness of long-acting nifedipine in pheochromocytoma. Jpn Heart J. 1989;30:751–757.

45. Bevan EG, McInnes GT, Use of beta-blockade in a patient with pheochromocytoma and asthma. ScottMed J. 1992;37(2),53–54.
46. Ramachandran R, Rewari V. Current perioperative management of pheochromocytomas. Indian J Urol. 2017;33(1):19-25. doi: 10.4103/0970-1591.194781.
47. Thomas RM, Ruel E, Shantavasinkul PC, et al. Endocrine hypertension: An overview on the current etiopathogenesis and management options. World J Hypertens. 2015;5(2):14-27.
48. Whitelaw BC, Praque JK, Mustafa OG, et al. Pheochromocytoma crisis. Clinical Endocrinology, 2014;80,13-22.
49. Kwon SY, Lee KS, Lee JN, et al. Risk factors for hypertensive attack during pheochromocytoma resection. Investig Clin Urol. 2016;57(3):184-90. Doi: 10.4111/icu.2016.57.3.184.
50. Bruynzeel H, Feelders RA, Groenland TH, et al. Risk Factors for Hemodynamic Instability During Surgery for Pheochromocytoma. J Clin Endocrinol Metab. 2010;95:67.
51. Aksakal N, Agcaoglu O, Sahbaz NA, et al. Predictive factors of operative hemodynamic instability for pheochromocytoma. Am Surg. 2018;84(6):920-923.
52. Up to Date (2019). Treatment of pheochromocytoma in adults. http//www.uptodate.com/contents/treatment-of-pheochromocytoma-in-adults/print.
53. Ramakrishna, H. Pheochromocytoma resection: Currentconcepts in anesthetic management. J. Anaesthesiol. Clin Pharmacol. 2015;31,317–323.
54. Ma C, Sun E, Lu B. Giant malignant pheochromocytoma in an elderly patienr: A case report. Medicine (Baltimore). 2018; 97(19):e0614. Doi: 10.1097/MD.0000000000010614.
55. Mazza A, Armigliato M, Marzola MC, et al. Anti-hypertensive treatment in pheochromocytoma and paraganglioma: current management and therapeutic features. Endocrine. 2014;45:469–478. Doi 10.1007/s12020-013-0007-y.i
56. Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and Treatment of Primary Adrenal Insufficiency: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016;101,364–389. Doi: 10.1210/jc.2015-1710.
57. Namekawa T, Utsumi T, Kawamura K, et al. Clinical predictors of prolonged postresection hypotension after laparoscopic adrenalectomy for pheochromocytoma. Surgery. 2016;159,763–770.
58. Herget-Rosenthal S, Saner, F, Chawla LS. Approach to hemodynamic shock and vasopressors. Clin J Am Soc Nephrol. 2008;3, 546–553.
59. Maas JJ, Pinsky MR, de Wilde RB, et al. Cardiac output response to norepinephrine in postoperative cardiac surgery patients: Interpretation with venous return and cardiac function curves. Crit Care Med. 2013;41,143–150.
60. Mamilla D, Katherina A, Brofferio A, et al. Postoperative management in patients with pheochromocytoma and paraganglioma. Cancers (Basel). 2019,3;11(7).
61. Stenström G, Swolin K. Pheochromocytoma in pregnancy. Experience of treatment with phenoxybenzamine in three patients. Acta Obstet Gynecol Scand. 1985;64, 357.
62. Bussmann WD, Kenedi P, von Mengden HJ, et al. Comparison of nitroglycerin with nifedipine in patients with hypertensive crisis or severe hypertension. Clin Investig. 1992;70,1085–1088.
63. Pearce CJ, Wallin JD. Labetalol and other agents that block both a- and b-adrenergic receptors. Cleve Clin J Med. 1994;61,59–69.
64. Biggar MA, Lennard TW. Systematic review of phaeochromocytoma in pregnancy. Br J Surg. 2013;100,182–190. doi: 10.1002/bjs.8976
65. Molitch ME. Endocrine emergencies in pregnancy. Baillieres Clin Endocrinol Metab. 1992,6(1), 167–191.
66. Levy JH. Treatment of perioperative hypertension. Anesthesiol Clin NAm. 1999,17,569–570.