MİKROANJİOPATİK VE DİĞER HASARA BAĞLI HEMOLİTİK ANEMİLER

14. BÖLÜM

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Giriş

Mikroanjiyopatik Hemolitik Anemi (MAHA) eritrositlerin nonimmün mekanizmalarla intravasküler sahada parçalanması sonucu gelişen anemilerdir. MAHA eritrositlerin mikrodolaşımda trombositten ve fibrinden zengin trombüsü geçerken mekanik olarak parçalanmasıyla oluşur. Parçalanmış eritrositler periferik kanda şistositler şeklinde görülür (1). Arteriol ve kapillerlerde trombüsler ile karakterizedir. Prostetik kalp kapakları ve intrakardiyak cihazlar da MAHA' ya sebep olabilir. Karakteristik laboratuvar bulguları; direk antiglobulin (coombs) testi negatifliği, serum laktat dehidrogenaz (LDH) artışı, serum indirekt bilirubin artışı ve haptoglobin azalmasıdır.

Trombotik Mikroanjiopatiler (TMA)

Bütün MAHA' lar TMA' ya sebep olmazlar, ama TMA' ların hepsinde MAHA ve trombositopeni görülür (2). Trombotik mikroanjiopati arteriol ve kapillerlerin duvarındaki mikrotrombüslerle seyreden patolojik lezyonları tanımlar. TMA' ların kesin tanısı doku biyopsisi ile konulur.

Edinsel TTP ilk tanı konulan ve en iyi tanımlanan TMA'dır (1). TTP' de böbrekteki yaygın mikrotrombüslere karşın böbrek fonksiyonlarındaki bozulma hafiftir (1).

Trombotik mikroanjiyopatiler:

1. Edinsel (otoimmün) Trombotik trombositopenik purpura (TTP)

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KAYNAKÇA

1. BRAIN MC, DACIE J V, HOURIHANE DO. Microangiopathic haemolytic anaemia: the possible role of vascular lesions in pathogenesis. *Br J Haematol*. 1962;8:358-374. doi:10.1111/j.1365-2141.1962.tb06541.x
2. Rock GA, Shumak KH, Buskard NA, et al. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. Canadian Apheresis Study Group. *N Engl J Med*. 1991;325(6):393-397. doi:10.1056/NEJM199108083250604
3. Bendapudi PK, Hurwitz S, Fry A, et al. Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study. *Lancet Haematol*. 2017;4(4):e157-e164. doi:10.1016/S2352-3026(17)30026-1
4. McMinn JR, George JN. Evaluation of women with clinically suspected thrombotic thrombocytopenic purpura-hemolytic uremic syndrome during pregnancy. *J Clin Apher*. 2001;16(4):202-209. doi:10.1002/jca.10005
5. Booth KK, Terrell DR, Vesely SK, George JN. Systemic infections mimicking thrombotic thrombocytopenic purpura. *Am J Hematol*. 2011;86(9):743-751. doi:10.1002/ajh.22091
6. George JN. Systemic malignancies as a cause of unexpected microangiopathic hemolytic anemia and thrombocytopenia. *Oncology (Williston Park)*. 2011;25(10):908-914.
7. Antman KH, Skarin AT, Mayer RJ, Hargreaves HK, Canellos GP. Microangiopathic hemolytic anemia and cancer: a review. *Medicine (Baltimore)*. 1979;58(5):377-384. doi:10.1097/00005792-197909000-00004
8. Levi M, Toh CH, Thachil J, Watson HG. Guidelines for the diagnosis and management of disseminated intravascular coagulation. British Committee for Standards in Haematology. *Br J Haematol*. 2009;145(1):24-33. doi:10.1111/j.1365-2141.2009.07600.x
9. ROSE JC, HUFNAGEL CA, FREIS ED, HARVEY WP, PARTENOPE EA. The hemodynamic alterations produced by a plastic valvular prosthesis for severe aortic insufficiency in man. *J Clin Invest*. 1954;33(6):891-900. doi:10.1172/JCI102962
10. Eyster E, Rothchild J, Mychajliw O. Chronic intravascular hemolysis after aortic valve replacement. Long-term study comparing different types of ball-valve prostheses. *Circulation*. 1971;44(4):657-665. doi:10.1161/01.cir.44.4.657
11. Alkhouli M, Farooq A, Go RS, Balla S, Berzingi C. Cardiac prostheses-related hemolytic anemia. *Clin Cardiol*. 2019;42(7):692-700. doi:10.1002/clc.23191
12. Shapira Y, Hirsch R, Kornowski R, et al. Percutaneous closure of perivalvular leaks with Amplatzer occluders: feasibility, safety, and shortterm results. *J Heart Valve Dis*. 2007;16(3):305-313.
13. Okita Y, Miki S, Kusuhara K, Ueda Y, Tahata T, Yamanaka K. Propranolol for intractable hemolysis after open heart operation. *Ann Thorac Surg*. 1991;52(5):1158-1160. doi:10.1016/0003-4975(91)91301-b
14. Shapira Y, Bairey O, Vatury M, Magen-Nativ H, Prokocimer M, Sagie A. Erythropoietin can obviate the need for repeated heart valve replacement in high-risk patients with severe mechanical hemolytic anemia: case reports and literature review. *J Heart Valve Dis*. 2001;10(4):431-435.
15. Ward A, Clissold SP. Pentoxifylline. A review of its pharmacodynamic and phar-

macokinetic properties, and its therapeutic efficacy. *Drugs*. 1987;34(1):50-97. doi:10.2165/00003495-198734010-00003
16. Ai T, Azemoto R, Saisho H. Prevention of gallstones by ursodeoxycholic acid after cardiac surgery. *J Gastroenterol*. 2003;38(11):1071-1076. doi:10.1007/s00535-003-1198-4
17. Silver RM, Branch DW, Scott JR. Maternal thrombocytopenia in pregnancy: time for a reassessment. *Am J Obstet Gynecol*. 1995;173(2):479-482. doi:10.1016/0002-9378(95)90269-4
18. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4(2):295-306. doi:10.1111/j.1538-7836.2006.01753.x
19. Hulstein JJJ, van Runnard Heimel PJ, Franx A, et al. Acute activation of the endothelium results in increased levels of active von Willebrand factor in hemolysis, elevated liver enzymes and low platelets (HELLP) syndrome. *J Thromb Haemost*. 2006;4(12):2569-2575. doi:10.1111/j.1538-7836.2006.02205.x
20. Egerman RS, Sibai BM. HELLP syndrome. *Clin Obstet Gynecol*. 1999;42(2):381-389. doi:10.1097/00003081-199906000-00022
21. Tsai HM, Lian EC. Antibodies to von Willebrand factor-cleaving protease in acute thrombotic thrombocytopenic purpura. *N Engl J Med*. 1998;339(22):1585-1594. doi:10.1056/NEJM199811263392203
22. George JN, Nester CM, McIntosh JJ. Syndromes of thrombotic microangiopathy associated with pregnancy. *Hematol Am Soc Hematol Educ Progr*. 2015;2015:644-648. doi:10.1182/asheducation-2015.1.644
23. James N George AC. Pathophysiology of acquired TTP and other primary thrombotic microangiopathies (TMAs).
24. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. *Blood*. 2010;116(20):4060-4069. doi:10.1182/blood-2010-07-271445
25. Ashida A, Matsumura H, Sawai T, et al. Clinical features in a series of 258 Japanese pediatric patients with thrombotic microangiopathy. *Clin Exp Nephrol*. 2018;22(4):924-930. doi:10.1007/s10157-018-1531-0
26. Eknoyan G, Riggs SA. Renal involvement in patients with thrombotic thrombocytopenic purpura. *Am J Nephrol*. 1986;6(2):117-131. doi:10.1159/000167066
27. Zander CB, Cao W, Zheng XL. ADAMTS13 and von Willebrand factor interactions. *Curr Opin Hematol*. 2015;22(5):452-459. doi:10.1097/MOH.0000000000000169
28. George JN. Measuring ADAMTS13 activity in patients with suspected thrombotic thrombocytopenic purpura: when, how, and why? *Transfusion*. 2015;55(1):11-13. doi:10.1111/trf.12885
29. Chauhan AK. Degradation of platelet-von Willebrand factor complexes by plasmin: an alternative/backup mechanism to ADAMTS13. *Circulation*. 2014;129(12):1273-1275. doi:10.1161/CIRCULATIONAHA.114.008298
30. Blombery P, Scully M. Management of thrombotic thrombocytopenic purpura: current perspectives. *J Blood Med*. 2014;5:15-23. doi:10.2147/JBM.S46458
31. George JN. The importance of clinical judgment for the diagnosis of thrombotic thrombocytopenic purpura. *Transfusion*. 2017;57(11):2558-2561. doi:10.1111/trf.14357
32. Shah N, Sarode R. Thrombotic thrombocytopenic purpura-what is new? *J Clin Apher*. 2013;28(1):30-35. doi:10.1002/jca.21264

33. Page EE, Kremer Hovinga JA, Terrell DR, Vesely SK, George JN. Clinical importance of ADAMTS13 activity during remission in patients with acquired thrombotic thrombocytopenic purpura. *Blood*. 2016;128(17):2175-2178. doi:10.1182/blood-2016-06-724161
34. Balduini CL, Gugliotta L, Luppi M, et al. High versus standard dose methylprednisolone in the acute phase of idiopathic thrombotic thrombocytopenic purpura: a randomized study. *Ann Hematol*. 2010;89(6):591-596. doi:10.1007/s00277-009-0877-5
35. Zeigler ZR, Shadduck RK, Gryn JF, et al. Cryoprecipitate poor plasma does not improve early response in primary adult thrombotic thrombocytopenic purpura (TTP). *J Clin Apher*. 2001;16(1):19-22. doi:10.1002/jca.1003
36. Rizvi MA, Vesely SK, George JN, et al. Complications of plasma exchange in 71 consecutive patients treated for clinically suspected thrombotic thrombocytopenic purpura-hemolytic-uremic syndrome. *Transfusion*. 2000;40(8):896-901. doi:10.1046/j.1537-2995.2000.40080896.x
37. Bell WR, Braine HG, Ness PM, Kickler TS. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. Clinical experience in 108 patients. *N Engl J Med*. 1991;325(6):398-403. doi:10.1056/NEJM199108083250605
38. Allford SL, Hunt BJ, Rose P, Machin SJ. Guidelines on the diagnosis and management of the thrombotic microangiopathic haemolytic anaemias. *Br J Haematol*. 2003;120(4):556-573. doi:10.1046/j.1365-2141.2003.04049.x
39. Swisher KK, Terrell DR, Vesely SK, Kremer Hovinga JA, Lämmle B, George JN. Clinical outcomes after platelet transfusions in patients with thrombotic thrombocytopenic purpura. *Transfusion*. 2009;49(5):873-887. doi:10.1111/j.1537-2995.2008.02082.x
40. McDonald V, Manns K, Mackie IJ, Machin SJ, Scully MA. Rituximab pharmacokinetics during the management of acute idiopathic thrombotic thrombocytopenic purpura. *J Thromb Haemost*. 2010;8(6):1201-1208. doi:10.1111/j.1538-7836.2010.03818.x
41. Peyvandi F, Scully M, Kremer Hovinga JA, et al. Caplacizumab for Acquired Thrombotic Thrombocytopenic Purpura. *N Engl J Med*. 2016;374(6):511-522. doi:10.1056/NEJMoa1505533
42. Tsai E, Chapin J, Laurence JC, Tsai H-M. Use of eculizumab in the treatment of a case of refractory, ADAMTS13-deficient thrombotic thrombocytopenic purpura: additional data and clinical follow-up. *Br J Haematol*. 2013;162(4):558-559. doi:10.1111/bjh.12387
43. Feng S, Liang X, Kroll MH, Chung DW, Afshar-Kharghan V. von Willebrand factor is a cofactor in complement regulation. *Blood*. 2015;125(6):1034-1037. doi:10.1182/blood-2014-06-585430
44. McNamara LA, Topaz N, Wang X, Hariri S, Fox L, MacNeil JR. High Risk for Invasive Meningococcal Disease Among Patients Receiving Eculizumab (Soliris) Despite Receipt of Meningococcal Vaccine. *MMWR Morb Mortal Wkly Rep*. 2017;66(27):734-737. doi:10.15585/mmwr.mm6627e1
45. Scully M, Knöbl P, Kentouche K, et al. Recombinant ADAMTS-13: first-in-human pharmacokinetics and safety in congenital thrombotic thrombocytopenic purpura. *Blood*. 2017;130(19):2055-2063. doi:10.1182/blood-2017-06-788026
46. Westwood J-P, Thomas M, Alwan F, et al. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. *Blood Adv*. 2017;1(15):1159-1166. doi:10.1182/bloodadvances.2017008268

47. Roriz M, Landais M, Desprez J, et al. Risk Factors for Autoimmune Diseases Development After Thrombotic Thrombocytopenic Purpura. *Medicine (Baltimore)*. 2015;94(42):e1598. doi:10.1097/MD.0000000000001598
48. Karmali MA. Host and pathogen determinants of verocytotoxin-producing Escherichia coli-associated hemolytic uremic syndrome. *Kidney Int Suppl*. 2009;(112):S4-7. doi:10.1038/ki.2008.608
49. Butler T. Haemolytic uraemic syndrome during shigellosis. *Trans R Soc Trop Med Hyg*. 2012;106(7):395-399. doi:10.1016/j.trstmh.2012.04.001
50. Freedman SB, Xie J, Neufeld MS, et al. Shiga Toxin-Producing Escherichia coli Infection, Antibiotics, and Risk of Developing Hemolytic Uremic Syndrome: A Meta-analysis. *Clin Infect Dis an Off Publ Infect Dis Soc Am*. 2016;62(10):1251-1258. doi:10.1093/cid/ciw099
51. Nitschke M, Sayk F, Härtel C, et al. Association between azithromycin therapy and duration of bacterial shedding among patients with Shiga toxin-producing enteroaggregative Escherichia coli O104:H4. *JAMA*. 2012;307(10):1046-1052. doi:10.1001/jama.2012.264
52. Obrig TG. Escherichia coli Shiga Toxin Mechanisms of Action in Renal Disease. *Toxins (Basel)*. 2010;2(12):2769-2794. doi:10.3390/toxins2122769
53. Menne J, Nitschke M, Stingele R, et al. Validation of treatment strategies for enterohaemorrhagic Escherichia coli O104:H4 induced haemolytic uraemic syndrome: case-control study. *BMJ*. 2012;345:e4565. doi:10.1136/bmj.e4565
54. Bresin E, Daina E, Noris M, et al. Outcome of renal transplantation in patients with non-Shiga toxin-associated hemolytic uremic syndrome: prognostic significance of genetic background. *Clin J Am Soc Nephrol*. 2006;1(1):88-99. doi:10.2215/CJN.00050505
55. Weil BR, Andreoli SP, Billmire DF. Bleeding risk for surgical dialysis procedures in children with hemolytic uremic syndrome. *Pediatr Nephrol*. 2010;25(9):1693-1698. doi:10.1007/s00467-010-1530-1
56. Van Dyck M, Proesmans W. Renoprotection by ACE inhibitors after severe hemolytic uremic syndrome. *Pediatr Nephrol*. 2004;19(6):688-690. doi:10.1007/s00467-004-1451-y