# Eozinofilna kardiomiopatija s trombom u lijevoj klijetci: ima li mjesta za nove oralne antikoagulanse u liječenju?

# Eosinophilic cardiomyopathy with thrombus in left ventricle: is there a place for new oral anticoagulants?

**Božo Vujeva, Katica Cvitkušić Lukenda, Domagoj Mišković***

Opća bolnica "Dr. Josip Benčević", Slavonski Brod, Hrvatska

General Hospital "Dr. Josip Benčević", Slavonski Brod, Croatia

**KLJUČNE RIJEČI:** hipereozinofilni sindrom, tromb u lijevoj klijetci, imatinib, antikoagulantna terapija.

**KEYWORDS:** hypereosinophilic syndrome, thrombus in the left ventricle, imatinib, anticoagulation therapy.

**CITATION:** Cardiol Croat. 2016;11(10-11):530-531. | **DOI:** http://dx.doi.org/10.15836/ccar2016.530

***ADDRESS FOR CORRESPONDENCE:** Domagoj Mišković, Opća bolnica "Dr. Josip Benčević", Andrije Štampara 42, HR-35000 Slavonski Brod, Croatia. / Phone: +385-98-760-767 / E-mail: domagoj1304@gmail.com

**ORCID:** Božo Vujeva, http://orcid.org/0000-0003-0490-3832 • Katica Cvitkušić Lukenda, http://orcid.org/0000-0001-6188-0708 Domagoj Mišković, http://orcid.org/0000-0003-4600-0498

**Uvod:** Hipereozinofilni sindrom je rijetki mijeloproliferativni poremećaj karakteriziran eozinofilijom i oštećenjem različitih organskih sustava.[1-3]

**Prikaz slučaja:** 23-godišnji bolesnik, hospitaliziran je zbog gubitka na težini, noćnog znojenja i kašlja. U laboratorijskim nalazima se verificira teška eozinofilija, uz anemiju i trombocitopeniju. 12-kanalni EKG je prikazan na **slici 1**. Učinjenim ultrazvukom srca (**slika 2**)verificiraju se morfološke promjene endomiokarda po tipu restriktivne dijastoličke disfunkcije uz umjerenu mitralnu regurgitaciju. Izuzev srca, nije nađena zahvaćenost drugih organskih sustava. U terapiju su uvedeni beta-blokator, ACE inhibitor, acetilsalicilatna kiselina te kortikosteroid. Trinaest dana po otpustu pacijent je hospitaliziran zbog paroksizmalne noćne dispneje i angine. Isključen je akutni koronarni sindrom. Na RTG-u pluća je opisan pleuralni izljev desno, a UZV-om srca se nađe pogoršanje mitralne regurgitacije. Pacijent je radi daljnje dijagnostike i terapije premješten u tercijarni centar gdje je započeto liječenje inhibitorom tirozin kinaze imatinibom. Na MR-u srca je verificiran tromb u lijevoj klijetci. Pacijent je premješten u našu ustanovu s preporukom daljnjeg uzimanja imatiniba i niskomolekularnog heparina (enoksaparin sc. u terapijskoj dozi).

**Zaključak:** Istovremeno uzimanje imatiniba i varfarina je kontraindicirano budući da se oba lijeka izlučuje putem jetre-supstrat su jetrenog enzima citokrom P450 3A4 te bi njihovo zajedničko uzimanje moglo povećati rizik od krvarenja. Kao alternativu enoksaparinu mogao bi se koristiti novi oralni antikoagulans (NOAC) dabigatran. Kao prednost u odnosu na enoksaparin navodimo peroralnu primjenu, a u odnosu na varfarin izbjegavanje enzimatskog sustava citokrom P450 3A4. Postoje i nedostatci jer dabigatran je substrat P-glikoproteinu, proteinu koji djeluje kao pumpa za prijenos tvari iz stanice, a imatinib inhibira djelovanje P-glikoproteina tako da može pojačati učinak dabigatrana i dovesti do krvarenja. U literaturi su opisani slučajevi uspješnog liječenja muralnih tromba dabigatranom te također zajedničkog uzimanja dabigatrana i imatiniba bez zabilježenih krvarenja. No, potreb-

**Background:** Hypereosinophilic syndrome is a myeloproliferative disorder characterized by eosinophilia that is associated with damage to multiple organs.[1-3]

**Case report:** 23-year-old patient, without comorbidity, was admitted to hospital because of weight loss, night's sweats and cough. Blood test result shows eosinophilia, anemia and thrombocytopenia. **Figure 1** shows 12-lead ECG. Transthoracic echocardiography (**Figure 2**) reveals endomyocardial fibrosis and restrictive diastolic dysfunction with moderate mitral regurgitation. Except the heart, there are no other organs involved. We started the treatment with beta-blockers, ACE inhibitors, aspirin and corticosteroids. Thirteen days after discharge, the patient was rehospitalized because of paroxysmal nocturnal dyspnea and angina. Acute coronary syndrome was ruled out. Right pleural effusion was seen on chest X-ray and further echocardiography showed worsening of mitral regurgitation. For the purpose of further diagnosis and treatment, patient was transferred to the University Hospital Center. Treatment by tyrosine kinase inhibitor imatinib was initiated. MRI exam verified thrombus in the left ventricle. The patient returned to our hospital with a recommendation by concomitant administration of imatinib 400 mg OD and subcutaneously enoxaparine 1 mg/kg BID.

**Conclusion:** Concomitant usage of imatinib and warfarin is not recommended since both drugs excreted by the liver-they are substrates of the liver enzyme citokrom P450 3A4 and taking them together could increase the risk of bleeding. As an alternative to enoxaparine, new oral anticoagulants (NOAC) dabigatran could be used. As an advantage compared to enoxaparin, we emphasize oral administration and in comparison to warfarin, dabigatran avoids enzymatic system cytochrome P450 3A4. There are also disadvantages because dabigatran is a substrate of P-glycoprotein, a protein that acts as a pump to transfer the substance from the cells. Imatinib inhibits the activity of P-glycoprotein so that can boost the effect of dabigatran and potentially lead to hemorrhage. There are reported cases of successful treatment of mural thrombi with dabigatran and also the reports of con-

**RECEIVED:**
**September 24, 2016**

**ACCEPTED:**
**October 10, 2016**

na su daljnja istraživanja koja bi dokazala učinkovitost i niski rizik krvarenja prilikom zajedničkog uzimanja dabigatrana ili ostalih NOAC-a i imatiniba u navedenoj situaciji.

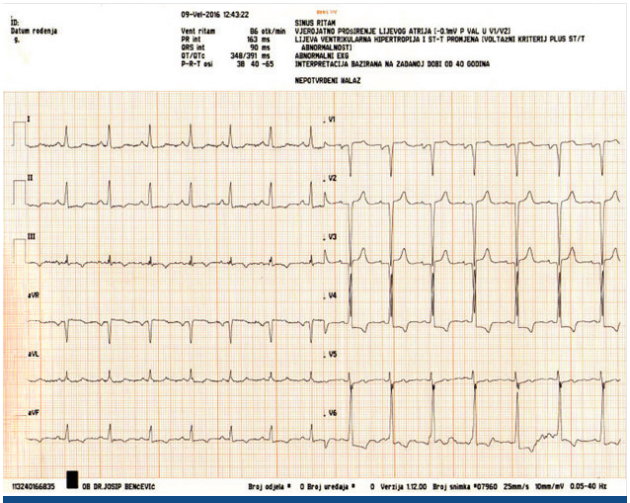

**FIGURE 1. Electrocardiographic signs of left atrial dilatation and left ventricular hypertrophy.**

comitant usage of dabigatran and imatinib without bleeding disorders. However, studies of parallel usage of dabigatran or other NOACs with imatinib in the hypereosinophilic syndrome are needed.

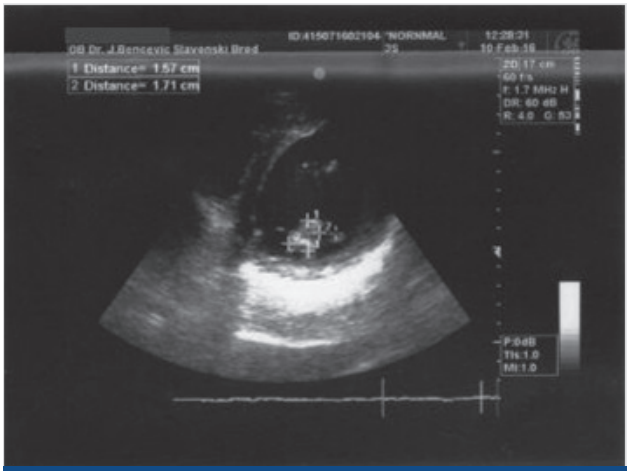


**FIGURE 2. Echocardiography – thrombus in the left ventricle size 1.57x1.71 cm.**

## LITERATURE

1. Adams JC, Dal-Bianco JP, Kumar G, Callahan MJ. Hypereosinophilic syndrome with characteristic left ventricular thrombus demonstrated by contrast echocardiography. Neth Heart J. 2009;17(4):169-70. **DOI:** http://dx.doi.org/10.1007/BF03086240
2. Cross P, Stewart R. Left Ventricular Mural Thrombus Treated With Dabigatran. J Case Rep Stud. 2014;2(4):402. **DOI:** http://dx.doi.org/10.15744/2348-9820.2.102
3. Short NJ, Connors JM. New Oral Anticoagulants and the Cancer Patient. Oncologist. 2014;19(1):82-93. **DOI:** http://dx.doi.org/10.1634/theoncologist.2013-0239