

Hypertensive Crises in the Adolescent: Evaluation of Suspected Renovascular Hypertension

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ABSTRAK

Krisis hipertensi dapat dibagi menjadi dua kelompok, yakni hipertensi emergensi dan hipertensi urgensi. Sebagian besar ahli mendefinisikan hipertensi emergensi sebagai suatu situasi yang membutuhkan penurunan tekanan darah segera dengan menggunakan obat parenteral akibat adanya ancaman kerusakan organ target yang akut dan bersifat progresif, sedangkan hipertensi urgensi merupakan suatu situasi dengan peningkatan tekanan darah yang nyata tetapi tanpa disertai gejala klinis yang berat atau kerusakan organ target yang progresif, namun tekanan darah tetap perlu diturunkan dalam hitungan jam dengan menggunakan obat oral. Pasien dewasa muda dengan hipertensi perlu dicurigai mengalami hipertensi renovaskular meskipun keadaan ini dapat juga disebabkan oleh faktor lain.

Laporan kasus ini menyajikan suatu kasus anak laki-laki berusia 16 tahun dengan krisis hipertensi suspek hipertensi renovaskular. Tekanan darahnya sebesar 240/120 mmHg saat masuk ke rumah sakit disertai retinopati hipertensi derajat III dan didapatkan peningkatan kreatinin setelah pemberian ACE-inhibitor; namun arteriografi menunjukkan hasil normal, pemeriksaan fisis lainnya dan pemeriksaan laboratorium juga menunjukkan hasil yang normal. Berdasarkan hal tersebut, disimpulkan bahwa pasien menderita hipertensi esensial. Oleh karena krisis hipertensi dapat muncul pada segala rentang usia, para dokter perlu mewaspadaai adanya kemungkinan hipertensi renovaskular pada pasien berusia muda dengan krisis hipertensi. Deteksi dini dan penanganan yang segera diperlukan untuk mencegah komplikasi akibat kerusakan organ target yang bersifat progresif.

Kata kunci: krisis hipertensi, dewasa muda.

ABSTRACT

Hypertensive crises can be divided into two categories as hypertensive emergency and hypertensive urgency. Most authorities have defined hypertensive emergency as a situation that requires immediate reduction in blood pressure (BP) with parenteral agents because of acute or progressive target organ damage, whereas hypertensive urgency is a situation with markedly elevated BP but without severe symptoms or progressive target organ damage, wherein the BP should be reduced within hours, often with oral agents. Adolescent with hypertension should be suspected of having renovascular hypertension in spite of other causes.

This case is presenting a 16-year-old boy with hypertensive crises due to suspected renovascular hypertension. His blood pressure was 240/120 at admission with hypertensive retinopathy grade III and there was increase in creatinine after administering ACE-inhibitor but his renal arteriography revealed normal, other physical examination and laboratory findings was normal. Regarding these findings, the conclusion was this patient got essential hypertension. As many hypertensive crises occur in any ages, clinicians should aware the possibility of renovascular hypertension in young patients with hypertensive crises. An early detection and urgent treatment are needed to prevent the implication of progressive target organ damage.

Key words: hypertensive crises, adolescent.

INTRODUCTION

Hypertension affects more than 1 billion people worldwide and is one of the leading causes of death. Among hypertension population, 70% is mild hypertension, 20% is moderate hypertension, 10% is severe hypertension, and 1% is hypertensive crises for each hypertension type. Depending on the degree of blood pressure (BP) elevation and presence of end-organ damage, severe hypertension can be defined as either a hypertensive emergency or a hypertensive urgency. A hypertensive emergency is associated with acute end-organ damage and requires immediate treatment with a titratable short-acting IV antihypertensive agent. Severe hypertension without acute end-organ damage is referred to as a hypertensive urgency and is usually treated with oral antihypertensive agents.¹ Secondary hypertension is more common in adolescent, with most cases caused by renal disease. Primary or essential hypertension is more common in adolescents and has multiple risk factors, including obesity and a family history of hypertension. Evaluation involves a thorough history and physical examination, laboratory tests, and specialized studies.¹

CASE ILLUSTRATION

A 16-year-old boy felt blurred vision in left eye without symptoms of itching, watery eyes, and eye redness within two weeks prior to admission. The Ophthalmologist at Cipto Mangunkusumo Hospital diagnosed as exudative retinal detachment with retinopathy on left eye and referred to rheumatology polyclinic to reveal any autoimmune or collagen disease, then he was referred to emergency room because of having blood pressure (BP) 240/180 mmHg. He denied any symptoms of headache, anxiety, loss of consciousness, feet edema, shortness of breath, chest pain, nosebleed, nausea and vomiting, rheumatic pain, cheek redness, photosensitivity, oral ulcers, palpitation, snoring, redness of urine, and small volume of urine. Urination and defecation were normal. There were no history of head trauma, hypertension, diabetes, heart disease, renal disease, allergy, or asthma. His mother has hypertension. He was a high school student. He never smoked or consumed any drugs before.

Physical examination revealed the BP was 240/180 mmHg, measured in both arms and legs, heart rate 88x/mins regular beat, respiratory rate 16x/mins, and normal temperature. IMT 24.2 kg/m² (overweight). There was gallop sounds on heart auscultation, other examinations were within normal limit.

Laboratory results showed hemoglobin level 13.7 g/dL, white blood cell 10.100/uL (diff count: -/3/75/20/2), platelet count 283.000/uL, creatinine 1.2 mg/dL, albumin 4.9 u/L, normal liver function and electrolyte level. Urinalysis showed proteinuria (+1) with protein excretion 556 mg/day. ECG showed LV strain. Chest X-ray showed cardiomegaly with rounded shaped of left heart border. Ophthalmologist diagnosed as hypertensive retinopathy OS gr III and hypertensive retinopathy OD gr II.

He was diagnosed as hypertensive emergency and was given O₂ 3L/mins, intravenous fluid drip (IVFD) of dextrose 5%/12 hours, nicardipine 10 mg/hr, clonidine 2x0.15 mg, captopril 3x25 mg, and bisoprolol 1x5 mg. In inpatient ward, he was diagnosed as hypertension stage II with history of hypertensive emergency and proteinuria. He was planned to undergo renal ultrasonography, renal Doppler ultrasound, magnetic resonance angiography (MRA), arteriography, aPTT, and serial ureum/creatinin. The BP was 160/110 mmHg in all extremities with Nicardipine 10 mg/hr and planning to tapering down gradually, renal diet 2100 kcals, clonidine 3x0.15 mg, captopril 3x25 mg, bisoprolol 1x5 mg. On the next day, the BP was increase to 240/170 mmHg on Nicardipine 1 mg/hr, so Nicardipine was increased to 2.5 mg/hr and later on to 5 mg/hr and given hydrochlorothiazide (HCT) 1x25 mg and alprazolam 2x0.5 mg, on the 5th day the BP was 140/110 mmHg and Nicardipine was tapering off gradually. During therapy, creatinin serial was increased from 1.2 to 1.7 and 2.2, so captopril was stopped and given amlodipine 1x10 mg. aPTT test was normal, MRA could not be done due to lack of facility.

Renal ultrasonography was normal, Renal Doppler Ultrasound shows suspicious of right renal artery stenosis. Coronary and renal arteriography was normal. He went home with clonidine 3x0.15 mg, amlodipine 1x10 mg, bisoprolol 1x5 mg, and HCT 1x25 mg and should have follow up in nephrology polyclinic.

DISCUSSION

Hypertensive emergency defined as a situation that requires immediate reduction in blood pressure (BP) with parenteral agents because of acute or progressing target organ damage.¹ **Table 1** shows the initial evaluation of patients with a hypertensive emergency.

Table 1. Initial evaluation of hypertensive emergency²

History
- Prior diagnosis and treatment of hypertension
- Intake of pressor agents: street drugs, sympathomimetics
- Symptoms of cerebral, cardiac, and visual dysfunction
Physical examination
- Blood pressure, Funduscopy, neurologic status, cardiopulmonary status
- Body fluid volume assessment, peripheral pulses
Laboratory evaluation
- Hematocrite and blood smear, urine analysis
- Automated chemistry: creatinine, glucose, electrolytes
- Plasma renin activity and aldosterone (if primary aldosteronism is suspected)
- Plasma renin activity before and 1 h after 25 mg captopril (if RVH is suspected)
- Spot urine or plasma for metanephrine (if pheochromocytoma is suspected)
Chest radiograph
Electrocardiogram

Physical examination revealed BP was 240/180 mmHg with hypertensive retinopathy OS gr III and hypertensive retinopathy OD gr II. These are the signs of hypertensive emergency with eye as target organ damage. This patient had gallop sound in heart auscultation, no abdominal bruit sound was found. If cardiomegaly is present, in some patients, a third heart sound (S3 or protodiastolic gallop) is audible. About 50% of patients with renovascular hypertension have an abdominal bruit.³

Laboratory examination revealed creatinine serial 1.2, 1.7, and 2.2 after given captopril 25 mg three times daily. Administration of ACEI can reduce glomerular capillary hydrostatic pressure to cause a decrease in glomerular ultrafiltration and produces a rise in serum creatinine. Filtration usually recovers rapidly after discontinuation of the offending drug. Unexplained deterioration of renal function associated with an ACEI should raise the possibility of renovascular hypertension⁴

Proteinuria was 556 mg/day. The renal lesion associated with malignant hypertension consists of fibrinoid necrosis of the afferent arterioles, sometimes extending into the glomerulus, and may result in focal necrosis of the glomerular tuft. Clinically, macroalbuminuria (>300 mg/d) or microalbuminuria (30–300 mg/d) are early markers of renal injury.⁵

aPTT was normal, excluding hypercoagulable states concerning Anti Phospholipids Syndrome. There was no hypokalemia, excluding hyperaldosteronism, plasma aldosterone to renin ratio was unable to be performed due to lack of facility. Vanolic Mandelic Acid (VMA) also was unable to be performed due to lack of facility, to exclude pheochromocytoma, but there were no symptoms of flushing and autonomic instability.

Electrocardiography (ECG) shows left ventricular hypertrophy. Hypertensive heart disease (HHD) is the result of structural and functional adaptations leading to left ventricular hypertrophy and diastolic dysfunction. Renovascular hypertension is associated with increased sympathetic neural activity leading to target organ injury, including left ventricular hypertrophy.⁶

Chest radiography shows cardiomegaly with rounded appearance of left heart border which is the sign of left ventricular hypertrophy. Renal Ultrasonography shows normal interpretation. Renal Doppler ultrasound shows suspicious of right renal artery stenosis, the distal portion was unable to be examined because of thick peritoneal fat and presence of bowel gas. Limitations of Doppler ultrasound are often related to inadequate examinations, particularly in obese patients and overlying bowel gas. Measuring peak systolic velocity (PSV), end-diastolic velocity and the ratio of the PSV in the renal artery to PSV in the aorta, gives its high sensitivity and specificity to 90% and 95%.⁷

Renal Doppler ultrasound shows Renal Aortic velocity Ratio (RAR) in right renal artery 2.78 (<3.5), this ratio represents renovascular hypertension if >3.5 but at ratio of 2.78, there's a possibility of renovascular hypertension.⁸

PSV >200 cm/s and RAR >2.0 were the flow velocity criteria utilized to indicate hemodynamically significant fibromuscular dysplasia (FMD), but it has limited specificity so most studies used RAR >3.5 as accepted standard. Some studies revealed that RAR >3.5

was found in 40% and RAR between 2.5-3.5 was found in 60% of patients. Doppler abnormalities in mid-to-distal location and occasionally extending into primary branches, suggested renal artery FMD, but subsequent renal angiography demonstrated normal or nearly normal, rather than the classic beaded appearance.⁹

MRA could not be done because of lack of facility and costly. MRA is the screening investigation of choice for renal artery stenosis in most centers. Advantages are that it is non invasive, avoids ionizing radiation, and uses a non-nephrotoxic contrast agent (gadolinium). Its has high sensitivity and specificity exceeding 95%.¹⁰

Arteriography shows normal coronary and renal arteriography. Arteriography with contrast remains the gold standard to determine the degree and location of renal artery stenosis, however it provides no information about the functional role and the clinical significance of the lesion.¹¹

Renovascular hypertension is one of the causes of hypertensive crises, presenting between 0.2%-32% and it has been reported about 1-5% of an entire hypertensive population has renovascular hypertension.¹²

Two most etiologies of renovascular hypertension are atherosclerosis (90%) and FMD (10%). Atherosclerosis generally occurs at the proximal portion of the artery in older patients with typical cardiovascular risk factors and in the contrary, FMD occurs in the middle or distal arterial segments in younger patients.¹³ **Table 2** below shows the clinical clues for renovascular hypertension.

This patient was suspected of RVH because having clinical clues which are onset of hypertension is before 30 years old, abrupt onset or worsening of hypertension, severe hypertension, worsening renal function with ACE inhibitor, advanced hypertensive retinopathy, moderate proteinuria, and elevated serum creatinine. Renal Doppler ultrasound shows suspicious of right renal artery stenosis (RAR 2,78).

There are many screening tests available for detecting RA stenosis including measurement of plasma renin activity, captopril-stimulated plasma renin activity, nuclear renography, intravenous pyelography, magnetic resonance angiography (MRA), renal Doppler, intravascular ultrasonography (IVUS), digital subtraction angiography, spiral CT imaging, and renal

Table 2. Clinical clues for renovascular hypertension¹⁷

History
- Onset of hypertension before age 30
- Abrupt onset or worsening of hypertension
- Severe or resistant hypertension
- Symptoms of atherosclerotic disease elsewhere
- Smoker
- Worsening renal function with ACE inhibitor or ARB
- Recurrent flash pulmonary edema
Examination
- Abdominal bruits, other bruits, advanced hypertensive retinopathy
Laboratory
- Secondary aldosteronism: higher plasma renin, low K, low Na
- Proteinuria, usually moderate
- Elevated serum creatinine
- >1.5 cm difference in kidney size on sonography
- Cortical atrophy on CT angiography

arteriography. The reported sensitivities and specificities range from 75% to 95%.

There is no specific algorithm because a rigid diagnostic approach for every case of suspected RVH is neither possible nor advisable. A general recommendation for a diagnostic approach to patients with suspected renovascular hypertension is presented in **Figure 1**. In some cases, it may be prudent to use a combination of studies. **Figure 2** is another algorithm presented for suspicious of RAS.

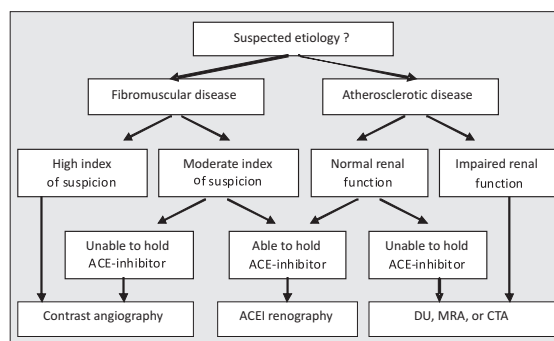


Figure 1. Suggested algorithm for suspected renovascular hypertension¹⁸

Treatment of hypertensive crises requires immediate control of the BP to terminate ongoing end-organ damage within the first 1-2 hours with intravenous anti hypertension agent but BP should not be lower than 25% of MABP, then within 2-6 hours should be reached 160/100 mmHg or MABP 120 mmHg, then if stable we can add oral drugs and reduce BP to normal limit.¹

This patient had BP 160/110 mmHg with Nicardipine 10 mg/h and planning to tapering down gradually to 1 mg/h and increase oral dose when we tapering down, his BP was increased to 240/170 mmHg, so we increased Nicardipine dose to 2.5 mg/h and later to 5 mg/h and given HCT 1x25 mg and alprazolam 2x0,5 mg.

On the 5th day, his BP was 140/110 mmHg so Nicardipine was tapering off and his blood pressure was stable (130/80 mmHg), oral drugs were given continually. Nicardipine has 100 times more water soluble than nifedipine, and, therefore it can be administered IV, making nicardipine a titratable IV calcium channel blocker. The onset of action of IV nicardipine is between 5-10 min, with a duration of action of 15-30 min and may exceed to 4 hours. Nicardipine can be given in 5-15 mg/h and increase 2.5 mg/h every 5 mins to a max of 15 mg/h. **Table 3** shows the iv antihypertensive medications which available in Indonesia.

During therapy, he was given captopril 3x25 mg and creatinin serial revealed increase of creatinine from 1.2, 1.7, and 2.2, so captopril was stopped and was given amlodipine 1x10 mg. ACEI is widely accepted as being superior in controlling renovascular hypertension. The major concern about ACEI is their potential to precipitate acute renal failure in patients with renovascular hypertension.¹⁷

This patient was concluded to have essential hypertension due to complication of chronic hypertension and normal arteriography.

Table 3. Dosages of i.v antihypertensive medications¹⁹

Drugs	Dosage	OOA	DOA
Conidine 150 ug	6 amp/250 cc gluc 5% microdrip	30-60 min	24 hrs
Nitroglycerin	10-50 ug per 500 cc	2-5 min	5-10 min
Nicardipine	0.5-6 ug/kg/min	1-5 min	15-30 min
Diltiazem	5-15 ug/kg/min then 1-5 ug/kg/min	1-5 min	15-30 min
Nitroprussid	0.25 ug/kg/min	Immediate	2-3 min

CONCLUSION

As many hypertensive crises occur in any ages, clinicians should remember the possibility of renovascular hypertension in young patients with hypertensive crises. An early detection and urgent treatment are needed to prevent the complications of progressive target organ damage.

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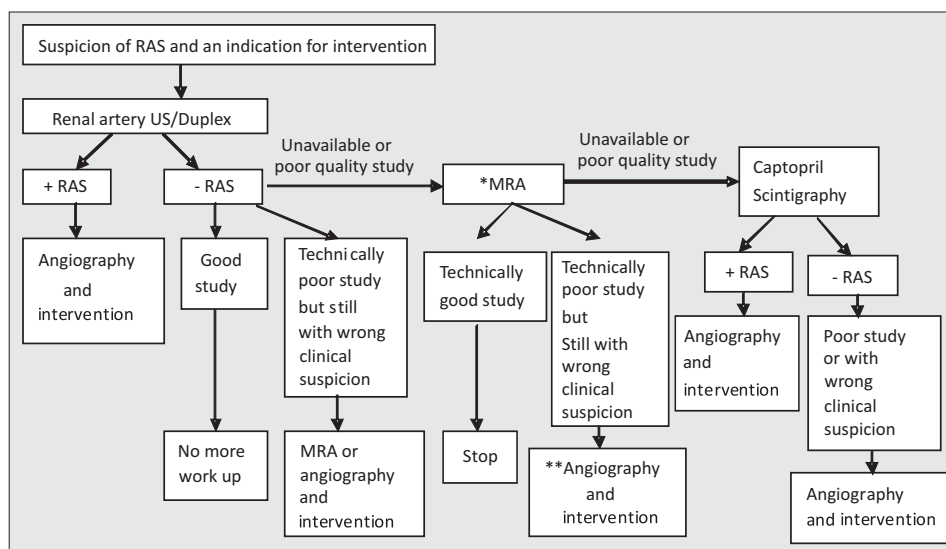


Figure 2. Algorithm for suspicion of renal artery stenosis¹⁸

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