15. Bölüm

İDİYOPATİK PULMONER FİBROZİS GENETİK VE GENOMİKLERİ

Maşuk ÇELİKEL[1]
Selvi AŞKAR[2]

GİRİŞ

İdiyopatik pulmoner fibrozis(İPF), kronik fibrotik ve akciğer fonksiyonlarında giderek artan azalma ile karakterize etiyolojik olarak karmaşık bir interstisyel akciğer hastalığıdır[1]. İPF, sıklıkla orta yaşlı ve yaşlı erişkinlerde ortaya çıkar. Olağan interstisyel pnömoniye özgü bir histopatolojik veya radyolojik patern ile ilişkilidir[2]. En sık karşılaşılan semptom ve bulgular; ilerleyen nefes darlığı, kuru öksürük, bibaziler velkro raller ve çomak parmaktır[3].Uluslararası kılavuzlar, İPF tanısının, İAH'nin bilinen nedenlerinin dışlanmasını ve yüksek çözünürlüklü bilgisayarlı tomografi (HRCT) veya cerrahi akciğer biyopsisinde olağan bir usual interstisyel pnömoni (UİP) varlığını gerektiren çok disiplinli bir düzeyde yapılmasını önermektedir[4]. Traksiyon bronşektazisi olan veya olmayan bal peteği kistleri, subplevral tutulum ve baskın retikülasyon varlığında tek başına HRCT'ye dayanarak radyolojik bir 'kesin UIP' tanısı konulabilir ve cerrahi biyopsi ihtiyacını ortadan kaldırır[5]. Çok sayıda epidemiyolojik ve genetik çalışma, genetik ve

[1] Arş. Gör. Dr., Van YYÜ Tıp Fakültesi, Göğüs Hastalıkları AD, masuk4343@gmail.com
[2] Doç. Dr., Van YYÜ Tıp Fakültesi, Göğüs Hastalıkları AD, selviasker@gmail.com

KAYNAKÇA

1. Michalski JE, Schwartz DA. Genetic Risk Factors for Idiopathic Pulmonary Fibrosis: Insights into Immunopathogenesis. Journal of Inflammation Research. 2020;13:1305.
2. King Jr TE, Pardo A, Selman M. Idiopathic pulmonary fibrosis. The Lancet. 2011;378(9807):1949-1961.
3. KIRKIL G. İdiyopatik Pulmoner Fibrozis: Tanım, Sınıflama, Klinik ve Genetik Bulgular, Yeni Biyobelirteçler.
4. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. American journal of respiratory and critical care medicine. 2011;183(6):788-824.
5. Barratt SL, Creamer A, Hayton C, et al. Idiopathic Pulmonary Fibrosis (IPF): An Overview. Journal of Clinical Medicine. 2018;7(8):201.
6. Daccord C, Maher TM. Recent advances in understanding idiopathic pulmonary fibrosis. F1000Research. 2016;5.
7. Kropski JA, Blackwell TS, Loyd JE. The genetic basis of idiopathic pulmonary fibrosis. European Respiratory Journal. 2015;45(6):1717-1727.
8. Kaur A, Mathai SK, Schwartz DA. Genetics in idiopathic pulmonary fibrosis pathogenesis, prognosis, and treatment. Frontiers in medicine. 2017;4:154.
9. Allen RJ, Guillen-Guio B, Oldham JM, et al. Genome-wide association study of susceptibility to idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2020;201(5):564-574.
10. Kropski JA, Young LR, Cogan JD, et al. Genetic evaluation and testing of patients and families with idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2017;195(11):1423-1428.
11. Network IPFCR. Prednisone, azathioprine, and N-acetylcysteine for pulmonary fibrosis. New England Journal of Medicine. 2012;366(21):1968-1977.
12. Heukels P, Moor C, Von der Thüsen J, et al. Inflammation and immunity in IPF pathogenesis and treatment. Respiratory Medicine. 2019;147:79-91.
13. Kolahian S, Fernandez IE, Eickelberg O, et al. Immune mechanisms in pulmonary fibrosis. American journal of respiratory cell and molecular biology. 2016;55(3):309-322.
14. Zhang G-Y, Liao T, Gao W-Y. MUC5B promoter polymorphism and pulmonary fibrosis. N Engl J Med. 2011;365(2):178.
15. Nakano Y, Yang IV, Walts AD, et al. MUC5B promoter variant rs35705950 affects MUC5B expression in the distal airways in idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2016;193(4):464-466.
16. Peljto AL, Zhang Y, Fingerlin TE, et al. Association between the MUC5B promoter polymorphism and survival in patients with idiopathic pulmonary fibrosis. Jama. 2013;309(21):2232-2239.
17. Seibold MA, Wise AL, Speer MC, et al. A common MUC5B promoter polymorphism and pulmonary fibrosis. New England Journal of Medicine. 2011;364(16):1503-1512.
18. Seibold MA, Smith RW, Urbanek C, et al. The idiopathic pulmonary fibrosis honeycomb cyst contains a mucocilary pseudostratified epithelium. PloS one. 2013;8(3):e58658.
19. Hunninghake GM, Hatabu H, Okajima Y, et al. MUC5B promoter polymorphism and interstitial lung abnormalities. New England Journal of Medicine. 2013;368(23):2192-2200.
20. Fahy JV, Dickey BF. Airway mucus function and dysfunction. New England Journal of Medicine. 2010;363(23):2233-2247.
21. Roy MG, Livraghi-Butrico A, Fletcher AA, et al. Muc5b is required for airway defence. Nature. 2014;505(7483):412-416.

22. Bhowmik A, Chahal K, Austin G, et al. Improving mucociliary clearance in chronic obstructive pulmonary disease. Respiratory medicine. 2009;103(4):496-502.
23. Kreda SM, Davis CW, Rose MC. CFTR, mucins, and mucus obstruction in cystic fibrosis. Cold Spring Harbor perspectives in medicine. 2012;2(9):a009589.
24. Robinson M, Bye PT. Mucociliary clearance in cystic fibrosis. Pediatric pulmonology. 2002;33(4):293-306.
25. Bonser LR, Erle DJ. Airway mucus and asthma: the role of MUC5AC and MUC5B. Journal of clinical medicine. 2017;6(12):112.
26. Molyneaux PL, Cox MJ, Willis-Owen SA, et al. The role of bacteria in the pathogenesis and progression of idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2014;190(8):906-913.
27. Paolocci G, Folletti I, Torén K, et al. Occupational risk factors for idiopathic pulmonary fibrosis in southern Europe: a case-control study. BMC pulmonary medicine. 2018;18(1):1-6.
28. Baumgartner KB, Samet JM, Coultas DB, et al. Occupational and environmental risk factors for idiopathic pulmonary fibrosis: a multicenter case-control study. American journal of epidemiology. 2000;152(4):307-315.
29. Han MK, Zhou Y, Murray S, et al. Lung microbiome and disease progression in idiopathic pulmonary fibrosis: an analysis of the COMET study. The Lancet Respiratory Medicine. 2014;2(7):548-556.
30. O'Dwyer DN, Ashley SL, Gurczynski SJ, et al. Lung microbiota contribute to pulmonary inflammation and disease progression in pulmonary fibrosis. American journal of respiratory and critical care medicine. 2019;199(9):1127-1138.
31. Hancock LA, Hennessy CE, Solomon GM, et al. Muc5b overexpression causes mucociliary dysfunction and enhances lung fibrosis in mice. Nature communications. 2018;9(1):1-10.
32. Mathai SK, Schwartz DA, Warg LA. Genetic susceptibility and pulmonary fibrosis. Current opinion in pulmonary medicine. 2014;20(5):429-435.
33. Armanios M. Telomerase and idiopathic pulmonary fibrosis. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 2012;730(1-2):52-58.
34. Armanios M, Blackburn EH. The telomere syndromes. Nature Reviews Genetics. 2012;13(10):693-704.
35. Petrovski S, Todd JL, Durheim MT, et al. An exome sequencing study to assess the role of rare genetic variation in pulmonary fibrosis. American journal of respiratory and critical care medicine. 2017;196(1):82-93.
36. Armanios MY, Chen JJ-L, Cogan JD, et al. Telomerase mutations in families with idiopathic pulmonary fibrosis. New England Journal of Medicine. 2007;356(13):1317-1326.
37. Cronkhite JT, Xing C, Raghu G, et al. Telomere shortening in familial and sporadic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2008;178(7):729-737.
38. Minagawa S, Araya J, Numata T, et al. Accelerated epithelial cell senescence in IPF and the inhibitory role of SIRT6 in TGF-β-induced senescence of human bronchial epithelial cells. American Journal of Physiology-Lung Cellular and Molecular Physiology. 2011;300(3):L391-L401.
39. Whitsett JA, Wert SE, Weaver TE. Alveolar Surfactant Homeostasis and the Pathogenesis of Pulmonary Disease. Annual Review of Medicine. 2010;61(1):105-119.
40. Lawson W, Grant S, Ambrosini V, et al. Genetic mutations in surfactant protein C are a rare cause of sporadic cases of IPF. Thorax. 2004;59(11):977-980.
41. Wang Y, Kuan PJ, Xing C, et al. Genetic defects in surfactant protein A2 are associated with pulmonary fibrosis and lung cancer. The American Journal of Human Genetics. 2009;84(1):52-59.
42. Mulugeta S, Nguyen V, Russo SJ, et al. A surfactant protein C precursor protein BRICHOS domain mutation causes endoplasmic reticulum stress, proteasome dysfunction, and caspase 3 activation. American journal of respiratory cell and molecular biology. 2005;32(6):521-530.

43. Kropski JA, Lawson WE, Young LR, et al. Genetic studies provide clues on the pathogenesis of idiopathic pulmonary fibrosis. Disease models & mechanisms. 2013;6(1):9-17.
44. Fingerlin TE, Murphy E, Zhang W, et al. Genome-wide association study identifies multiple susceptibility loci for pulmonary fibrosis. Nature genetics. 2013;45(6):613-620.
45. Polivka L, Hadj-Rabia S, Bal E, et al. Epithelial barrier dysfunction in desmoglein-1 deficiency. Journal of Allergy and Clinical Immunology. 2018;142(2):702-706. e707.
46. Huber O, Petersen I. 150th anniversary series: desmosomes and the hallmarks of cancer. Cell communication & adhesion. 2015;22(1):15-28.
47. Mathai SK, Pedersen BS, Smith K, et al. Desmoplakin variants are associated with idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2016;193(10):1151-1160.
48. Takeda K, Kaisho T, Akira S. Toll-like receptors. Annual review of immunology. 2003;21(1):335-376.
49. Kawasaki T, Kawai T. Toll-like receptor signaling pathways. Frontiers in immunology. 2014;5:461.
50. Kawai T, Akira S. The role of pattern-recognition receptors in innate immunity: update on Toll-like receptors. Nature immunology. 2010;11(5):373.
51. O'Dwyer DN, Armstrong ME, Trujillo G, et al. The Toll-like receptor 3 L412F polymorphism and disease progression in idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2013;188(12):1442-1450.
52. Kelly BG, Lok SS, Hasleton PS, et al. A rearranged form of Epstein–Barr virus DNA is associated with idiopathic pulmonary fibrosis. American journal of respiratory and critical care medicine. 2002;166(4):510-513.
53. Lok S, Haider Y, Howell D, et al. Murine gammaherpes virus as a cofactor in the development of pulmonary fibrosis in bleomycin resistant mice. European Respiratory Journal. 2002;20(5):1228-1232.
54. Ebrahimi B, Dutia BM, Brownstein DG, et al. Murine gammaherpesvirus-68 infection causes multi-organ fibrosis and alters leukocyte trafficking in interferon-γ receptor knockout mice. The American journal of pathology. 2001;158(6):2117-2125.
55. Zhang G, Ghosh S. Negative regulation of toll-like receptor-mediated signaling by Tollip. Journal of Biological Chemistry. 2002;277(9):7059-7065.
56. Didierlaurent A, Brissoni B, Velin D, et al. Tollip regulates proinflammatory responses to interleukin-1 and lipopolysaccharide. Molecular and cellular biology. 2006;26(3):735-742.
57. Go H, Koh J, Kim HS, et al. Expression of toll-like receptor 2 and 4 is increased in the respiratory epithelial cells of chronic idiopathic interstitial pneumonia patients. Respiratory medicine. 2014;108(5):783-792.
58. Zhu L, Wang L, Luo X, et al. Tollip, an intracellular trafficking protein, is a novel modulator of the transforming growth factor-β signaling pathway. Journal of Biological Chemistry. 2012;287(47):39653-39663.
59. van der Mark VA, Ghiboub M, Marsman C, et al. Phospholipid flippases attenuate LPS-induced TLR4 signaling by mediating endocytic retrieval of Toll-like receptor 4. Cellular and molecular life sciences. 2017;74(4):715-730.