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CASE REPORT

An adolescent with isolated systolic hypertension – case report and diagnostic and therapeutic approach

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ABSTRACT

Primary hypertension (PH) is the most common cause of arterial hypertension in adolescents; many of these patients present with isolated systolic hypertension (ISH).

The study presents a case of a 16-year-old male adolescent with PH. The patient had ISH in both 24-hour-ambulatory and office measurements. Secondary causes and hypertension-mediated organ damage were excluded. Evaluation of the vascular phenotype revealed low central systolic blood pressure (109 mm Hg), high peripheral augmentation index (27 mm Hg), and high arterial elasticity. The boy was started on non-pharmacological treatment. The manuscript discusses up-to-date knowledge on the pathogenesis and evolution of ISH in young people. A diagnostic and therapeutic approach according to the European Society of Hypertension is presented.

Adolescents with ISH require evaluation of the vascular phenotype. There is a need for further studies on the evolution and long-term outcome in young people with this form of arterial hypertension.

KEY WORDS:

adolescent, central blood pressure, primary hypertension, isolated systolic hypertension.

INTRODUCTION

Arterial hypertension (AH) is found in approximately 3–5% of paediatric patients and 10% of adolescents (significantly more commonly in boys) [1]. Older data [2] and new ones [3] suggest that primary hypertension (PH) covers approximately 50% of all cases of AH in children. Undoubtedly, primary (or essential) hypertension is the leading cause after puberty.

Primary hypertension is a disease of unknown aetiology, but numerous theories on pathogenetic pathways in PH have been developed in recent years. The most popular theories explaining the rise in blood pressure include the following: hyperkinetic circulation, activation of renin-angiotensin-aldosterone and sympathetic systems, the impact of central obesity, hyperinsulinemia and insulin resistance, oxidative stress, endothelial dysfunction, hyperuricemia, low-grade inflammation and autoimmune mechanisms, premature (early) aging of vital systems like arteries, the immune system, or even the skeletal system (early biological aging concept), and increased salt sensitivity (Guyton hypothesis) [4–6]. Environmental determinants of hypertension, such as a sedentary lifestyle, unhealthy diet, and stimulants, including tobacco smoking, should also be considered. All these pathogenetic aetiologies are likely to play a role. Genetic factors are important, but the role of single polymorphisms is practically negligible [7].

The most common vascular phenotype of PH is isolated systolic hypertension (ISH). Recent research has shown that many of these adolescents have normal central blood pressure and no hypertension-mediated organ damage (HMOD), and a rise in peripheral blood pressure is caused by hyperkinetic circulation and increased arte-

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rial leading to abnormal augmentation of systolic blood pressure in upper arm arteries [5].

Considering its prevalence, PH has become one of adolescents' most common chronic diseases. Hence, every paediatrician should know the diagnostic and therapeutic approach to an adolescent with elevated blood pressure. This paper underlines the most important diagnostic and therapeutic steps in an adolescent with ISH regarding up-to-date Polish and international recommendations.

CASE REPORT

A 16-year-old boy was referred to our department with suspicion of AH. In anamnesis, elevated blood pressure was first noted 3 months earlier during routine screening at the doctor's office (paediatric balance examination). Since then, his home blood pressure measurements have been in the range of 140/70 to 150/80 mm Hg. The patient reported no complaints that could be related to hypertension. Past medical history was as follows: he was born from the first pregnancy, spontaneous delivery in the 40th week of gestation, his birth weight was 3250 g, with an Apgar score of 10. At the age of 10 months he was hospitalized due to intussusception; he underwent resection of a small bowel segment and appendix. At 10 years of age, torsion of the right testicle was treated surgically. There were no other diseases or allergies. His medical history was negative for symptoms of kidney diseases or urinary tract infections. The patient never smoked cigarettes or used other stimulants. His physical activity was average. He exercised in physical education classes and did not engage in additional physical activity. His mother suffered from arterial hypertension, diagnosed at the age of 15 years – no diagnostic tests aimed at secondary causes were performed on the mother. His father and 12-year-old sister were healthy with normal blood pressure.

On admission, physical examination revealed no abnormalities. His height was 189 cm (95th percentile according to Polish normative values [8]), weight was 90 kg (95th percentile [8]), and body mass index was 25.2 kg/m^2 (88th percentile [8]). His blood pressure measured with an oscillometric validated device was 136/80 – 145/70 – 145/80 mm Hg, and his blood pressure on an auscultatory (sphygmomanometer) was 140/80 mm Hg. In 24-h ambulatory blood pressure, ISH was confirmed – 24 h – 142/72 mm Hg, activity period – 146/74 mm Hg, resting period – 126/62 mm Hg. Vascular phenotype evaluation was performed (Figures 1, 2). It revealed high peripheral augmentation of central blood pressure (central systolic blood pressure – cSBP: 109 mm Hg, peripheral systolic blood pressure 136 mm Hg, systolic blood pressure augmentation 27 mm Hg) and high elasticity of large arteries – negative augmentation index normalized to the heart rate of 75 beats per minute: –17%, and normal aortic pulse wave velocity (aPWV) – 5.5 m/s (25–50th percentile [9]).

In laboratory tests, the patient was found to have normal kidney function – creatinine 0.65 mg/dl, normal serum ions (sodium 140 mmol/l, potassium 4.3 mmol/l, calcium 9.8 mg/dl), no anomalies in lipids (total cholesterol 120 mg/dl, LDL-cholesterol 60 mg/dl, HDL-cholesterol 47 mg/dl, triglycerides 57 mg/dl), and normal blood gases. His urinalysis was also normal. Tests to exclude secondary blood pressure forms revealed the following: on ultrasound – normal kidney, urinary tract and adrenal glands, and normal renal artery blood flow spectrum (Doppler ultrasonography), normal aortic arch on echocardiography, normal thyroid function assessed as free

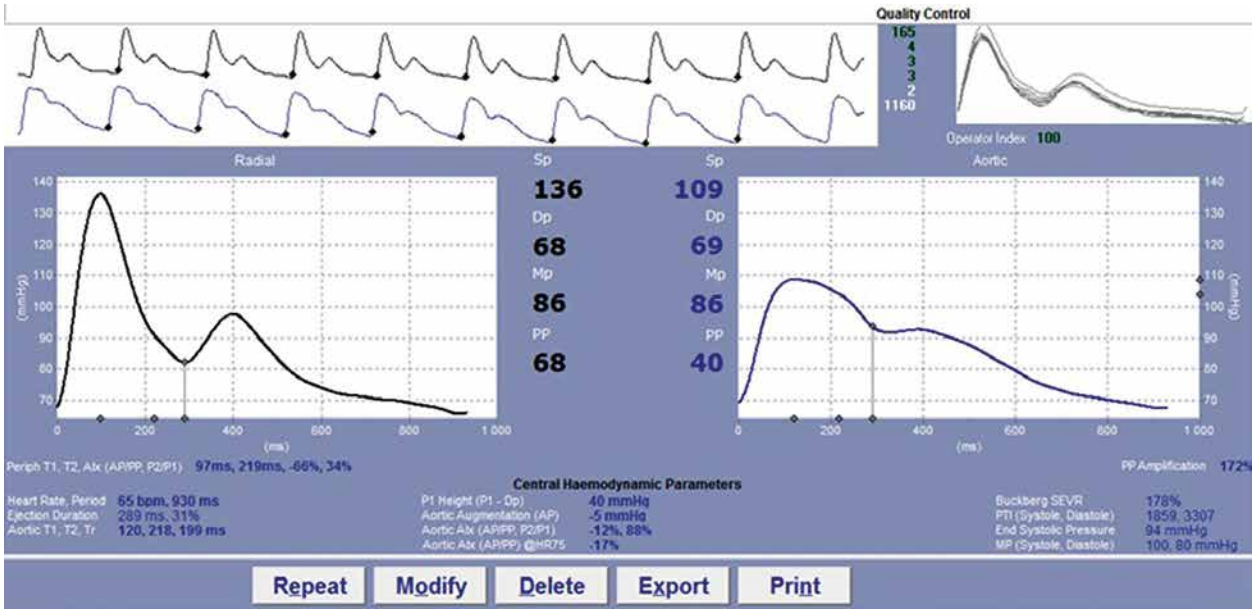

FIGURE 1. Vascular phenotype analysis in a patient with isolated systolic hypertension – pulse wave analysis and central blood pressure – Sphygmocor, AtCor Medical, Australia

FIGURE 2. Vascular phenotype analysis in a patient with isolated systolic hypertension – aortic pulse wave velocity – Sphygmocor, AtCor Medical, Australia

thyroxine (fT4) and thyroid-stimulating hormone concentrations, normal renin and aldosterone concentrations after 2 hours in a supine position, normal plasma metoxycatecholamines, and normal cortisol circadian profile.

Tests for HMOD were as follows: left ventricular mass index 90 g/m^2 (normal value for males and male adolescents ≥16 years 49–115 g/m^2 [10]), urinary albumin-creatinine ratio 18.0 mg/g (normal value < 30 mg/g [10]), fundoscopy – no signs of hypertensive angiopathy, aPWV 5.5 m/s (25–50th percentile [9]), and common carotid artery intima media thickness 0.348 mm (10–25th percentile according to [11]).

Because secondary causes were excluded and no HMOD was found, the patient was started on non-pharmacological treatment according to [10, 12] – low-sodium diet, intermediate everyday physical activity, weight loss with target BMI below 85th percentile, and restriction from illegal substances with special emphasis on tobacco smoking.

After 6 months of observation, the patient still presents with asymptomatic ISH (140–150/70–80 mm Hg), and his cSBP is 110 mm Hg. Further follow-up and continuation of non-pharmacological treatment were recommended.

DISCUSSION

The presented case demonstrates a typical adolescent with ISH with a model vascular phenotype. According to Polish and European guidelines, AH is diagnosed in children and adolescents when systolic and diastolic blood pressure is equal to or exceeds the 95th percentile for sex, age, and height on 3 separate occasions. Adolescents aged 16 years or older are an exception because they should be diagnosed using adult thresholds [10, 12]. Different definitions are used in the 2017 American Academy of Pediatrics Guidelines [13]. The definition of AH according to various guidelines is shown in Table 1 [10, 12–14].

Once AH is confirmed, the patient should be reviewed for aetiology, comorbidities, and HMODs. The general rule for excluding secondary causes is "the younger the patient and the higher blood pressure, the more likely are second-

TABLE 1. Criteria for diagnosis of arterial hypertension in children according to different guidelines

Parameters	Children and younger adolescents	Older adolescents
European Society of Hypertension – 2016 [9] and Polish Society of Hypertension – 2019 [11]	Age < 16 years Systolic and/or diastolic blood pressure ≥ 95th percentile for sex, age, and height on 3 separate visits	Age 16–17 Systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg on 3 separate visits
Polish Society for Paediatric Nephrology – 2015 [13]	Same for all age groups Systolic and/or diastolic blood pressure ≥ 95th percentile for sex, age, and height on 3 separate visits	
American Academy of Pediatrics – 2017 [12]	Age < 13 years Systolic and/or diastolic blood pressure ≥ 95th percentile for sex, age, and height on 3 separate visits	Age 13–17 years Systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 80 mm Hg on 3 separate visits

ary forms of hypertension". The Polish Society of Hypertension recommends a 3-step approach in diagnostics for secondary causes of AH [12]. In the presented case, tests from the first and second steps were performed although the patient was after puberty, presented with the first grade of AH, and was without HMOD; the decision to widen the diagnostic test was dictated by positive family history.

The patient was diagnosed with primary hypertension, which is always the exclusion diagnosis but is the most prevalent cause of AH in adolescents. Although ISH is the typical phenotype for primary hypertension, this does not justify the exclusion of secondary forms of hypertension. Primary hypertension is significantly more common in overweight or obese adolescents, and metabolic syndrome is found in as many as 15–20% of adolescents with PH [15]. There is an ongoing debate about whether PH in lean and in obese adolescents (or adults) is the same entity. The study by Litwin *et al.* is important in this debate. The authors found that even lean adolescents with PH are characterized by the same metabolic disturbances as obese ones, i.e. sarcopenia and increased body fat percentage [4, 15].

As already mentioned, ISH is the leading form of PH in adolescents and young adults. This entity has been distinguished in the 2016 European Society of Hypertension [10] and 2019 Polish Society of Hypertension guidelines [12]. Isolated systolic hypertension is found in overweight, obese, and slim, athletic adolescents. There are numerous concepts explaining the mechanism of ISH in youngsters. They are as follows: hyperkinetic concentration with high heart rate and stroke volume, increased sympathetic tone, high salt sensitivity, and high elasticity of arteries [5]. Recently, our group revealed that ISH patients differ from systolic-diastolic hypertension patients in no or neglectable rise in blood renin concentration compared to healthy children [16].

The blood pressure pattern differs through the arterial tree. The aorta and its largest branches are elastic arteries. During the systole phase, they accumulate the energy of left ventricular stroke, thus decreasing systolic blood pressure. The degree of this accumulation and blood pressure decrease is related to the elasticity of the aorta. In contrast, medium and small artery walls (e.g. the brachial artery) are composed mainly of vascular smooth muscle cells; thus, they do not change their lumen significantly during the heart cycle. Due to the difference in the wall structure, and according to Poisson's law, the pulse wave shape is different, and the systolic blood pressure is significantly higher in peripheral "muscle" arteries compared to large elastic arteries. Of note, no significant differences are noted for diastolic and mean blood pressure (Figure 1). The blood pressure in the aorta (commonly called central or aortic blood pressure – CBP or AoBP) is also influenced by backward waves. The pulse wave rebounds from the peripheral arteries predominantly at the division of the arteries and returns to the aorta affecting the central pressure. The pulse wave travels relatively slowly in young adults with elastic arteries and returns to the aorta in diastole, increasing diastolic pressure. Such people are characterized by a slow pulse wave velocity and a so-called negative augmentation index, which are considered markers of healthy arteries (Figure 1). In contrast, in older patients or those with early vascular aging (e.g. AH or chronic kidney disease), as a consequence of arterial stiffening, the pulse wave is fast and reaches the aorta during systole, increasing central systolic pressure, which is measured as a positive augmentation index [5, 17].

It was revealed that many patients with ISH are characterized by normal central blood pressure and the absence of HMOD. Thus, they seem not to have "true" hypertension but rather "spurious" hypertension, which probably does not lead to negative cardiovascular sequelae [18]. The European Society of Hypertension proposed an approach to young patients with ISH (Figure 3). If possible, cSBP ought to be measured in these patients. Afterward, the presence of HMOD should be checked in the patient. Provided cSBP is normal and HMOD (especially left ventricular hypertrophy) is absent, the patient probably does not require antihypertensive treatment and may be left under medical observation for non-pharmacological treatment only [5]. This approach raises numerous questions. Firstly, what is the threshold of normal and elevated cSBP? In children, we have normative values established by the German group using an oscillometric device [19]. The question is whether these norms can be used when central blood pressure is measured using the applanation tonometry technique. There are significant differences in, e.g., pulse wave velocity measured using both these modalities. Secondly, what is at least the short-term outcome of patients with spurious hypertension? The data by Obrycki *et al.* suggest that some of these individuals progress towards true hypertension with elevated CBP [20]. Moreover, the same group recently revealed that even patients with normal central blood pressure may have left ventricular hypertrophy [21], questioning whether "spurious" ISH is actually a benign condition. Thus, repeated assessment of both peripheral and central blood pressure and HMOD is required in these individuals.

Our patient had normal cSBP and no HMOD; thus, he was excluded from pharmacological treatment; after 6 months, he remained asymptomatic with normal cSBP, and further follow-up was recommended. Due to metabolic disturbances commonly observed in adolescents with PH, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers (ARB) remain the medications of choice in the case of indications for pharmacological therapy. Interestingly, different classes of antihypertensives exert different actions on central BP. Angiotensin-converting enzyme inhibitors, ARBs, and dihydropyridine calcium channel blockers were found to decrease blood pressure, whereas beta-blockers may even elevate CBP [22]. Interestingly, nebivolol, thanks to its vasodilating and vasoprotective actions, positively impacts

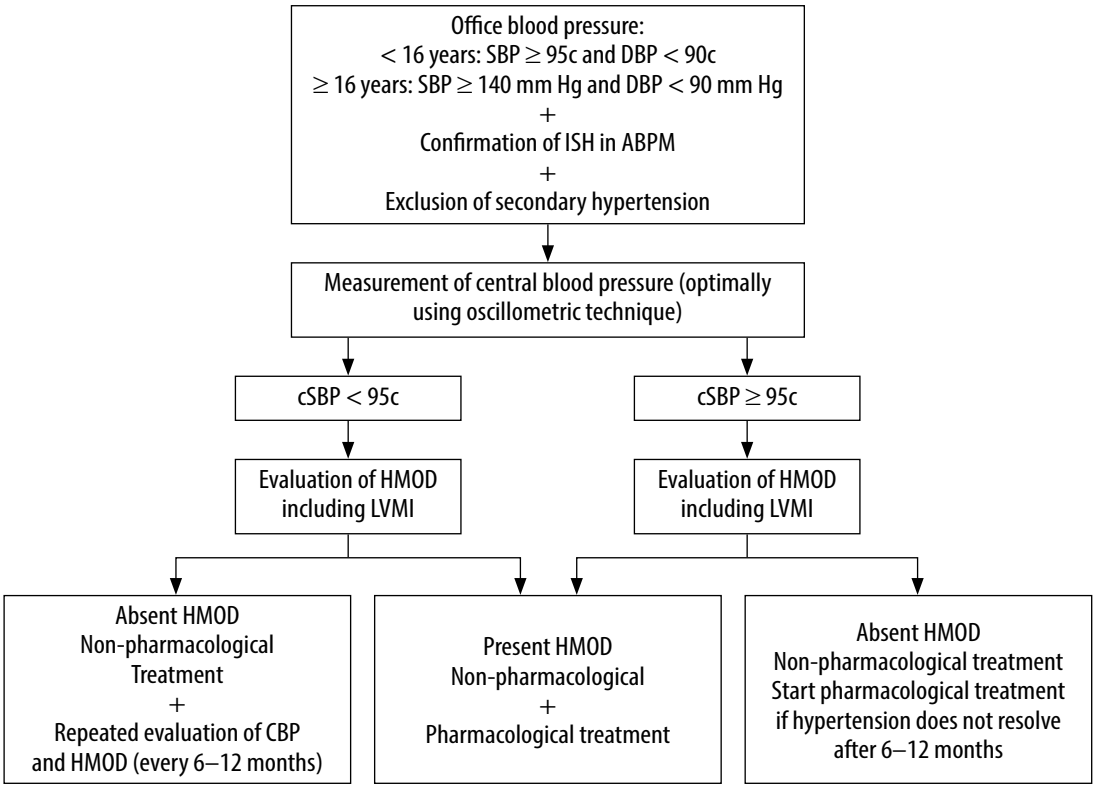

FIGURE 3. Proposed approach to an adolescent with isolated systolic hypertension according to [5] in our own modification

ABPM – ambulatory blood pressure monitoring, CBP – central blood pressure, cSBP – central systolic blood pressure, DBP – peripheral diastolic blood pressure, HMOD – hypertension-mediated organ damage, ISH – isolated systolic hypertension, LVMI – left ventricular mass index, SBP – peripheral systolic blood pressure

the vascular wall, decelerates the pulse wave, and thus was found to lower cSBP [23].

CONCLUSIONS

To summarize, AH is a common entity in the paediatric population, affecting up to 5% of individuals. In the second decade of life, its prevalence rises to 10%. Primary hypertension constitutes the most prevalent cause of AH in adolescents, and many adolescents with PH present with isolated systolic hypertension. Nevertheless, it is crucial to rule out secondary forms of hypertension also in adolescents presenting with isolated systolic hypertension. If possible, measurement of central blood pressure is recommended in patients with ISH because these teenagers commonly have normal cSBP and high peripheral systolic blood pressure amplification. Patients with normal central blood pressure and no HMOD may not require pharmacological treatment. It must be emphasized that these patients require strict follow-up (including repeated measures of CBP and HMOD), and, as always, individualization of the medical approach is crucial.

DISCLOSURE

The authors declare no conflict of interest.

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