

# BÖLÜM 10

## İlacı Bağlı Trombositopeni

Öykü ARSLAN<sup>1</sup>

Platelet olarak da adlandırılan trombositler kemik iliği megakaryositlerinden sentezlenir ve 7-10 gün kaldıkları dolaşıma salınır. Trombositopeni, periferik kandaki normal trombosit sayısı dağılımının 2.5. alt persentil değeri olan  $150 \times 10^9/L$  nin altındaki trombosit sayısı olarak tanımlanır (1). Trombositopeninin kemik iliği üretiminde azalma, tüketim artışı, yıkım artışı, dalak sekestrasyonu veya bu nedenlerin bir kombinasyonu gibi çok sayıda konjenital ve edinsel nedeni vardır (2). Trombosit sayısında azalmayı tetikleyebilecek birçok bozukluk arasında, ilacı bağli trombositopeni (İBT) özel bir odaklanmayı hak ediyor. İBT; gıdalar, içecekler, bitkisel ilaçlar ve besin takviyeleri dahil olmak üzere çok çeşitli ilaç ve bileşenlerin uygulanmasından sonra ortaya çıkabilir (3). İBT'de çok sayıda ilaç belirlenmiş olmasına rağmen, altta yatan patogenetik mekanizmalar temel olarak iki ana kategoriye ayrılır: trombosit üretiminin baskılanması ve periferik trombosit yıkımı veya klirensinde artış (Tablo-1).

**Tablo-1: İlacı bağli trombositopeni mekanizmaları**

Kemik iliği baskılanması veya megakaryosit hasarı
Tüm hematopoietik <b>hücre dizilerinde</b> veya megakaryosit soyunda sitotoksik miyelosupresyon
Hücre matürasyonu ile çatışma (megakaryopoez)
Megakaryosit proapoptotik etki
<b>Periferik trombosit</b> yıkımında artış
Non-immün İBT

## Kaynaklar

1. Eto K, Kunishima S. Linkage between the mechanisms of thrombocytopenia and thrombopoiesis. *Blood* 2016;127(10): 1234-1241.
2. Nagalla S, Sarode R. Recent advances in understanding and management of acquired thrombocytopenia. *F1000Res.* 2018;(7):68.
3. George JN, Aster RH. Drug-induced thrombocytopenia: pathogenesis, evaluation, and management. *Hematology Am Soc Hematol Educ Program.* 2009:153-158.
4. Aster RH. Drug-induced immune cytopenias. *Toxicology* 2005;209(02):149-153.
5. Gale RP. Antineoplastic chemotherapy myelosuppression: mechanisms and new approaches. *Exp Hematol* 1985;13(Suppl 16):3-7.
6. Danese E, Montagnana M, Favalaro EJ et al. Drug-induced thrombocytopenia: Mechanisms and laboratory diagnostics. *Semin Thromb Hemost.* 2020;46(3):264-274.
7. Majhail NS, Lichtin AE. What is the best way to determine if thrombocytopenia in a patient on multiple medications is druginduced? *Cleve Clin J Med* 2002;69(03):259-262.
8. Greinacher A, Fuerll B, Zinke H et al. Megakaryocyte impairment by eptifibatide-induced antibodies causes prolonged thrombocytopenia. *Blood* 2009;114(6):1250-1253.
9. De Silva E, Kim H. Drug-induced thrombocytopenia: focus on platelet apoptosis. *Chem Biol Interact* 2018;284:1-11.
10. Sadler JE, Moake JL, Miyata T et al. Recent advances in thrombotic thrombocytopenic purpura. *Hematology Am Soc Hematol Educ Program* 2004:407-423.
11. Prechel M, Walenga JM. Heparin-induced thrombocytopenia: an update. *Semin Thromb Hemost* 2012;38(5):483-496.
12. Shantsila E, Lip G, Chong BH. Heparin-induced thrombocytopenia. *Chest* 2009;135(6):1651-1664.
13. Vayne C, Guéry EA, Rollin J et al. Pathophysiology and diagnosis of drug-induced immune thrombocytopenia. *J Clin Med.* 2020 Jul 13;9(7):2212.
14. Bakchoul T, Jouni R, Warkentin TE. Protamine (heparin)-induced thrombocytopenia: a review of the serological and clinical features associated with anti-protamine/heparin antibodies. *J Thromb Haemost.* 2016;14(9):1685-1695.
15. Cuker A, Arepally GM, Chong BH et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: Heparin-induced thrombocytopenia. *Blood Adv.* 2018;2(22):3360-3392.
16. Pouplard C, Amiral J, Borg J, et al. Decision analysis for use of platelet aggregation test, carbon 14-serotonin release assay, and heparin-platelet factor 4 enzyme-linked immunosorbent assay for diagnosis of heparin-induced thrombocytopenia. *Am J Clin Pathol.* 1999;111(5):700-706.
17. Minet V, Dogne JM, Mullier F. Functional assays in the diagnosis of heparin-induced thrombocytopenia: a review. *Molecules* 2017;22(4):E617.
18. Aster RH, Bougie DW. Drug-induced immune thrombocytopenia. *N Engl J Med* 2007;157(6):580-587.
19. Vayne C, Guery EA, Rollin J et al. Pathophysiology and diagnosis of drug-induced immune thrombocytopenia. *J Clin Med* 2020;9(7):2212.
20. Visentin GP, Liu CY. Drug-induced thrombocytopenia. *Hematol Oncol Clin North Am* 2007;21(4):685-696.
21. Grossjohann B, Eicher P, Greinacher A et al. Ceftriaxone causes drug-induced immune thrombocytopenia and hemolytic anemia: characterization of targets on platelets and red blood cells. *Transfusion* 2004;44(7):1033-1040.
22. Verrotti A, Scaparrotta A, Grosso S et al. Anticonvulsant drugs and hematological disease. *Neurol Sci* 2014;35(7):983-993.

23. Loo AS, Gerzenshtein L, Ison MG. Antimicrobial drug-induced thrombocytopenia. A review of the literature. *Semin. Thromb. Hemost.* 2012;38(8):818-829.
24. Chong BH, Du XP, Berndt MC et al. Characterization of the binding domains on platelet glycoproteins Ib-IX and IIb/IIIa complexes for the quinine/quinidine-dependent antibodies. *Blood* 1991;77(10):2190-2199.
25. Topol EJ, Byzova TV, Plow EF. Platelet GPIIb/IIIa blockers. *Lancet* 1999;353(9148):227-231.
26. The RESTORE Investigators. Effects of platelet glycoprotein IIb/IIIa blockade with tirofiban on adverse cardiac events in patients with unstable angina or acute myocardial infarction undergoing coronary angioplasty. *Circulation* 1997;96(5):1445-1453.
27. Koster A, Morshuis M, Birschmann I. Abciximab/heparin during acute heparin-induced thrombocytopenia: a word of caution. *Ann Thorac Surg* 2018;106(1):309.
28. Dery JP, Braden GA, Lincoff AM et al. Final results of the ReoPro readministration registry. *Am J Cardiol* 2004;93(8):979-984.
29. Mascelli MA, Lance ET, Damaraju L et al. Pharmacodynamic profile of short-term abciximab treatment demonstrates prolonged platelet inhibition with gradual recovery from GP IIb/IIIa receptor blockade. *Circulation* 1998;97(17):1680-1688.
30. Aster RH. Can drugs cause autoimmune thrombocytopenic purpura? *Semin Hemaatol* 2000;37(3):229-238.
31. Griem P, Gleichmann E. Metal ion induced autoimmunity. *Curr Opin Immunol* 1995;7(6):831-838.
32. Chong BH, Choi PY, Khachigian L et al. Drug-induced immune thrombocytopenia. *Hematol Oncol Clin North Am* 2013;27(3):521-540.
33. Arnold DM, Nazi I, Warkentin TE et al. Approach to the diagnosis and management of drug-induced immune thrombocytopenia. *Transfus Med Rev* 2013;27(3):137-145.
34. Arnold DM, Curtis BR, Bakchoul T; Platelet Immunology Scientific Subcommittee of the International Society on Thrombosis and Hemostasis. Recommendations for standardization of laboratory testing for drug-induced immune thrombocytopenia: communication from the SSC of the ISTH. *J Thromb Haemost.* 2015;13(4):676-678.