

ENFEKSİYONLARA BAĞLI HEMOLİTİK ANEMİLER VE TOKSİK AJANLARA BAĞLI HEMOLİTİK ANEMİLER

**15.
BÖLÜM**

Pınar ÇAKMAK¹

Giriş

Enfeksiyon hastalıkları ekstrensek hemolitik anemilere doğrudan neden olabileceği gibi var olan hemolizin şiddetini artırabilir. En sık karşılaştığımız mekanizmalar immün aracı hemolitik anemi, eritrositlerin direk yıkımıyla giden non-immün hemolitik anemi ve mikroanjiyopatik hemolitik anemi şeklindedir (1).

I. ENFEKSİYONLARA BAĞLI HEMOLİTİK ANEMİLER

1. Otoimmün Hemolitik Anemi ve Enfeksiyonlar

Eritrositlerin konak immüniteleri aracı yıkımı ile karakterizedir. Enfeksiyonla indüklenen otoimmün hemolitik anemiler, soğuk aglutinin aracı, sıcak aglutinin aracı ve paroksismal soğuk hemoglobinüri şeklinde incelenebilir (2).

- **Soğuk Aglutinin Aracılı Hemoliz**

Soğuk aglutininler, eritrosit yüzeyindeki kan grubu抗原leri ile reaksiyona girerler. Antikorlar Ig M tipindedir. Antigenler ise eritrosit yüzeyinde tipik olarak 'I' veya 'i' dir. Soğuk aglutininin hastalığından sorumlu esas patojenler *Mycoplasma pneumoniae* ve Epstein Barr virustur. *Klebsiella* enfeksiyonları, kabakulak, sitomegalovirus, Lejyoner hastalığı ve visseral leishmaniasis' ten sonra da soğuk aglutinin aracı hemoliz bildirilmiştir (3,4).

Mycoplasma pneumoniae

Hücre duvarından yoksun olduğu için gram boyamada görülmez. Beta laktamlara ve hücre duvarı sentezini inhibe eden diğer antibiyotiklere doğal direnç-

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KAYNAKÇA

1. Dhaliwal G, Cornett PA, Tierney LM. Hemolytic Anemia. *Am Fam Physician*. 2004;69:2599-2607
2. Sokol RJ, Hewitt S. Autoimmune hemolysis: a critical review. *Crit Rev Oncol Hematol* 1985;4(2):125-54
3. Woodruff AW, Topley E, Knight R. The anaemia of kala azar. *Br J Haematol* 1972; 22:319
4. Pirofsky B. Infectious disease and autoimmune hemolytic anemia, in Autoimmunization and the Autoimmune Hemolytic Anemias. Waverly Press, Baltimore. 1969
5. Luby JP. Pneumonia caused by *Mycoplasma pneumoniae* infection. *Clin Chest Med* 1991; 12:237.
6. Waites KB, Talkington DF. *Mycoplasma pneumoniae* and its role as a human pathogen. *Clin Microbiol Rev* 2004;17(4):697-728.
7. Daxböck F, Zedtwitz-Liebenstein K, Burgmann H. Severe hemolytic anemia and excessive leukocytosis masking mycoplasma pneumonia. *Ann Hematol* 2001;80(3):180-2.
8. Khan FY, Yassin M. *Mycoplasma pneumoniae* associated with severe autoimmune hemolytic anemia: case report and literature review. *Braz J Infect Dis* 2009;13(1):77-9.
9. Großhennig S, Ischebeck T, Gibhardt J, et al. Hydrogen sulfide is a novel potential virulence factor of *Mycoplasma pneumoniae*: characterization of the unusual cysteine desulfurase/desulphydrase HapE. *Mol Microbiol* 2016; 100:42.
10. Valade S, Biard L, Lemiale V, et al. Severe atypical pneumonia in critically ill patients: a retrospective multicenter study. *Ann Intensive Care* 2018; 8:81.
11. Stein B, DeCredico N, Hillman L. Evaluation of the Direct Antiglobulin Test (DAT) in the Setting of *Mycoplasma pneumoniae* Infection. *JAMA* 2018; 319:1377.
12. Brodsky RA. Warm Autoimmune Hemolytic Anemia. *N Engl J Med* 2019; 381:647.
13. Santos Malavé C, Shady DL, Hartman SK. Paroxysmal cold hemoglobinuria in a child with RSV: an underrecognized cause of hemolytic anemia. *Am J Emerg Med* 2016; 34:2252.e5.
14. Götsche B, Salama A, Mueller-Eckhardt C. Donath-Landsteiner autoimmune hemolytic anemia in children. A study of 22 cases. *Vox Sang* 1990; 58:281.
15. Sokol RJ, Booker DJ, Stamps R. Erythropoiesis: Paroxysmal Cold Haemoglobinuria: A Clinico-Pathological Study of Patients with a Positive Donath-Landsteiner Test. *Hematology* 1999; 4:137.
16. Brugnara C, Barcellini W. Paroxysmal cold hemoglobinuria clinical manifestations typical age. UpToDate review version May 2020
17. Tunçbilek S. Enfeksiyonlar ve Mikroorganizmalara Bağlı Hemolitik Anemiler. *Turkiye Klinikleri J Hematol-Special Topics*. 2016;9(1):70-6
18. Aklan MZ, Sönmez Tamer G. Plasmodium türleri. Willke Topcu A, Söyletir G, Doğanay M. Enfeksiyon Hastalıkları ve Mikrobiyolojisi 3.baskı İstanbul: Nobel Kitapevleri; 2008: 2486-502
19. Dünya Sitma Raporu 2018. Dünya Sağlık Örgütü; Cenevre, 2018
20. Zuccala ES, Baum J. Cytoskeletal and membrane remodelling during malaria parasite invasion of the human erythrocyte. *Br J Haematol*. 2011;154(6):680.
21. Fairhurst RM, Wellemes TE. Plasmodium Species. In: Mandell GL, Bennett JE, Dolin R. Principles and Practice of Infectious Diseases. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010: 3437-62.

22. Adams JH, Sim BK, Dolan SA. A family of erythrocyte binding proteins of malaria parasites. *Proc Natl Acad Sci U S A.* 1992;89(15):7085.
23. Wyler DJ. Plasmodium and Babesia. In: Gorbach, Barlett, Neil (eds). *Infectiosus Disease*, Philadelphia, WB Saunders Company, 1998; 2407
24. Brown W H. *Basic Clinical Parasitology*. 4st ed. New York: Appleton Century Crofts; 1975: 75-87
25. Boele van Hensbroek M, Calis JC, Phiri KS. Pathophysiological mechanisms of severe anaemia in Malawian children. *PLoS One.* 2010;5(9):e12589.
26. Tran TH, Day NP, Ly VC, et al. Blackwater fever in southern Vietnam: a prospective descriptive study of 50 cases. *Clin Infect Dis* 1996; 23:1274.
27. Ndila CM, Uyoga S, Macharia AW, et al. Human candidate gene polymorphisms and risk of severe malaria in children in Kilifi, Kenya: a case-control association study. *Lancet Haematol* 2018; 5:e333.
28. Aidoo M, Terlouw DJ, Kolczak MS, et al. Protective effects of the sickle cell gene against malaria morbidity and mortality. *Lancet* 2002; 359:1311.
29. Wiesenfeld SL. Sickle-cell trait in human biological and cultural evolution. Development of agriculture causing increased malaria is bound to gene-pool changes causing malaria reduction. *Science* 1967; 157:1134.
30. White NJ. Anaemia and malaria. *Malar J* 2018; 17:371.
31. World Health Organization. Guidelines for the treatment of malaria, 3rd, WHO, Geneva 2015. <http://www.who.int/malaria/publications/atoz/9789241549127/en/> (Accessed on June 29, 2018).
32. Hunfeld KP, Hildebrandt A, Gray JS. Babesiosis: recent insights into an ancient disease. *Int J Parasitol* 2008; 38: 1219-1237
33. Herwaldt BL, Linden JV, Bosserman E, et al. Transfusion-associated babesiosis in the United States: a description of cases. *Ann Intern Med* 2011; 155:509.
34. Brennan MB, Herwaldt BL, Kazmierczak JJ, et al. Transmission of Babesia microti Parasites by Solid Organ Transplantation. *Emerg Infect Dis* 2016; 22.
35. Cornett JK, Malhotra A, Hart D. Vertical transmission of babesiosis from a pregnant, splenectomized mother to her neonate. *Infect Dis Clin Pract* 2012; 20:408.
36. Vannier EG, Diuk-Wasser MA, Ben Mamoun C. Babesiosis. *Infect Dis Clin Kuzey Am* 2015; 29: 357.
37. Sun T, Tenenbaum MJ, Greenspan J, et al. Morphologic and clinical observations in human infection with Babesia microti. *J Infect Dis* 1983; 148:239–248.
38. Otsuka Y, Yamasaki M, Yamato O, Maede Y. Increased generation of superoxide in erythrocytes infected with Babesia gibsoni. *J Vet Med Sci* 2001; 63:1077.
39. Gelfand JA, Vannier EG. Babesia Species. In Mandell GL, Bennett JE, Dolin R (eds) *Principles and practice of infectious diseases*. 7th edition, 2010; 3539-45.
40. Laval RE. Daniel Alcides Carrion. *Rev Chilena Infectol* 2003; 20:36.
41. Maguina VC, Ugarte-Gil C, Brena CP, et al. Update of Carrion's disease. *Rev Med Hered* 2008; 19:36.
42. Maguiña C, Guerra H, Ventosilla P. Bartonellosis. *Clin Dermatol* 2009; 27: 271–280
43. Characterization of Bartonella bacilliformis flagella and effect of antiflagellin antibodies on invasion of human erythrocytes. *Infect Immun* 1993;61(12):4962-71
44. Maguina C, Garcia PJ, Gotuzzo E, et al. Bartonellosis (Carrión's disease) in the modern era. *Clin Infect Dis* 2001; 33:772.
45. Maguiña C, Gotuzzo E. Bartonellosis. New and old. *Infect Dis Clin North Am* 2000;14:1-

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46. Shurin SB, Anderson P, Zollinger J. Pathophysiology of hemolysis in infections with *Hemophilus influenzae* type b. *J Clin Invest* 1986;77(4):1340-8.
47. Biswas T, Ghosh DK, Mukherjee N, Ghosal J. Lipid peroxidation of erythrocytes in visceral leishmaniasis. *J Parasitol* 1997;83(1):151-2.
48. Justin Cochrane, Lacie Bland, and Mary Noble, Intravascular Hemolysis and Septicemia due to *Clostridium perfringens* Emphysematous Cholecystitis and Hepatic Abscesses, Hindawi Publishing Corporation, Volume 2015
49. McIlwaine K, Leach MT. *Clostridium perfringens* septicaemia. *Br J Haematol* 2013;163(5): 549.
50. Awad MM, Bryant AE, Stevens DL, Rood JL. Virulence studies on chromosomal alpha-toxin and theta-toxin mutants constructed by allelic exchange provide genetic evidence for the essential role of alpha-toxin in *Clostridium perfringens*-mediated gas gangrene. *Mol Microbiol* 1995; 15:191.
51. Hübl W, Mostbeck B, Hartleb H, et al. Investigation of the pathogenesis of massive hemolysis in a case of *Clostridium perfringens* septicemia. *Ann Hematol* 1993; 67:145.
52. C. van Bunderen, M. K. Bomers, E. Wesdorp. *Clostridium perfringens* septicaemia with massive intravascular haemolysis: a case report and review of the literature. *Netherlands Journal of Medicine* 2010 vol. 68- 9, pp. 343–346
53. Seval GC, Aylı M. *Turkiye Klinikleri J HematolSpecial Topics* 2016; 9(1): 34
54. Aigner C, Schmidt A, Gaggl M. An updated classification of thrombotic microangiopathies and treatment of complement gene variant-mediated thrombotic microangiopathy. *Clin Kidney J* 2019; 12:333.
55. Banatvala N, Griffin PM, Greene KD, et al. The United States National Prospective Hemolytic Uremic Syndrome Study: microbiologic, serologic, clinical, and epidemiologic findings. *J Infect Dis* 2001; 183:1063.
56. Mody RK, Luna-Gierke RE, Jones TF, et al. Infections in pediatric postdiarrheal hemolytic uremic syndrome: factors associated with identifying shiga toxin-producing *Escherichia coli*. *Arch Pediatr Adolesc Med* 2012; 166:902.
57. Fitzpatrick M. Hemolytic uremic syndrome and *E. coli* O157. *BMJ* 1999; 318:684.
58. Niaudet P, Boyer GO. Clinical manifestations of shiga toxin producing e.coli stec hus in children. UpToDate review version Jun 2020
59. Küçükkaya RD, Adıgüzel C. Trombotik trombositopenik purpura tanı ve tedavi kılavuzu. Sürüm 1-Temmuz 2011.
60. Ray PE, Liu XH. Pathogenesis of Shiga toxininduced hemolytic uremic syndrome. *Pediatr Nephrol* 2001;16(10):823-39
61. Cheung V, Trachtman H. Hemolytic uremic syndrome: toxins, vessels, and inflammation. *Front Med (Lausanne)* 2014;1:42.
62. Khalid M, Andreoli S. Extrarenal manifestations of the hemolytic uremic syndrome associated with Shiga toxin-producing *Escherichia coli* (STEC HUS). *Pediatr Nephrol* 2019; 34: 2495. Epub 2018 Nov 1
63. Brad Yuan, Melvyn H. Klein, Robert S. Contiguglia. The role of aluminum in the pathogenesis of anemia in an outpatient hemodialysis population. 1989;11: 2-3, 91-96
64. Khurana V, Gambhir I, Kishore D. Microangiopathic hemolytic anemia following disseminated intravascular coagulation in aluminum phosphide poisoning, *Indian Journal of Medical Sciences* 2009; Vol. 63, Issue 6

65. Beutler E . Hemolytic anemia due to chemical and physical agents. In: Beutler E, Lichtman MA, Coller BS, Kipps TJ, eds . Williams Hematology. 5th ed. New York: McGraw Hill; 1995 : 670-73
66. Means RT, Glader B. Acquired nonimmune hemolytic disorders. In: Greer JP, Arber DA, Glader B, List AF, Means RT, Paraskevas F, et al., eds. Wintrobe's Clinical Hematology. 13th ed. Philadelphia USA: Lippincott Williams & Wilkins; 2014. p.809-22.
67. McIntyre N, Clink HM, Levi AJ. Hemolytic anemia in Wilson's disease. N Engl J Med 1967; 276:439
68. Boulard M, Blume K, Beutler E: The effect of copper on red cell enzyme activities. J Clin Invest 1972; 51:459
69. Gamakaranaage CS, Rodrigo C, Weerasinghe S. Complications and management of acute copper sulphate poisoning; a case discussion. J Occup Med Toxicol 2011;6(1):34.
70. Lewis RJ Sr. Hawley's Condensed Chemical Dictionary 15th edn New York John Wiley, 2007 Inc pg.1028
71. Radding J. Acute renal tubular failure-a report of two cases with an unusual mechanism of poisoning due to sodium chlorate. Calif Med, 1958: vol 88; 446-450
72. Staudinger KC, Roth VS: Occupational lead poisoning. Am Fam Physician 1998; 57:719
73. Fischbein A, Wallace J, Sassa S, et al: Lead poisoning from art restoration and pottery work: unusual exposure source and household risk. J Environ Pathol Toxicol Oncol 1992; 11:7
74. Valentine WN, Paglia DE, Fink K. Lead poisoning: association with hemolytic anemia, basophilic stippling, erythrocyte pyrimidine 5'-nucleotidase deficiency, and intraerythrocytic accumulation of pyrimidines. J Clin Invest 1976;58(4): 926-32.
75. Piomelli S. Chemical toxicity of red cells. Environ Health Perspect 1981;39:65-70.
76. Volney G, Tatusov M, Yen A C, et al. Naphthalene Toxicity: Methemoglobinemia and Acute Intravascular Hemolysis. Cureus 2018;10(8): e3147.
77. Gold BS, Dart RC, Barish RA. Bites of venomous snakes. N Engl J Med 2002; 5; 347-356.
78. McDade J, Aygun B, Ware R. Brown recluse spider (*Loxosceles reclusa*) envenomation leading to acute hemolytic anemia in six adolescents. J Pediatr. 2010; 156(1): 155–157.
79. Yousefpoor Y, Amani A, Divsalar A. Assessment of hemolytic activity of bee venom against some physicochemical factors. Journal of Asia-Pacific Entomology 2019 : 22;4: 1129-1135
80. Roodt AR, Salomón OD, Orduna TA. Poisoning by bee sting. Gac Med Mex 2005;141(3):215-22.