


Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) as Hypertension-Mediated Organ Damage (HMOD) in Hypertensive Emergencies

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ABSTRACT

Hypertensive emergencies are characterized by severe increases in blood pressure with evidence of hypertension-mediated organ damage (HMOD) and are associated with an increased risk of cardiovascular events, i.e. coronary heart disease (CHD) and mortality. **Case:** A 75-year-old man with typical chest pain with nausea and vomiting 1 hour before admission. Blood pressure was 200/100 mmHg, ECG showed T inversion in leads II, III, AVF, V1-V6 and prolonged QT interval, cardiomegaly on chest x-ray, laboratory results show leukocytosis, hyperglycemia, and hypokalemia. The diagnoses were non-ST elevation acute coronary syndrome (NSTE-ACS), hypertensive emergency, and T2DM. Treatment in the ICCU consists of intravenous antihypertensive, antiplatelet, anticoagulant, statin, nitrate, insulin, and potassium chloride for electrolyte correction. The patient was admitted to the ICCU for further observation and management.

Keywords: HMOD, hypertensive emergencies, ischemic heart disease.

ABSTRAK

Hipertensi emergensi ditandai dengan kenaikan tekanan darah yang berat disertai bukti kerusakan organ yang progresif *(hypertension-mediated organ damage* - HMOD*)*. Keadaan ini berkaitan dengan peningkatan risiko kejadian penyakit kardiovaskular, seperti penyakit jantung koroner bahkan kematian. **Kasus:** Seorang laki-laki usia 75 tahun dengan nyeri dada tipikal sejak 1 jam sebelum datang ke rumah sakit disertai mual dan muntah. Tekanan darah 200/100 mmHg, pada EKG didapatkan inversi T pada *lead* II, III, AVF, V1-V6, dan pemanjangan interval QT. Pada pemeriksaan *X-ray* dada didapatkan kardiomegali, hasil laboratorium menunjukkan leukositosis, hiperglikemi, dan hipokalemi. Pasien didiagnosis *non-ST elevation acute coronary syndrome* (NSTE-ACS), hipertensi emergensi, dan diabetes melitus tipe 2. Tata laksana di ICCU menggunakan anti-hipertensi intravena, *anti-platelet*, anti-koagulan, *statin*, nitrat, insulin, dan kalium klorida untuk koreksi elektrolit. Pasien dirawat di ICCU untuk observasi dan tata laksana lebih lanjut. **Karina Puspaseruni, Edmond Da Rizka, Wisnu Sakulat. *Non-ST Elevation Acute Coronary Syndrome* (NSTE-ACS) sebagai *Hypertension-Mediated Organ Damage* (HMOD) pada Hipertensi Emergensi.**

Kata kunci: HMOD, hipertensi emergensi, penyakit jantung iskemik.

INTRODUCTION

Hypertension is a major public health challenge worldwide due to its high prevalence and increased risk of cardiovascular diseases.[1] Globally, the proportion of hypertension was estimated to have a 29% rise from 2000 to 2025, and more than 80% of deaths from hypertension and related cardiovascular diseases occur in low- and middle-income countries.[1] Riskesdas data showed an increase in prevalence of hypertension in the >18-year population from 25.8% to 34.11% within the 5 years.[2]

Elevated blood pressure is a major risk factor for the development of hypertension-mediated organ damage (HMOD) and subsequent cardiovascular diseases.[3] Hypertension and diabetes mellitus are common coexisting conditions and increase the short-term as well as long-term risk of various cardiovascular complications including stroke, CAD (coronary arterial diseases), heart failure, atrial fibrillation, and peripheral vascular disease.[4]

CASE

A 75-year-old man with a history of uncontrolled hypertension and type II diabetes mellitus was admitted to the emergency department with typical chest pain 1 hour before admission along with nausea and vomiting. The patient was conscious with a blood pressure of 200/100 mmHg, pulse rate of 92 bpm, and respiration rate of 22/minute with 98% oxygen saturation in room air. No increase of jugular venous pressure. No rhonchi or wheezing was found in both lungs. A cardiac examination showed

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widened left sternal border with normal cardiac sound. Capillary refill time is normal, with no edema in extremities. ECG showed T inversion in lead II, III, AVF, V1-V6, and QTc 519 msec (**Figure**). Chest x-ray showed cardiomegaly with a cardiothoracic ratio (CTR) of 80%. Laboratory findings were slight leukocytosis (11.800/mm^3), hyperglycemia (305 mg/dL), and hypokalemia (3.47 mmol/L). The diagnosis was non-ST elevation acute coronary syndrome (NSTE-ACS), hypertensive emergency, with type-2 DM. The patient was treated with dual antiplatelet therapy (DAPT) oral clopidogrel 300 mg and aspirin 320 mg, subcutaneous fondaparinux 2.5 mg, oral atorvastatin 40 mg, candesartan 16 mg, nifedipine GITS 30 mg, sublingual nitrate 5 mg continued with nitroglycerine pump 1 mg/hour, ranitidine 50 mg iv, ondansetron 4 mg iv, insulin 4 IU iv, and potassium chloride infusion 37.5 mEq in 500 mL normal saline for 1 hour. The patient was treated in ICCU (Intensive Care Coronary Unit) for further observation and treatment.

DISCUSSION

Hypertension is a heterogeneous group of disorders characterized by sustained high blood pressure.[5] It is often associated with other risk factors such as diabetes mellitus or dyslipidemia.6 The average age of patients admitted to hospital with hypertensive emergency is between 55 and 60 years old.[5]

A hypertensive emergency is a sudden increase in systolic blood pressure above 180 mmHg and/or diastolic blood pressure above 120 mmHg with the presence of acute target organ damage.[7] HMOD (hypertension-mediated organ damage) refers to structural and functional changes in arteries or end organs such as the heart, brain, eyes, kidneys, and blood vessels.[5] HMOD has been associated with an increased risk of mortality and CV events; the incidence of cardiac death, CHD, ischaemic and hemorrhagic stroke was also significantly higher in HMOD patients.[6] Manifestations of cardiac organ damage include typical chest discomfort indicating myocardial infarction; back pain may indicate aortic dissection; and dyspnoea may indicate pulmonary edema or congestive heart failure.[8]

Chest discomfort is defined as a retrosternal sensation of pain, pressure, or heaviness ('angina') radiating to the left, right, or both arms, neck, or jaw, with additional symptoms such as sweating, nausea, epigastric pain, dyspnoea, and syncope.[9] This patient presents with new-onset chest pain that radiates into the left arm for 1 hour and does not improve with rest. No symptoms of dyspnoea, limb edema, or back pain. Older age, male sex, family history of CAD, diabetes, hyperlipidemia, smoking, hypertension, renal dysfunction, a previous manifestation of CAD, and peripheral or carotid artery disease increase the likelihood of NSTE-ACS.[9]

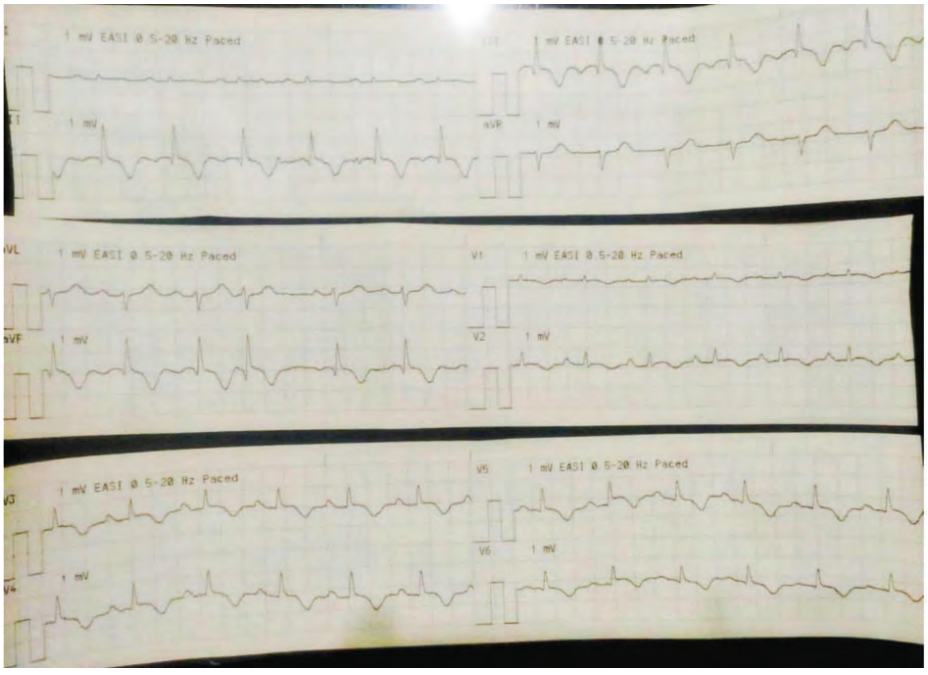

Figure. ECG on admission.

Directly exposed to high blood pressure, the heart is the main organ affected by hypertension.[10] The extent of left ventricular hypertrophy (LVH) is mainly related to the duration of hypertension and the level of elevated blood pressure; it initially occurs as an adaptation to increased ventricular wall stress.[10] Long-term primary hypertension can cause arteriolosclerosis and accelerate the atherosclerotic process.[5]

A basic metabolic profile including a complete blood count, urinalysis, ECG, and chest x-ray is indicated in all patients with a suspected hypertensive emergency.[11] Further investigations should be symptom-based and related to the differential diagnosis.[5] Cardiac enzymes should be performed in patients with acute coronary events but were not performed in this case due to limited facilities. Based on signs and symptoms; blood pressure 200/100 mmHg with typical chest pain, no ST elevation but T inversion on ECG, cardiomegaly on x-ray with hyperglycemia and hypokalemia, the diagnosis was NSTE-ACS, hypertensive emergency, and T2DM.

Current treatment of hypertensive emergencies is rapid blood pressure control with parenteral antihypertensive drugs (**Table 1**).[7] Hospital admission and close monitoring in the ICCU is recommended for continuous monitoring of arterial pressure levels, assessment and treatment of target organ damage[1] and administration of intravenous antihypertensive drugs.[12]

American College of Cardiology (ACC)/ American Heart Association (AHA) recommends intravenous esmolol, labetalol, nicardipine, or nitroglycerin for a hypertensive emergency with ACS (acute myocardial infarction with or without ST-segment elevation and unstable angina).[12] Similarly, the European Society of Cardiology (ESC)/European Society of Hypertension (ESH) recommends nitroglycerin and labetalol to lower SBP reaching <140 mmHg.[13] Nitroglycerine, a vasodilator that mainly reduces the preload and decreases the cardiac oxygen demands,[7] was used in this patient due to its availability **(Table 2)**.

Diabetes mellitus, hypertension, CVD, and kidney disease are known to share the same pathological mechanisms (activation of the renin-angiotensin-aldosterone system,


reactive oxygen species, inflammation), and simultaneously form a vicious cycle and interconnected complications.[4] Endothelial dysfunction, a hallmark of hypertension and diabetes mellitus, is the primary initiator for atherosclerosis and thrombosis, eventually leading to acute events such as myocardial infarction and stroke.[4] Salagre, *et al*, found 39.7% of hypertensive emergency patients also have diabetes mellitus.[14] Al Bannay also found that the prevalence of emergency hypertension among diabetes mellitus patients was higher (59.3%) than in the non-diabetic mellitus group (24.3%).[15] Diabetes mellitus combined with very high blood pressure can be a major contributor to the development of hypertensive emergencies.[4]

Hypertension is the most modifiable risk factor for CVD and stroke, and contributes to premature morbidity and mortality.[5] Older age, poor access to health care facilities, non-compliance with prescribed antihypertensive drug therapy, and comorbid conditions have been linked to risks of hypertensive crises and hypertensive emergencies.[4] According to Riskesdas data, good compliance with hypertension medication in the ≥18 years was only 54.4%, 32.27% were not compliant and the rest (13.33%) did not take drugs at all.[2] Similar results were also observed in routine blood pressure checks among the population ≥18 years; only 12% routinely took blood pressure measurements, 47% only occasionally, and 41% did not have a measurement.[2] Older age, non-adherence to treatment, and comorbid diabetes mellitus become several factors for hypertension emergency in this case.

Regular treatment combined with lifestyle modifications; reducing salt consumption, healthy diet, weight reduction, smoking cessation, regular physical activity, reducing stress, and inducing mindfulness can prevent high blood pressure also high blood glucose, and reduce CV risk.[13] The patient did not routinely control his hypertension and diabetes mellitus for many years and did not consume anti-hypertensive and/or anti-diabetic drugs regularly.

The mortality rate of hypertensive emergency is higher (4.6%) compared with hypertensive urgencies (0.8%) with a 29% 90-day readmission rate with the same diagnosis in hypertensive crisis.[16] The 6-year incidence of all-cause death was higher in the HMOD group than in the non-HMOD group (22.5% vs. 9.0%).[6] The in-hospital and one-year mortality for a hypertensive emergency are 13% and 39%, respectively.[17] These data demonstrate that hypertensive emergencies have both short- and long-term risks.[17]

Table 1. Blood pressure reduction strategies in cases of emergency hypertension.[12]

Clinical Presentation	Timeline and Target for BP Reduction	First-line Treatment	Alternative
Malignant hypertension with or without acute renal failure	Several hours Reduce MAP by 20%-25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediately reduces MAP	Nitroglycerine, labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediately reduces SBP to <140 mmHg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduces SBP to <120 mmHg AND heart rate to <60 bpm	Esmolol and nitroprusside or nitroglycerine or nicardipine	Labetalol OR metoprolol
Eclampsia and severe pre-eclampsia/HELLP	Immediately reduces SBP to <160 mmHg AND DBP to <105 mmHg	Labetalol or nicardipine and magnesium sulfate	Consider delivery

BP= blood pressure; bpm= beat per minute; DBP= diastolic blood pressure; HELLP= hemolysis, elevated liver enzymes, and low platelets; MAP= mean arterial pressure; SBP= systolic blood pressure.

Table 2. Characteristics of drug options for emergency hypertension.[12]

Drug	Onset of Action	Duration of Action	Doses	Contraindications	Adverse Effects
Esmolol	1-2 min	10-30 min	0.5-1 mg/kg as i.v. bolus; 50-300 µg/kg/min as i.v. infusion	Second or third-degree AV block, systolic heart failure, asthma, bradycardia	Bradycardia
Labetalol	5-10 min	3-6 h	0.25-0.5 mg/kg i.v. bolus; 2-4 mg/min infusion until goal BP is reached, thereafter 5-20 mg/h	Second or third-degree AV block, systolic heart failure, asthma, bradycardia	Bronchoconstriction, fetal bradycardia
Nicardipine	5-15 min	30-40 min	5-15 mg/h i.v. infusion, starting dose 5 mg/h, increase every 15-30 min with 2.5 mg until goal BP, thereafter decrease to 3 mg/h	Liver failure	Headache, reflex tachycardia
Nitroglycerine	1-5 min	3-5 min	5-200 µg/min i.v. infusion 5 µg/min increase every 5 min	-	Headache, reflex tachycardia

BP= blood pressure; i.v.= intravenous

CONCLUSION

Cardiovascular events associated with hypertensive emergencies are life-threatening situations requiring an immediate evaluation to protect end-organs, reduce the risk of complications, and improve patient outcomes. Hypertensive emergency needs careful but immediate blood pressure control. Early detection of target organ damage and proper treatment are key determinants for reducing morbidity and mortality.

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