20.
BÖLÜM

ONKOLOJİK TEDAVİYE BAĞLI PERİFERİK VASKÜLER HASTALIKLAR VE İNME

Yusuf Sinan AYDIN [1]

ONKOLOJİK TEDAVİYE BAĞLI PERİFERİKVASKÜLER HASTALIKLAR VE İNMENİN PATOFİZYOLOJİSİ VE KLİNİK TANISI

Kardiyoonkoloji, kemoterapi ve radyoterapinin yan etkisi olarak ortaya çıkan kardiyovasküler hastalıkların saptanması, takibi ve tedavisine odaklanan kardiyolojinin yeni bir alanıdır. Onkolojik popülasyonda tedaviye bağlı mortalite ve morbidite artışına yol açan çeşitli kardiyovasküler olaylar görülebilmektedir. Bu tedaviler miyositleri, endotel hücrelerini ve kan hücrelerini etkileyerek farklı mekanizmalar yoluyla kardiyovasküler toksisiteyi indükleme potansiyeline sahiptirler. Hastalara tedavi öncesi ayrıntılı kardiyovasküler değerlendirme yapılmalı, tedavinin herhangi bir aşamasında gelişebilecek istenmeyen olaylar açısından yakın takibe alınmaları önerilmektedir. Özellikle kardiyovasküler olay açısından yüksek riskli olan bireylerin onkolog ve kardiyolog arasında işbirliği içinde birlikte takip edilmeleri giderek önem kazanmaktadır. (1,2)

Periferik arter hastalığı

Periferik arter hastalığı, kardiyovasküler risk faktörleri ve uygulanan onkolojik tedaviye ikincil bir komplikasyon olarak yaklaşık%30'a varan bir insidansla ortaya çıkabilir. (3) Risk faktörleri arasında hipertansiyon, hiperlipidemi, diyabet, geçirilmiş tromboz ve inme, ileri yaş, erkek cinsiyeti, sigara kullanımı, obezite, düzensiz ilaç alımı, uygulanan kemoterapinin dozu ve süresi yer almaktadır. (4) Kronik miyeloid löseminin (KML) tedavisinde kullanılan tirozinkinaz inhibitörleri (TKİ), periferik arter hastalığı ve kardiyovasküler istenmeyen olayların gelişiminden sorumlu ana anti-neoplastik ajanlardır. KML hastalarında "altın standart" tedavi olarak kabul edilen imatinibe karşı ortaya

[1] Uzm. Dr., SBÜ Dr. Siyami Ersek Göğüs ve Kalp Damar Cerrahisi Eğitim Araştırma Hastanesi, Kardiyoloji Kliniği aydins76@gmail.com

nekroz, fibroz, vasavazorumlarda obstrüksiyon ve hızlanmış ateroskleroz yer alır. (35,36)

KAYNAKLAR

1. Kostakou PM, Kouris NT, Kostopoulos VS, Damaskos DS, Olympios CD.Cardio-oncology: a newanddevelopingsector of researchandtherapy in thefield of cardiology. Heart 2019 Jan;24(1):91-100
2. Alexandre J, Alexandre J, Cautela J, Ederhy S, Damaj GL, Salem JE et al. Cardiovasculartoxicityrelatedtocancer treatment: a pragmaticapproachtotheAmericanandEuropeancardio-oncology guidelines. J AM HeartAssoc. 2020 Sep 15;9 (18):e018403
3. Zamorano JL,Lancellotti P, RodriguezMuñoz D, AboyansV et al. TheTask Force forcancertreatmentsandcardiovasculartoxicity of theEuropeanSociety of Cardiology (ESC). EurHeart J.2016 Sep 21;37 (36):2768-2801.
4. Valent P,Hadzijusufovic E, Hoermann G, FürederW etal.Risk factorsandmechanismscontributingto TKI-inducedvascularevents in patientswith CML. LeukRes. 2017 Aug;59:47-54
5. O'Hare T, Eide CA, Deininger MW. Bcr-ablkinase domain mutations, drugresistance, andtheroadtoacureforchronicmyeloidleukemia. Blood. 2007;110:2242–9.
6. Radich JP. Monitoringresponsetotyrosinekinase inhibitör therapy, mutationalanalysis, andnewtreatmentoptions in chronicmyelogenousleukemia. J NatlComprCancNetw. 2013;11:663–6.
7. Aichberger KJet al. Progressiveperipheralarterialocclusivediseaseandothervascularevents duringnilotinibtherapy in CML. Am J Hematol. 2011;86:533–9
8. Kim TD, et al. Peripheralarteryocclusivedisease in chronicphasechronicmyeloidleukemiapatientstreatedwithnilotiniborimatinib. Leukemia. 2013;27:1316–21.
9. Le Coutre P, Rea D, Abruzzese E, Dombret H, Trawinska MM, Herndlhofer S, et al. Severe peripheralarterialdiseaseduringnilotinibtherapy. J NatlCancerInst. 2011;103:1347-8.
10. Giles FJ, Mauro MJ, Hong F, Ortmann CE, McNeill C, Woodman RC, et al. Rates of peripheralarterialocclusivedisease in patientswithchronicmyeloidleukemia in thechronicphasetreatedwithimatinib, nilotinib, ornon-tyrosinekinasetherapy: A retrospectivecohortanalysis. Leukemia. 2013;27:1310–5.
11. Valent P, Hadzijusufovic E, Schernthaner GH, Wolf D, Rea D, le Coutre P. Vascularsafetyissues in CML patientstreatedwith BCR/ABL1 kinaseinhibitors. Blood. 2015;125:901–6.
12. Mirault T, Rea D, Azarine A, Messas E. Rapidonset of peripheralarterydisease in a chronicmyeloidleukemiapatientwithoutpriorarterialdisorder: Direct relationshipwithnilotinibexposureandclinicaloutcome. Eur J Haematol. 2015;94:363–7.
13. Quintás-Cardama A, Kantarjian H, Cortes J. Nilotinib-associatedvascularevents. ClinLymphomaMyelomaLeuk. 2012;12:337–40.
14. Gover-Proaktor A, Granot G, Shapira S, Raz O, Pasvolsky O, Nagler A, et al. Ponatinibreducesviability, migration, andfunctionality of humanendothelialcells. LeukLymphoma. 2017;58:1455–67.
15. Sekijima T, Tanabe A, Maruoka R, Fujishiro N, Yu S, Fujiwara S, et al. Impact of platinum-basedchemotherapy on theprogression of atherosclerosis. Climacteric. 2011;14:31–40.
16. Serrano-Castro PJ, Guardado-Santervás P, Olivares-Romero J. Ischemicstrokefollowingcisplatinand 5-fluorouracil therapy: A transcranialdopplerstudy. EurNeurol. 2000;44:63–4.
17. El Amrani M, Heinzlef O, Debroucker T, Roullet E, Bousser MG, Amarenco P. Brain infarctionfollowing 5-fluorouracil andcisplatintherapy. Neurology. 1998;51:899–901.
18. Kinno R, Kii Y, Uchiyama M, Owan Y, Yamazaki T, Fukui T. 5-fluorouracil-induced leukoencephalopathywithacutestroke-likepresentationfulfillingcriteriaforrecombinanttissueplasminogenactivatortherapy. J StrokeCerebrovascDis. 2014;23:387–9.
19. Li J, Lee JJ, Chu E, Baehring JM. Reversibleleukoencephalopathywithstroke-likepresentation in a patientwith 5-dihydropyrimidine dehydrogenasedeficiencytreatedwithcontinuous 5-fluorouracil infusion. ClinColorectalCancer. 2012;11:215–7.

20. Nguyen MT, Stoianovici R, Brunetti L. Chemotherapyinducedstrokemimic: 5-fluorouracil encephalopathyfulfillingcriteriafortissueplasminogenactivatortherapy. Am J EmergMed. 2017;35:1389–90.
21. Fraum TJ, KreislTN, Sul J, Fine HA, Iwamoto FM. Ischemicstrokeandintracranialhemorrhage in gliomapatients on antiangiogenictherapy. J Neurooncol. 2011;105:281–9.
22. Letarte N, Bressler LR, Villano JL. Bevacizumabandcentralnervoussystem (CNS) hemorrhage. CancerChemotherPharmacol. 2013;71:1561–5.
23. Kuenen BC. Analysis of prothromboticmechanismsandendothelialperturbationduringtreatmentwithangiogenesisinhibitors. PathophysiolHaemostThromb. 2003;33(Suppl 1):13–4.
24. DiLisi D, Madonna R, Zito C, Bronte E, Badalamenti G, Parrella P, et al. Anticancertherapy-inducedvasculartoxicity: VEGF inhibitionandbeyond. Int J Cardiol. 2017;227:11–7
25. Chaosuwannakit N, D'Agostino R, Jr, Hamilton CA, Lane KS, Ntim WO, Lawrence J, et al. Aorticstiffnessincreasesuponreceipt of anthracyclinechemotherapy. J ClinOncol. 2010;28:166–72.
26. Drafts BC, Twomley KM, D'Agostino R, Jr, Lawrence J, Avis N, Ellis LR, et al. Lowtomoderatedoseanthracycline-basedchemotherapy is associatedwithearlynoninvasiveimagingevidence of subclinicalcardiovasculardisease. JACC CardiovascImaging. 2013;6:877–85.
27. Grover S, Lou PW, Bradbrook C, Cheong K, Kotasek D, Leong DP, et al. Earlyandlatechanges in markers of aorticstiffnesswithbreastcancertherapy. InternMed J. 2015;45:140–7
28. Gao Y, Ma G, Liu S, Teng Y, Wang Y, Su Y. Thalidomideandmultiplemyeloma serum synergisticallyinduce a hemostaticimbalance in endothelialcells *in vitro*.ThrombRes. 2015;135:1154–9.
29. De Bruin ML, Dorresteijn LD, van'tVeer MB, Krol AD, van der Pal HJ, Kappelle AC, et al. Increased risk of strokeandtransientischemicattack in 5-year survivors of hodgkinlymphoma. J NatlCancerInst. 2009;101:928–37.
30. Woodward WA, Durand JB, Tucker SL, Strom EA, Perkins GH, Oh J, et al. Prospectiveanalysis of carotidarteryflow in breastcancerpatientstreatedwithsupraclavicularirradiation 8 ormoreyearspreviously: No increase in ipsilateralcarotidstenosisafterradiationnoted. Cancer. 2008;112:268–73.
31. Levinson SA, Close MB, Ehrenfeld WK, Stoney RJ. Carotidarteryocclusivediseasefollowingexternalcervicalirradiation. ArchSurg. 1973;107:395–7.
32. Hayward RH. Arteriosclerosisinducedbyradiation. SurgClin North Am. 1972;52:359–66.
33. Cheng SW, Ting AC, Wu LL. Ultrasonicanalysis of plaquecharacteristicsandintimal-medialthickness in radiation-inducedatheroscleroticcarotidarteries. Eur J VascEndovascSurg. 2002;24:499–504.
34. Fonkalsrud EW, Sanchez M, Zerubavel R, Mahoney A. Serialchanges in arterialstructurefollowingradiationtherapy. SurgGynecolObstet. 1977;145:395–400.
35. Louis EL, McLoughlin MJ, Wortzman G. Chronicdamagetomediumandlargearteriesfollowingirradiation. J Can AssocRadiol. 1974;25:94–104.
36. Fajardo LF. Thepathology of ionizingradiation as definedbymorphologicpatterns. ActaOncol. 2005;44:13–22.