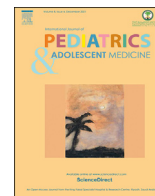


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International Journal of Pediatrics and Adolescent Medicine

journal homepage: <http://www.elsevier.com/locate/ijpam>

Case report

Coarctation of Aorta in Turner Mosaicism

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ARTICLE INFO

Article history:

Received 23 November 2019

Received in revised form

8 February 2020

Accepted 16 March 2020

Available online 18 March 2020

Keywords:

Hypertension

Secondary hypertension

Adolescence

Coarctation of aorta

Turner syndrome

ABSTRACT

The prevalence of hypertension in the pediatric age range is estimated at 1–5% worldwide, with higher rates in adolescence. Although primary hypertension is more common, due to the increasing prevalence of obesity and metabolic syndrome among adolescents, secondary hypertension should be always considered and excluded. We present the case of an adolescent with secondary hypertension and a challenging diagnosis associated with coarctation of aorta and Turner Mosaicism.

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1. Background

The definition of hypertension (HT) in children and adolescents has been changing in recent years. According to the American Academy of Paediatrics (2017), in children <13 years of age, hypertension is defined as systolic and diastolic blood pressure (BP) \geq 95th percentile for age, sex, and height on \geq 3 occasions. However, for adolescents \geq 13 years of age, hypertension is now defined as BP \geq 130/80, regardless of age, sex, or height [1]. The prevalence of HT in children is estimated at 1–5% worldwide, with higher rates in adolescence [2].

Primary hypertension (PH) has been increasing in the pediatric age and is associated with metabolic syndrome, which is considered the main cause of HT in adolescents, affecting millions around the world [3]. Secondary causes of hypertension (SH) are more common among infants and young children. Up to 85% of children with HT have an identifiable cause [4]. (Table 1).

It is recommended that all children with confirmed HT be evaluated for underlying causes. The most common causes of SH

vary with age [5]. Coarctation of the aorta (CoAo), renal artery stenosis or thrombosis, and congenital renal malformations present with newborn HT. In children older than 6 years, renal artery stenosis and renal parenchymal are major causes of HT. Around 80% of children with SH have renal abnormalities [6]. Besides an underlying renal parenchymal disease, endocrine disease (pheochromocytoma, hyperthyroidism), vascular disease (renovascular disease), or neurological conditions (neurofibromatosis) should always be considered as the main causes of SH in pediatric age [7,8]. In adolescent females, oral contraceptives have been associated with HT, and this should be valued too.

However, if the pathology does not present an obvious sign or symptom, the diagnosis may be delayed until an older age. In order of an attempted diagnosis, clinical history, and a complete physical evaluation must be always performed [9].

A comprehensive physical examination could suggest the underlying cause of HT in children. The initial evaluation of HT should be complemented with a urinalysis, serum creatinine, and echocardiography to evaluate for LVH (left ventricular hypertropia). Renal ultrasound doesn't need to be performed routinely in obese adolescents with a normal physical examination and normal urinalysis results [2].

We present a case of SH with a challenging diagnosis.

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Peer review under responsibility of King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia.

Table 1

The classification of primary and secondary hypertension in children.

Primary (essential) hypertension	Secondary hypertension
It occurs without an identifiable cause. Some identifiable risk factors are: <ul style="list-style-type: none"> • Overweight or obesity • Family history of high blood pressure • Type 2 diabetes or a high fasting blood sugar level • High cholesterol • Diet salt intake • Race: black or hispanic • Male sex • Smoking or exposure to second-hand smoke • Sedentarism 	It is caused by a specific condition. The principle causes are: <ul style="list-style-type: none"> • Chronic kidney disease • Polycystic kidney disease • Heart problems, such as coarctation of the aorta • Adrenal disorders • Hyperthyroidism • Pheochromocytoma • Renal artery stenosis • Sleep disorders, especially obstructive sleep apnea • Certain medications, such as decongestants, oral contraceptives, and steroids • Drugs, such as cocaine

2. Case report

LNC is a 17-year-old female adolescent with a personal history of hospital admissions due to respiratory infections in the first year of life (two episodes of urinary tract infections) and a urinary tract infection at 4 months. Due to this urinary infection in the first year of life, she performed a renal ultrasound with no alterations and a DMSA scan 6 months after the infection, excluding the possibility of reflux nephropathy.

Physical development occurred within normal parameters – weight evolution at the 50th percentile and height evolution between 5th and 10th. Menarche at age 13. She started an oral contraceptive because of irregular cycles.

No family history of consanguinity or hereditary pathology were found.

LNC was observed in the emergency department due to headache episodes and malaise during exercise, which improved spontaneously. At the examination was objectified high BP - 169–100 mmHg (>P95). A few minutes later, a second measurement identified BP of 110–60 mmHg. In this context, suspecting HT, she was referred to a pediatric appointment.

In the first appointment, she described similar episodes with a year of evolution, associated with headaches and hypertensive spikes. Consequently, electrocardiogram and analytical were performed with no abnormal findings. HT was confirmed (BP 59–83 mmHg and 138–87 mmHg, pulse rate 77 bpm; weight 55 Kg; height 153; BMI 23.5). Physical examination revealed a disproportion between upper and lower body segments.

To investigate secondary causes of HT, she repeated the blood serum analysis, including blood cell count, serum electrolytes, renal function, and measurements of aldosterone and renin serum levels.

No alterations were found. The thyroid function was normal too (Table 2).

Urinalysis, vanillylmandelic acid, homovanillic acid, and catecholamines in urine were also negative. Abdominopelvic ultrasound showed no alterations. Renal ultrasound, including the Doppler study, raised the possibility of reduced caliber renal arteries, which was excluded after MRI.

To exclude target organ damage and because BP in lower limbs was difficult to measure, she underwent a telemedicine echocardiographic study – which highlighted the diagnosis of coarctation of the aorta (CoAO). Because of the disproportion of the limbs, a karyotype was performed and two cell lines – 88–90% with two X chromosomes and about 10–12% of the cells presented only one X chromosome – were detected, confirming the presence of mosaicism for Turner Syndrome.

A study by Angio-CT confirmed a hemodynamically important CoAO, which motivated referral to Cardiothoracic Surgery. She underwent surgery and since then presented a normal range of BP for age, gender, and height.

3. Discussion

Coarctation of the aorta (CoAo) is one of the rare causes of severe HT and accounts for approximately 6%–8% of all congenital heart diseases. It is more common among the male sex [10].

The timing and manifestations of CoA depend on the severity of narrowing, relationship with arch vessels, and adequacy of collateral vessel formation. Lower body hypoperfusion results in activation of the renin-angiotensin-aldosterone system and consequent upper body hypertension [11].

CoA that remains undetected until adulthood is less severe and

Table 2

Complementary investigation of hypertension performed in the patient.

Blood	Full blood count Plasma sodium, potassium and calcium, urea nitrogen, creatinine Fasting plasma glucose Serum lipids (cholesterol, LDL cholesterol, HDL cholesterol) Fasting serum triglycerides Thyroid function (T4L and TSH) Plasma renin activity Plasma aldosterone concentration
Urine	Urinalysis plus quantitative measurement of microalbuminuria and proteinuria Uroculture Urine and plasma catecholamines or metanephrines
Imaging	Renal ultrasonography Color Doppler ultrasonography Chest Xray 2-D echocardiography Angio-CT scan
Genetic	Karyotype

is often not accompanied by symptoms, besides the HT. When present, symptoms and complications are usually secondary to HT and include headaches, shortness of breath due to left ventricular dysfunction, exercise intolerance, and rarely ruptured cerebral artery aneurysms [12]. The measurement of BP in the four limbs should be performed routinely because the CoAo can be asymptomatic during infancy and the diagnosis may be delayed [13].

The clinical suspicion can be confirmed with different approaches. The electrocardiogram in a patient with CoAo can demonstrate increased voltage in the lateral precordial leads consistent with left ventricular hypertrophy, but not rarely is normal. The echocardiogram will demonstrate left ventricular hypertrophy in older ages. There also can be mitral regurgitation and left atrial dilation. The echocardiogram can demonstrate a narrowing in the aortic arch at the level of the isthmus (just beyond the left subclavian) with Doppler velocities increased in this region. CT scanning and MRI are useful for providing a detailed anatomy of the aortic arch before and after treatment and are nowadays, a very accurate means of diagnosis [13].

The treatment for CoAo is to eliminate the narrowed segment. This can be accomplished surgically or via transcatheter techniques. Surgery requires removal of the coarctation segment and direct anastomosis of the normal aorta. The transcatheter technique utilizes a balloon and stent angioplasty. Most institutions perform surgery for neonates and small children. Many institutions will perform cardiac catheterization and primary stent angioplasty in adolescents and adults. Balloon angioplasty has been performed in neonates and children [12]. Even after an intervention, there is an increased risk of developing essential hypertension. There is also an increased risk of cerebral aneurysms in patients with CoAo (treated or untreated). Follow up care is vital as recurrence of coarctation and HT is not uncommon [14].

CoAo is usually associated with other malformations, such as a bicuspid aortic valve (up to 80%), ventricular septal defect, patent ductus arteriosus, atrioventricular canal defects, transposition of the great arteries or left-sided obstructive heart defects [15]. The association of CoAo and Turner syndrome is not completely established. However, the presence of HT is common in both pathologies. Around one third to one-half of individuals with Turner syndrome are born with a heart defect and 17% had a documented CoAo [16,17].

The relationship between CoAo and Turner syndrome mosaicism is even less established [18]. At least 12.6% of girls born with CoAo have karyotype confirmation of Turner syndrome. Such a high frequency, combined with the clinical benefit of an early diagnosis, supports the benefit of genetic screening in girls with CoAo [18]. Numerous institutions around the world offer a genetic diagnosis for children with CoAo [19].

In this particular case, the disproportion of limbs associated with HT raised the suspicion of a genetic association with Turner syndrome and supported the genetic screening. The presence of only 10% of cells with mosaicism may explain the late diagnosis and the absence of other typical manifestations, such as edema or neck skin folds.

This case highlights the possibility of this association that must be studied in early life to avoid late diagnosis and eventual complications. The correct diagnosis and management allow us to control BP with surgical correction and did not require additional pharmacological therapy until now.

4. Conclusion

Although essential HT accounts for most cases of HT in adolescence, secondary causes must be remembered and investigated.

The careful anamnesis and a complete objective examination are the essential clues to the diagnosis. The presence of HT and CoAo associated with clinical findings may suggest the presence of a concomitant syndrome that must be investigated. In this case, the investigation of HT allowed us to diagnose an asymptomatic adolescent with CoAo and Turner syndrome.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Vanessa Gorito: Conceptualization, Methodology, Writing - original draft. **Cristina Baptista:** Data curation, Writing - original draft. **Paulo Santos:** Visualization, Investigation. **Ana Margarida Costa:** Supervision. **Joana Carvalho:** Supervision, Validation.

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