

PSÖRIATİK ARTRİT

6. BÖLÜM

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Giriş

Psöriatik artrit (PsA), psöriazisle ilişkili olan inflamatuar bir kas-iskelet sistemi hastalığıdır. Histopatolojik, klinik özellikleri ve insan lökosit antijeni (HLA:Human leukocyte antigen) ile ilişkisi nedeniyle seronegatif spondiloartropati (SpA) olarak sınıflandırılır. PsA hastaları, psöriazis, tırnak psöriazisi, periferik eklem hastlığı, spondilit, entezit ve daktilit dahil olmak üzere heterojen klinik bulgulara sahiptir. Hastalıkın klinik heterojenitesi nedeniyle hastalarda sıkılıkla işlev bozukluğuna ve yaşam kalitesinin düşmesine neden olduğu kabul edilmektedir (1). Bu bölümde PsA'nın klinik bulguları, tanısı ve tedavisi tartışılmacaktır.

Epidemiyoloji

Psöriatik Artrit Prevalansı ve İnsidansı

PsA'da kadın ve erkek eşit olarak etkilendir. Genel popülasyonda insidans yılda her 100,000 kişide yaklaşık 6 kişidir. Dünyada yapılan prevalans çalışmaları incelendiğinde Amerika Birleşik Devletleri'nde PsA prevalansı %0,06-0,25, Avrupa ülkelerinde %0,21-0,5, Çin'de %0,02 oranlarındanadır (2-6). PsA prevalansı genel popülasyonda düşük olmasına rağmen, psöriazisli hastalarda daha yaygındır. Psöriazis olan hastalarda PsA prevalan-

sı %4-30 aralığında değişmektedir. 2019 yılında yapılan bir meta-analizde psöriazis olanlarda PsA prevalansı %19,7 iken, orta ve şiddetli psöriazis hastalarında %24,6 olarak bildirilmiştir. (7). Avrupa'da yapılan çok merkezli 1560 psöriazis hastası içeren bir çalışmada, 30 yıldan sonra psöriazis hastaların %31'inde PsA geliştiği ve zamanla PsA gelişme riskinin azalmadığı gösterilmiştir (8).

PsA hastaların %70'inde psöriazis, artrit başlangıcından önce mevcuttur, %20'sinde cilt ve eklem bulguları birlikte başlarken, daha nadiren %10'unda eklem bulguları cilt tutulumundan önce gelişir (9). Psöriazis tanısını takiben artrit başlangıcı arasındaki zaman aralığı 15 yıldan fazla ve bazı hastalarda 40 yıla kadar yüksek olabilmektedir (10). Psöriazisin şiddeti ile eklem tutulumu arasında zayıf ilişki vardır (11).

Sınıflandırma Kriterleri

PsA için ilk sınıflandırma kriterleri 1973 yılında Moll ve arkadaşları tarafından önerilmiştir (12). 2006 yılında Psöriatik Artrit Sınıflandırma Kriterleri (CASPAR) geliştirilmiştir (Tablo 1). Bu kriterlerin özgüllüğü %98,7 ve duyarlılığı %91,4 olarak bildirilmiştir (13). Günümüzde hastaları klinik çalışmalara kaydetmek ve klinisyenlere rehberlik etmek amacıyla kullanılmaktadır.

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lığı, oto-immun hastalıkların indüklenmesi ve paradoksal durumlar gibi yan etkiler gözlenebilir (77). Farmakoterapiye ek olarak, inflamasyonu kontrol etmenin önemi hakkında hastanın eğitimi de önemlidir. Sigara bırakma, kilo verme, fiziksel aktivite ve stres yönetimi PsA tedavisinde önemli unsurlardır (36). PsA'da kullanılan tedaviler tabloda sunulmuştur (Tablo 2).

SONUÇ

PsA insidansı ve prevalansı dünya çapında değişiklik göstermektedir. PsA için erken tanı ve tedavi önemlidir. Psöriazis olan bir hastada artrit olduğunda mutlaka bir romatoloğa danışılmalıdır. PsA tedavisinin kararı, klinik belirtiler, komorbidite ve eklem fonksiyonunun sürdürülmesi de dahil olmak üzere hastalığın tüm yönleri ile vervilmelidir.

KAYNAKÇA

- Calabresi E, Monti S, Governato G, et al. One year in review 2018: psoriatic arthritis. *Clin Exp Rheumatol.* 2019;37(2):167-178.
- Brockbank J, Gladman D. Diagnosis and management of psoriatic arthritis. *Drugs.* 2002;62(17):2447-2457. Doi:10.2165/00003495-200262170-00004
- Catanoso M, Pipitone N, Salvarani C. Epidemiology of psoriatic arthritis. *Reumatismo.* 2012;64(2):66-70. Doi:10.4081/reumatismo.2012.66
- Madland TM, Apalset EM, Johannessen AE, et al. Prevalence, disease manifestations, and treatment of psoriatic arthritis in Western Norway. *J Rheumatol.* 2005;32(10):1918-1922.
- Shbbee M, Uramoto KM, Gibson LE, et al. The epidemiology of psoriatic arthritis in Olmsted County, Minnesota, USA, 1982-1991. *J Rheumatol.* 2000;27(5):1247-1250.
- Zeng QY, Chen R, Darmawan J, et al. Rheumatic diseases in China. *Arthritis Res Ther.* 2008;10(1):R17. Doi:10.1186/ar2368
- Alinaghi F, Calov M, Kristensen LE, et al. Prevalence of psoriatic arthritis in patients with psoriasis: A systematic review and meta-analysis of observational and clinical studies. *J Am Acad Dermatol.* 2019;80(1):251-265.e19. Doi:10.1016/j.jaad.2018.06.027
- Christophers E, Barker JN, Griffiths CE, et al. The risk of psoriatic arthritis remains constant following initial diagnosis of psoriasis among patients seen in European dermatology clinics. *J Eur Acad Dermatol Venereol.* 2010;24(5):548-554. Doi:10.1111/j.1468-3083.2009.03463.x
- Liu JT, Yeh HM, Liu SY, et al. Psoriatic arthritis: Epidemiology, diagnosis, and treatment. *World J Orthop.* 2014;5(4):537-543. Doi:10.5312/wjo.v5.i4.537
- Tillett W, Charlton R, Nightingale A, et al. Interval between onset of psoriasis and psoriatic arthritis comparing the UK Clinical Practice Research Database with a hospital-based cohort. *Rheumatology (Oxford).* 2017;56(12):2109-2113.
- Cohen MR, Reda DJ, Clegg DO. Baseline relationships between psoriasis and psoriatic arthritis: analysis of 221 patients with active psoriatic arthritis. Department of Veterans Affairs Cooperative Study Group on Seronegative Spondyloarthropathies. *J Rheumatol.* 1999;26(8):1752-1756.
- Moll JM, Wright V. Familial occurrence of psoriatic arthritis. *Ann Rheum Dis.* 1973;32(3):181-201. Doi:10.1136/ard.32.3.181
- Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum.* 2006;54(8):2665-2673. Doi:10.1002/art.21972
- Eder L, Chandran V, Gladman DD. What have we learned about genetic susceptibility in psoriasis and psoriatic arthritis?. *Curr Opin Rheumatol.* 2015;27(1):91-98.
- O'Reilly DD, Jani M, Rahman P, et al. The Genetics of Psoriasis and Psoriatic Arthritis. *J Rheumatol Suppl.* 2019;95:46-50. Doi:10.3899/jrheum.190119
- Cauli A, Mathieu A. Psoriatic arthritis: genetics and pathogenesis. *Reumatismo.* 2012;64(2):71-78. Doi:10.4081/reumatismo.2012.71
- Nestle FO, Kaplan DH, Barker J. Psoriasis. *N Engl J Med.* 2009;361(5):496-509. Doi:10.1056/NEJMra0804595
- Eddy DJ, Johnston CF, Shaw C, et al. Neuropeptides in psoriasis: an immunocytochemical and radioimmunoassay study. *J Invest Dermatol.* 1991;96(4):434-438. Doi:10.1111/1523-1747.ep12469898
- Diluvio L, Vollmer S, Besgen P, et al. Identical TCR beta-chain rearrangements in streptococcal angina and skin lesions of patients with psoriasis vulgaris. *J Immunol.* 2006;176(11):7104-7111. Doi:10.4049/jimmunol.176.11.7104
- Espinosa LR, Berman A, Vasey FB, et al. Psoriatic arthritis and acquired immunodeficiency syndrome. *Arthritis Rheum.* 1988;31(8):1034-1040.

21. Scher JU, Ubeda C, Artacho A, et al. Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease. *Arthritis Rheumatol.* 2015;67(1):128-139.
22. Love TJ, Zhu Y, Zhang Y, et al. Obesity and the risk of psoriatic arthritis: a population-based study. *Ann Rheum Dis.* 2012;71(8):1273-1277. Doi:10.1136/annrheumdis-2012-201299
23. Chiricozzi A. Pathogenic role of IL-17 in psoriasis and psoriatic arthritis. *Actas Dermosifiliogr.* 2014;105 Suppl 1:9-20. Doi:10.1016/S0001-7310(14)70014-6
24. van Kuijk AW, Reinders-Blankert P, Smeets TJ, et al. Detailed analysis of the cell infiltrate and the expression of mediators of synovial inflammation and joint destruction in the synovium of patients with psoriatic arthritis: implications for treatment. *Ann Rheum Dis.* 2006;65(12):1551-1557. Doi:10.1136/ard.2005.050963
25. Menon B, Gullick NJ, Walter GJ, et al. Interleukin-17+CD8+ T cells are enriched in the joints of patients with psoriatic arthritis and correlate with disease activity and joint damage progression. *Arthritis Rheumatol.* 2014;66(5):1272-1281. Doi:10.1002/art.38376
26. Sherlock JP, Joyce-Shaikh B, Turner SP, et al. IL-23 induces spondyloarthropathy by acting on ROR- γ CD3+CD4-CD8- enthesal resident T cells. *Nat Med.* 2012;18(7):1069-1076. Doi:10.1038/nm.2817
27. Ritchlin CT, Haas-Smith SA, Li P, et al. Mechanisms of TNF-alpha- and RANKL-mediated osteoclastogenesis and bone resorption in psoriatic arthritis. *J Clin Invest.* 2003;111(6):821-831. Doi:10.1172/JCI16069
28. Peng H, Wright V, Usas A, et al. Synergistic enhancement of bone formation and healing by stem cell-expressed VEGF and bone morphogenetic protein-4. *J Clin Invest.* 2002;110(6):751-759. Doi:10.1172/JCI15153
29. Belasco J, Wei N. Psoriatic Arthritis: What is Happening at the Joint?. *Rheumatol Ther.* 2019;6(3):305-315. Doi:10.1007/s40744-019-0159-1
30. Gladman DD, Antoni C, Mease P, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis.* 2005;64 Suppl 2(Suppl 2):ii14-ii17. Doi:10.1136/ard.2004.032482
31. Gladman DD, Shuckett R, Russell ML, et al. Psoriatic arthritis (PSA)--an analysis of 220 patients. *Q J Med.* 1987;62(238):127-141.
32. Haddad A, Chandran V. Arthritis mutilans. *Curr Rheumatol Rep.* 2013;15(4):321. Doi:10.1007/s11926-013-0321-7
33. Gladman DD. Psoriatic arthritis. *Baillieres Clin Rheumatol.* 1995;9(2):319-329. Doi:10.1016/s0950-3579(05)80193-1
34. Jadon DR, Sengupta R, Nightingale A, et al. Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. *Ann Rheum Dis.* 2017;76(4):701-707. Doi:10.1136/annrheumdis-2016-209853
35. Torre Alonso JC, Rodriguez Perez A, Arribas Castillo JM, et al. Psoriatic arthritis (PA): a clinical, immunological and radiological study of 180 patients. *Br J Rheumatol.* 1991;30(4):245-250.
36. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis *N Engl J Med.* 2017;376(10):957-970. Doi:10.1056/NEJMra1505557
37. Gisondi P, Tinazzi I, El-Dalati G, et al. Lower limb enthesopathy in patients with psoriasis without clinical signs of arthropathy: a hospital-based case-control study. *Ann Rheum Dis.* 2008;67(1):26-30. Doi:10.1136/ard.2007.075101
38. Polacheck A, Li S, Chandran V, et al. Clinical Enthesitis in a Prospective Longitudinal Psoriatic Arthritis Cohort: Incidence, Prevalence, Characteristics, and Outcome *Arthritis Care Res (Hoboken).* 2017;69(11):1685-1691.
39. Cantini F, Salvarani C, Olivieri I, et al. Distal extremity swelling with pitting edema in psoriatic arthritis: a case-control study. *Clin Exp Rheumatol.* 2001;19(3):291-296.
40. Brockbank JE, Stein M, Schentag CT, et al. Dactylitis in psoriatic arthritis: a marker for disease severity?. *Ann Rheum Dis.* 2005;64(2):188-190.
41. Cassell SE, Bieber JD, Rich P, et al. The modified Nail Psoriasis Severity Index: validation of an instrument to assess psoriatic nail involvement in patients with psoriatic arthritis. *J Rheumatol.* 2007;34(1):123-129.
42. Williamson L, Dalbeth N, Dockerty JL, et al. Extended report: nail disease in psoriatic arthritis-clinically important, potentially treatable and often overlooked. *Rheumatology (Oxford).* 2004;43(6):790-794. Doi:10.1093/rheumatology/keh198
43. Abbouda A, Abicca I, Fabiani C, et al. Psoriasis and Psoriatic Arthritis-Related Uveitis: Different Ophthalmological Manifestations and Ocular Inflammation Features. *Semin Ophthalmol.* 2017;32(6):715-720. Doi:10.3109/08820538.2016.1170161
44. Johnson SR, Schentag CT, Gladman DD. Autoantibodies in biological agent naive patients with psoriatic arthritis. *Ann Rheum Dis.* 2005;64(5):770-772.
45. Alenius GM, Berglin E, Rantapää Dahlqvist S. Antibodies against cyclic citrullinated peptide (CCP) in psoriatic patients with or without joint inflam-

- mation. *Ann Rheum Dis.* 2006;65(3):398-400. Doi:10.1136/ard.2005.040998
46. Kane D, Stafford L, Bresnihan B, et al. A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. *Rheumatology (Oxford)*. 2003;42(12):1460-1468. Doi:10.1093/rheumatology/keg384
 47. Kane D, Greaney T, Bresnihan B, et al. Ultrasonography in the diagnosis and management of psoriatic dactylitis. *J Rheumatol.* 1999;26(8):1746-1751.
 48. McGonagle D, Conaghan PG, Emery P. Psoriatic arthritis: a unified concept twenty years on. *Arthritis Rheum.* 1999;42(6):1080-1086.
 49. Sudół-Szopińska I, Matuszewska G, Kwiatkowska B, et al. Diagnostic imaging of psoriatic arthritis. Part I: etiopathogenesis, classifications and radiographic features. *J Ultrason.* 2016;16(64):65-77. Doi:10.15557/JoU.2016.0007
 50. Haroon M, Rafiq Chaudhry AB, Fitzgerald O. Higher Prevalence of Metabolic Syndrome in Patients with Psoriatic Arthritis: A Comparison with a Control Group of Noninflammatory Rheumatologic Conditions. *J Rheumatol.* 2016;43(2):463-464. Doi:10.3899/jrheum.150757
 51. Rohekar S, Tom BD, Hassa A, et al. Prevalence of malignancy in psoriatic arthritis. *Arthritis Rheum.* 2008;58(1):82-87. Doi:10.1002/art.23185
 52. McDonough E, Ayearst R, Eder L, et al. Depression and anxiety in psoriatic disease: prevalence and associated factors. *J Rheumatol.* 2014;41(5):887-896.
 53. Ogdie A, Yu Y, Haynes K, et al. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study. *Ann Rheum Dis.* 2015;74(2):326-332. Doi:10.1136/annrheumdis-2014-205675
 54. Turkiewicz AM, Moreland LW. Psoriatic arthritis: current concepts on pathogenesis-oriented therapeutic options. *Arthritis Rheum.* 2007;56(4):1051-1066. Doi:10.1002/art.22489
 55. García-Kutzbach A, Chacón-Súchite J, García-Ferrer H, et al. Reactive arthritis: update 2018. *Clin Rheumatol.* 2018;37(4):869-874. Doi:10.1007/s10067-018-4022-5
 56. Wordsworth P. Arthritis and inflammatory bowel disease. *Curr Rheumatol Rep.* 2000;2(2):87-88. Doi:10.1007/s11926-000-0045-3
 57. Helliwell PS, Taylor WJ. Classification and diagnostic criteria for psoriatic arthritis. *Ann Rheum Dis.* 2005;64 Suppl 2(Suppl 2):ii3-ii8. Doi:10.1136/ard.2004.032318
 58. Perez-Ruiz F, Dalbeth N, Bardin T. A review of uric acid, crystal deposition disease, and gout. *Adv Ther.* 2015;32(1):31-41. Doi:10.1007/s12325-014-0175-z
 59. Zhang W, Doherty M, Leeb BF, et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. *Ann Rheum Dis.* 2009;68(1):8-17. Doi:10.1136/ard.2007.084772
 60. Gladman DD, Inman RD, Cook RJ, et al. International spondyloarthritis interobserver reliability exercise--the INSPIRE study: II. Assessment of peripheral joints, enthesitis, and dactylitis. *J Rheumatol.* 2007;34(8):1740-1745.
 61. Ritchlin CT, Kavanaugh A, Gladman DD, et al. Treatment recommendations for psoriatic arthritis. *Ann Rheum Dis.* 2009;68(9):1387-1394. Doi:10.1136/ard.2008.094946
 62. Nash P, Clegg DO. Psoriatic arthritis therapy: NSAIDs and traditional DMARDs. *Ann Rheum Dis.* 2005;64 Suppl 2(Suppl 2):ii74-ii77. Doi:10.1136/ard.2004.030783
 63. Kingsley GH, Kowalczyk A, Taylor H, et al. A randomized placebo-controlled trial of methotrexate in psoriatic arthritis. *Rheumatology (Oxford)*. 2012;51(8):1368-1377. Doi:10.1093/rheumatology/kes001
 64. Kaltwasser JP, Nash P, Gladman D, et al. Efficacy and safety of leflunomide in the treatment of psoriatic arthritis and psoriasis: a multinational, double-blind, randomized, placebo-controlled clinical trial. *Arthritis Rheum.* 2004;50(6):1939-1950. Doi:10.1002/art.20253
 65. Gupta AK, Grober JS, Hamilton TA, et al. Sulfasalazine therapy for psoriatic arthritis: a double blind, placebo controlled trial. *J Rheumatol.* 1995;22(5):894-898.
 66. Salvarani C, Macchioni P, Olivieri I, et al. A comparison of cyclosporine, sulfasalazine, and symptomatic therapy in the treatment of psoriatic arthritis. *J Rheumatol.* 2001;28(10):2274-2282.
 67. Lee JC, Gladman DD, Schentag CT, et al. The long-term use of azathioprine in patients with psoriatic arthritis. *J Clin Rheumatol.* 2001;7(3):160-165. Doi:10.1097/00124743-200106000-00005
 68. Mease P. A short history of biological therapy for psoriatic arthritis. *Clin Exp Rheumatol.* 2015;33(5 Suppl 93):S104-S108.
 69. Taurog JD, Chhabra A, Colbert RA. Ankylosing Spondylitis and Axial Spondyloarthritis. *N Engl J Med.* 2016;374(26):2563-2574. Doi:10.1056/NEJMra1406182
 70. Carmona L, Gómez-Reino JJ, Rodríguez-Valverde V, et al. Effectiveness of recommendations to prevent reactivation of latent tuberculosis infection in patients treated with tumor necrosis factor antagonists. *Arthritis Rheum.* 2005;52(6):1766-1772. Doi:10.1002/art.21043

71. Viganò M, Degasperi E, Aghemo A, et al. Anti-TNF drugs in patients with hepatitis B or C virus infection: safety and clinical management. *Expert Opin Biol Ther.* 2012;12(2):193-207. Doi:10.1517/14712598.2012.646986
72. Weitz JE, Ritchlin CT. Ustekinumab : targeting the IL-17 pathway to improve outcomes in psoriatic arthritis. *Expert Opin Biol Ther.* 2014;14(4):515-526.
73. Mease PJ, McInnes IB, Kirkham B, et al. Secukinumab Inhibition of Interleukin-17A in Patients with Psoriatic Arthritis. *N Engl J Med.* 2015;373(14):1329-1339. Doi:10.1056/NEJMoa1412679
74. Mease PJ, van der Heijde D, Ritchlin CT, et al. Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naïve patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1. *Ann Rheum Dis.* 2017;76(1):79-87. Doi:10.1136/annrheumdis-2016-209709
75. Kavanaugh A, Mease PJ, Gomez-Reino JJ, et al. Treatment of psoriatic arthritis in a phase 3 randomised, placebo-controlled trial with apremilast, an oral phosphodiesterase 4 inhibitor. *Ann Rheum Dis.* 2014;73(6):1020-1026. Doi:10.1136/annrheumdis-2013-205056
76. Mease P, Genovese MC, Gladstein G, et al. Abatacept in the treatment of patients with psoriatic arthritis: results of a six-month, multicenter, randomized, double-blind, placebo-controlled, phase II trial. *Arthritis Rheum.* 2011;63(4):939-948. Doi:10.1002/art.30176
77. Kilic E, Kilic G, Akgül Ö, et al. The Reported Adverse Effects Related to Biological Agents Used for the Treatment of Rheumatic Diseases in Turkey/Romatizmal Hastalıkların Tedavisinde Biyolojik Ajanların Kullanımına Baglı Türkiye'de Bildirilmiş Yan Etkiler. *Turk J Rheumatol* 2013;28(3):149-162. Doi: 10.5606/tjr.2013.3052
78. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic Arthritis *N Engl J Med.* 2017;376(10):957-970. Doi:10.1056/NEJMra1505557