Moždani udar, akutni koronarni sindrom i mišićna hipotrofija kao posljedica hiperhomocisteinemije

Stroke, acute coronary syndrome and muscle hypothrophy as a consequence of hyperhomocysteinemia

Jozica Šikić[1,2], Ante Pašalić[2]*, Jasna Čerkez Habek[2,3], Tea Friščić[2], Dario Gulin[2], Edvard Galić[1,2]

[1]Sveučilište u Zagrebu, Medicinski fakultet, Zagreb, Hrvatska
[2]Klinička bolnica „Sveti Duh", Zagreb, Hrvatska
[3]Hrvatsko katoličko sveučilište, Zagreb, Hrvatska

[1]University of Zagreb, School of Medicine, Zagreb, Croatia
[2]University Hospital "Sveti Duh", Zagreb, Croatia
[3]Catholic University of Croatia, Zagreb, Croatia

RECEIVED:
October 21, 2018

ACCEPTED:
November 5, 2018

KLJUČNE RIJEČI: hiperhomocisteinemija, hiperkoagulabilnost, akutni koronarni sindrom.

KEYWORDS: hyperhomocysteinemia, hypercoagulability, acute coronary syndrome.

CITATION: Cardiol Croat. 2018;13(11-12):303. | https://doi.org/10.15836/ccar2018.303

***ADDRESS FOR CORRESPONDENCE**: Ante Pašalić, Klinička bolnica „Sveti Duh", Sveti Duh 64, HR-10000 Zagreb, Croatia. / Phone: +385-99-3438-178 / E-mail: ante.pasalic@outlook.com

ORCID: Jozica Šikić, https://orcid.org/0000-0003-4488-0559 • Ante Pašalić, https://orcid.org/0000-0001-5989-6495
Jasna Čerkez Habek, https://orcid.org/0000-0003-3177-3797 • Tea Friščić, https://orcid.org/0000-0003-3189-8661
Dario Gulin, https://orcid.org/0000-0001-8502-7816 • Edvard Galić, https://orcid.org/0000-0002-5707-0961

Uvod: Hiperhomocisteinemija (Hhc) je rijedak poremećaj koji se javlja u 5% opće populacije, češće u osoba muškog spola. Najčešće nastaje kao posljedica mutacije MTHFR gena, odgovornog za kodiranje enzima metilentetrahidrofolat reduktaze. Ostali mogući uzroci su mutacija gena za metionin sintetazu, smanjeni unos vitamina B_6, B_{12} i folata. Hhc se povezuje s kardiovaskularnim bolestima, renalnom insuficijencijom, šećernom bolesti, mišićnom atrofijom i hiperkoagulabilnim stanjima, koji mogu rezultirati akutnim koronarnim sindromom (AKS), akutnim cerebrovaskularnim incidentom (ACI) i dubokom venskom trombozom (DVT)[1,2].

Prikaz slučaja: Prikazujemo slučaj 35-godišnjeg bolesnika koji je prebolio nekoliko moždanih udara i tranzitornih ishemijskih ataka, koje su rezultirale desnostranom hemiparezom i disfazijom. Neurološkom obradom verificiraju se brojne ishemijske lezije. Bolesnik ima blago reduciranu sistoličku funkciju lijeve klijetke (ejekcijska frakcija 50%), dilatiranu lijevu klijetku (5,8 cm), učestale epizode nodalnog ritma, bradikardiju (< 35/min), asistolička pauza > 3,8 sekundi. Implantiran mu je trajni VVI elektrostimulator srca. Radi mišićne hipotrofije učini se i biopsija kojom se isključi mišićna distrofija. U lipnju 2016. godine bolesnik je hospitaliziran zbog anginoznih tegoba, s urednim elektrokardiografskim (EKG) nalazom i vrijednostima troponina. Koronarografijom se isključi koronarna bolest srca (KBS). U ožujku 2017. godine, uslijed tjelesne aktivnosti, bolesnik ponovo razvija anginozne tegobe uz povišene vrijednosti troponina, a u EKG-u je zabilježena denivelacija ST-segmenta u inferoposteriornim odvodima. Koronarografijom se isključi postojanje KBS. Učini se dodatna obrada u svrhu određivanja urođenog hiperkoagulabilnog stanja. Analiza je pokazala da je bolesnik homozigot za MTHFR gen i heterozigot za 4G/5G PAI-I gen te se uvede peroralni antikoagulans, vitamin B_{12} i folati.

Zaključak: Hiperhomocisteinemija je rijetka bolest koja može biti povezana s mišićnom hipotrofijom, a izazivanjem hiperkoagulabilnog stanja može dovesti do AKS i ACI. Stoga je potrebno misliti na nju posebice u mlađih, do tada zdravih pojedinaca, poglavito stoga što se primijenjenom terapijom mogu prevenirati njezine posljedice.

Introduction: Hyperhomocysteinemia (Hhcy) is a rare condition, observed in 5% of the general population, more commonly in men. It is mostly caused by a mutation in the MTHFR gene responsible for encoding methylenetetrahydrofolate reductase. Other possible causes include mutations in methionine synthase gene, vitamin B_6, B_{12} or folate deficiency. It may be associated with cardiovascular diseases, renal failure, diabetes mellitus, muscle atrophy, and persistent hypercoagulable state, which can lead to acute coronary syndrome (ACS), acute cerebrovascular events (ACE) and deep venous thrombosis (DVT)[1,2].

Case report: We present a case of a young man, 35-years-old, who suffered multiple strokes and transient ischemic attacks, causing right sided hemiparesis and dysphasia. Extensive neurological evaluation showed numerous ischemic lesions. He had dilatated cardiomyopathy (5.8 cm) with mildly decreased left ventricular ejection fraction (50%), frequent episodes of nodal rhythm, bradycardia (<35 beats per minute), an asystolic pause >3.8 seconds. A permanent VVI pacemaker was implanted. Due to muscular hypotrophy, muscle biopsy was performed, which excluded any known dystrophy. In June 2016 patient was hospitalized with typical stenocardia with normal electrocardiographic (ECG) finding and troponin levels. Coronary angiography has been performed, and coronary artery disease (CAD) has been excluded. In March 2017, due to physical activity patient has had typical stenocardia again. We have found high troponin levels and ST depression in inferoposterior leads on the ECG. Coronary angiography again showed no signs of CAD. Extensive diagnostics were performed in order to see whether the patient suffers from a hereditary hypercoagulable state. Mentioned analysis has showed that patient is homozygous for MTHFR gene and heterozygous 4G/5G PAI-1 gene. Permanent oral anticoagulant therapy as well as vitamin B_{12} and folate were introduced.

Conclusion: Hyperhomocysteinemia is a rare condition which can be associated with muscle hypotrophy, as well as hypercoagulable state by which it can lead to ACS and ACE. Therefore, Hhcy should be taken into account in especially in healthy young adults especially because by using therapy, its consequences could be prevented.

LITERATURE

1. Maron BA, Loscalzo J. The treatment of hyperhomocysteinemia. Annu Rev Med. 2009;60:39-54. https://doi.org/10.1146/annurev.med.60.041807.123308
2. Veeranki S, Winchester LJ, Tyagi SC. Hyperhomocysteinemia associated skeletal muscle weakness involves mitochondrial dysfunction and epigenetic modifications. Biochim Biophys Acta. 2015 May;1852(5):732-41. https://doi.org/10.1016/j.bbadis.2015.01.008