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Case Report

The challenge to prove a rare cause of secondary arterial hypertension. A case report of a pediatric renal solitary fibrous tumor

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ABSTRACT

Background. Childhood hypertension is getting more attention in recent years. We present a case report of a rare cause of secondary arterial hypertension in a teenage girl - a solitary fibrous tumor of the kidney. The case demonstrates that standard imaging techniques, computed tomography and magnetic resonance imaging, are not fully reliable in the diagnosis of renovascular hypertension.

Case. A 15-year old girl was admitted to the Pediatric Department because of episodes of stiffness in the limbs, accompanied by pale skin and lips, dated 4 months back. During these episodes, high blood pressure up to 160/100 mmHg was measured. A 24-hour blood pressure monitoring demonstrated arterial hypertension stage II. Renovascular hypertension was suspected, but the computed tomography examination of the abdomen showed normal-sized renal arteries. In the left kidney hilum, an intraparenchymal formation was discovered. The data presented a non-specific lesion with a wide differential diagnosis. Given the fact that the patient had been treated with an ACE-inhibitor, serum renin level could not be correctly interpreted. The lesion was removed through a laparoscopic intervention. Intraoperatively, the tumor was compressing a small intra-renal vessel - a finding that hadn't been discovered by the previous imaging studies. The final pathologist diagnosis was: solitary fibrous tumor. During the next six months of follow-up, the maximal blood pressure values of the patient were up to 120/80 mmHg.

Conclusions. Solitary fibrous tumors of the kidneys are infrequent in children. The presented case displays a rare form of initial clinical manifestation of this tumor. It is also a demonstration that standard imaging techniques are not able to get a precise visualization of the small intra-renal vessels. At the same time, the decision of whether or not to perform a more invasive procedure should be based on the clinical conditions and risks of the individual patient.

Key words: hypertension, renal solitary fibrous tumor.

The current definition of hypertension (HTN) in children includes systolic and/or diastolic blood pressure above the 95th percentile for age, sex, and height. Children with values between the 90th and 95th percentile are classified as having high - normal blood pressure (BP).[1] Arterial hypertension is divided into primary, or essential, and secondary, in which an underlying disease is present. It is well-known, that primary hypertension is more common in adolescents, with the majority of those affected being overweight and/or with a family history of being overweight.[2] Secondary hypertension is considered more common among younger children, especially in those under 6 years of age.[3,4] The smaller the child, and the more severe and rapid the rise in the BP, the more likely they have secondary hypertension. However, recent reports demonstrate that the incidence of

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secondary hypertension in adolescents is not to be neglected.[3,4]

We present a case report of a rare cause of secondary hypertension in a teenage girl, which demonstrates that standard imaging techniques, computed tomography (CT) and magnetic resonance imaging (MRI), are not fully reliable in the diagnosis of renovascular hypertension due to the inability of incomplete visualization of small vessels.

Case Report

A 15-year-old girl was admitted to the Pediatric Department because of episodes of stiffness in the limbs, accompanied by pale skin and lips. During these episodes, high BP up to 160/100 mmHg was measured. The family history revealed that the grandfather (paternal) had arterial hypertension and the mother suffered from nephrolithiasis. Her complaints dated 4 months back and were accompanied by severe occipital and frontal headaches. Repeatedly, higher values of BP had been measured, up to 160/120 mmHg. Blood pressure remained high (140/80 mmHg) in between these periods. Angiotensin receptor blocker therapy was started but due to a lack of efficacy, the therapy was cancelled after a month. Subsequently, a combined medication was prescribed [angiotensin-converting enzyme inhibitor (ACEi) and calcium channel blocker (CCB)].

Upon admission, the patient was in satisfactory condition. Her stature and body mass index (BMI) for age and sex were normal (BMI 18.8 kg/m^2). The cardiac evaluation showed a rhythmic heart rate (95 bpm) and clear heart sounds. BP was 140/95 mmHg. Her pulse was well palpable, symmetrical on the upper and lower extremities. As pointed above, the current treatment was with a combined antihypertensive drug (ACEi + CCB).

The following examinations were performed:

- Complete blood count (CBC), renal function tests (BUN, creatinine, uric acid), liver enzymes (AST, ALT), and electrolytes - all within the reference values.
- Thyroid function (FT4 15.4 pmol/L, TSH 1.73 uIU/ml) - all within the reference values
- Serum cortisol levels and cortisol circadian rhythm were also in the normal range. 24-hour urine cortisol test showed elevated values: 306.80 μg/24h and 344.30 μg/24h (normal range up to 286 μg/24h). In this regard, the ACTH was repeatedly examined and showed normal values.
- Urinalysis - clear urine sample; protein/creatinine ratio was 8.98 mg/mmol (normal range up to 7.9 mg/mmol).
- Electrocardiogram and echocardiography - no abnormalities.

Given the treatment with an ACEi, serum renin and aldosterone levels could not be correctly evaluated.

A 24-hour blood pressure monitoring demonstrated arterial hypertension stage II. The mean daily BP values were 141.7/99.1 mmHg, night BP values were 117/80.6 mmHg, as 39.7% of the measured systolic values were above 140 mmHg. Maximal BP was 165/16 mmHg.

Renovascular hypertension was suspected, and a computed tomography (CT) examination of the abdomen was performed. The results showed normal-sized renal arteries, normal adrenal glands, and right kidney. In the left kidney hilum, an intraparenchymal mass was discovered. The tumor was oval-shaped, with smooth borders, sized 11/11 mm, located in the middle to the lower third of the parenchyma, projecting slightly to the hilum (Fig. 1). Such a lesion implied a broad differential diagnosis, so a magnetic resonance imaging (MRI) was performed. The tumor was iso- to slightly hypointense in comparison to the renal parenchyma, and after contrast injection, remained hypocontrasted to the rest of the parenchyma. The data presented a non-specific lesion with a wide differential diagnosis and included a renal cell carcinoma or another solid tumor (Fig. 2).

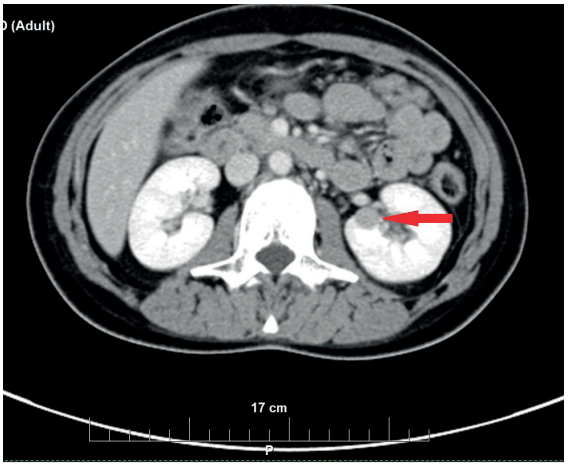

Fig. 1. Venous phase-contrast enhancement abdominal computed tomography scan showing a small homogenous well-defined hypovascular cortical neoplasm (marked by arrow).

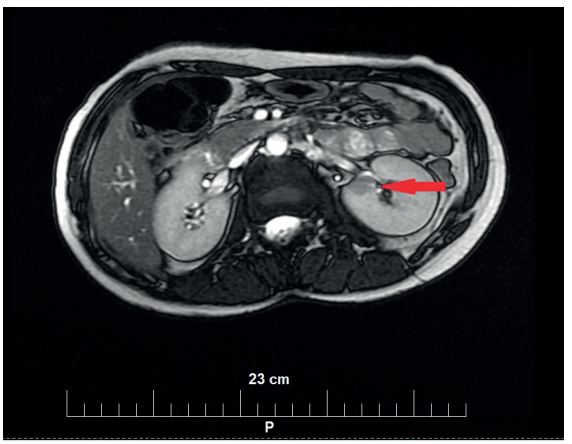

Fig. 2. Magnetic resonance imaging revealed a hypointense (on T2 images) well-defined lesion in the left kidney hilum (marked by arrow). No signal intensity changes found on the gadolinium-enhanced images, slightly increased signal intensity on DWI, slightly decreased signal intensity on ADC map (not presented).

A decision to act immediately was taken, and a laparoscopic intervention was performed to remove the lesion. Intraoperatively, the tumor was well-circumscribed with a grey color, compressing a small intra-renal vessel - a finding that hadn't been discovered by the previous imaging studies. A second smaller satellite nodule with the same morphology was also found nearby and removed together with the larger one.

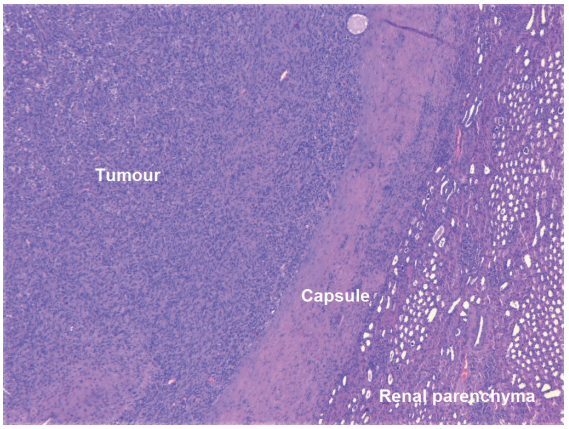

Fig. 3. Tumor biopsy (H&E, x40) showing a well-demarcated tumor with a thick fibrous capsule, partially surrounded by renal tissue.

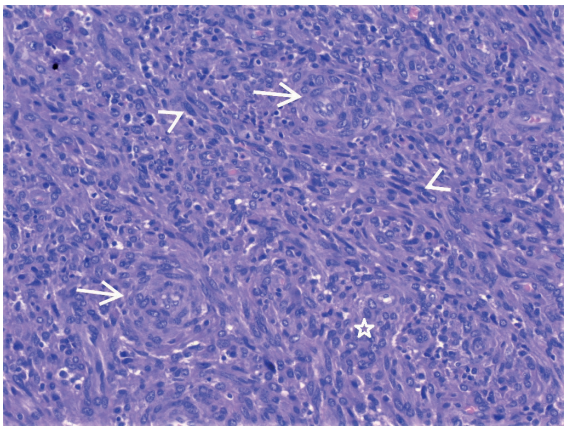

Fig. 4. Tumor biopsy (H&E, x200) showing. a tumor composed of intersecting bundles (arrowheads) and whorls (arrows) of spindle and round cells (star) without nuclear atypia and mitotic activity.

Histology revealed a well-demarcated, round tumor with a thick fibrous capsule, partially surrounded by renal tissue (Fig. 3), composed of intersecting bundles and whorls of spindle and round cells without nuclear atypia and mitotic activity (Fig. 4). Immunohistochemistry showed diffuse positivity for CD34 (Fig. 5), focal for CD99 and bcl2, sparse single S-100 positive cells, negative CK AE1/3, Ki-67 in less

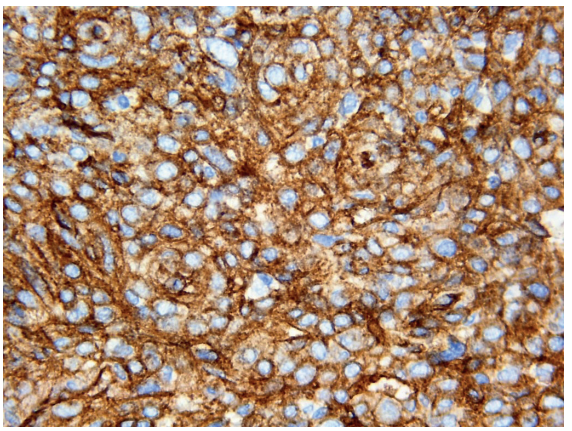

Fig. 5. Tumor biopsy with diffuse positivity for CD34 stating (x400).

than 10% of the nuclei. The smaller tumor had the same characteristics. The surrounding renal parenchyma appeared normal.

The differential diagnosis was required to rule out a renin-producing juxtaglomerular tumor that had a similar histomorphology. Since the juxtaglomerular cells have a smooth muscle cell origin, they show SMA expression. In our case, SMA marked only stromal vessel walls, and the tumor cells were SMA negative. The final pathologist's diagnosis was: solitary fibrous tumor.

The postoperative period went smoothly with rapid normalization of blood pressure values on the 1st postoperative day, with the possibility of a quick withdrawal of antihypertensive treatment. During the next six months of follow-up, the patient was feeling fine, with maximal BP values up to 120/80 mmHg.

Written informed consent for publication of the patient's clinical details and/or clinical images was obtained from the parent of the patient.

Discussion

Due to the patient's specific clinical presentation, a secondary renovascular HTN was suspected. The challenge was in the results of the imaging studies - CT and MRI - renal arteries without stenosis, and the presence of a tumor in one of the kidneys.

Renal pathology (renoparenchymal and renovascular) is the leading cause of secondary HTN in all age groups of the pediatric population and accounts for up to 80% of cases.[3,5,6] Glomerulonephritis causes secondary HTN in 42% of patients.[3] Reflux nephropathy ranks second. Frequent urinary tract infections and subsequent chronic kidney injury are considered major risk factors for the development of HTN.[7] In our patient, in particular, there were neither clinical nor laboratory markers for renal parenchymal disease.

Renovascular disease causes 6 to 10% of all childhood hypertension.[5,6,8] Renal artery stenosis accounts for up to 5% of all cases of secondary HTN, and fibromuscular dysplasia is considered the most common cause of renal artery stenosis in children.[3,6] Renal artery stenosis can be isolated (unilateral, bilateral, stenosis of a small intra-renal vessel), or can affect the abdominal aorta, as well.[9] Renovascular HTN should be considered in every single child with high-grade HTN, symptomatic HTN (presented with hypertensive encephalopathy, cardiac failure), and difficult to control HTN (with more than two antihypertensive drugs). This was the case in the presented patient, in whom a renovascular HTN or hormone-secreting tumor was discussed. However, the conducted imaging studies, CT and MRI, showed normal diameters of renal arteries and didn't confirm stenosis.

A CT scan with contrast demonstrates a high percentage of sensitivity and specificity for renal artery stenosis in children.[10] It is not yet fully understood how reliable the information is about small renal vessels in cases of suspected renovascular HTN.[8,10] MRI examinations also have some limitations concerning the diagnosis of renovascular HTN, mainly due to an uncooperative patient who won't hold their breath.[8,11] Conventional angiography remains the gold standard for a detailed

evaluation of small renal vessels. It provides precise information not only about the lumen of the renal arteries but also about their small branches. On the other hand, despite the obvious advantages of this imaging technique, it is an invasive procedure that carries risks. The main disadvantage is considered to be the higher levels of radiation in comparison to a properly conducted CT scan, and the risk of vascular damage.[8] In our patient, the information from this procedure would not have influenced the therapeutic decision since the tumor formation was subject to removal.

Given the presence of a tumor in the kidney that could potentially press a renal vessel or produce renin, the next step in the diagnostic process would be serum renin evaluation. Neuroblastoma, Wilms tumor, hemangiopericytoma, and other different types of tumors could press a renal vessel with a subsequence of kidney hypoperfusion. This could be verified through the evaluation of serum levels of renin and aldosterone. Although extremely rare (100 cases were reported in the literature), the juxtaglomerular cell tumor is capable of producing renin to a high concentration and presents clinically with moderate to severe HTN and symptoms such as headache, dizziness, and nausea.[12] Furthermore, there was an obvious macroscopic resemblance between the juxtaglomerular tumor and the tumor in our patient - well-circumscribed formation with a fibrous capsule and a grey-whitish color. Given the fact that the patient had been treated with an ACEi, serum renin level could not be correctly interpreted. Following the oral administration of an ACEi, plasma renin levels increase several times due to the feedback mechanism that exists between renin and angiotensin II.[13]

The most common endocrine disorders that cause secondary HTN are catecholamine secreting tumors (pheochromocytoma and paraganglioma), Cushing syndrome, hyperthyroidism, primary hyperaldosteronism, and congenital adrenal hyperplasia. Arterial HTN, palpitation, and headache are the most common initial clinical manifestations of catecholamine-secreting tumors, due to their ability to secrete adrenalin, noradrenalin, and dopamine in high concentrations in the serum.[14] In our patient, a 24-hour urine test for catecholamine wasn't performed because of the persistent manner of the HTN and the lack of a tumor in the adrenal glands or other parts of the sympathetic/parasympathetic nervous system. Besides, there was clear evidence of a tumor located in the left kidney, which was considered to be the potential cause of renovascular hypertension.

HTN is one of the main clinical manifestations of Cushing syndrome in up to 47% of cases.[15,16] Elevated 24-h urine cortisol in our patient didn't match with any clinical criteria such as stunted growth, pubertal arrest, visceral obesity, etc. Laboratory investigation also didn't reveal any other signs of increased glucocorticoid secretion. That is why increased urinary cortisol was considered more as a secondary event.

The histology result showed one very rare tumor in childhood: a solitary fibrous tumor of the kidney. This is a spindle cell neoplasm with a mesenchymal origin, firstly described in the pleura.[17] An extrapulmonary location has also been described, yet kidney origin represents one of the rarest locations. Typically manifested in adulthood, solitary fibrous tumors of the kidneys are extremely rare in children.[17,18] As far as we know, there are only a few pediatric cases described in the literature.[18-20] The current case is the only one clinically manifested with secondary arterial hypertension. The clinical presentation varies from an accidental finding to a palpable abdominal mass, abdominal pain, gross hematuria, and intermittent hypoglycemia.[17,21] The macroscopic appearance of the tumor shows a well-circumscribed mass, with a grey or tan-white surface. Histopathology resembles hemangiopericytoma. Differentiation between the solitary fibrous tumors and other spindle cell neoplasm is based on immunohistochemistry: they show high positivity for CD34, CD99, and bcl-2. In most of the described cases, the course is benign with no recurrences after removal.[18]

Malignancy occurs only rarely, but should not be neglected. A continuous follow-up is recommended.[21]

We think that the most probable cause for the high-grade HTN in the presented patient was the compression of a small renal vessel by the tumor, thus causing secondary renovascular HTN. As a shortcoming in the differential diagnosis, we take into account the fact that a conventional angiography wasn't performed. It would have given us more information regarding small vessels in advance. On the other hand, the procedure itself is not completely safe and carried some additional risks. To speed up the cure, our patient went directly to surgery. The assessment of whether to perform angiography or not should be based on the clinical condition of the individual patients and the impact of the resultant therapeutic behavior.

Childhood HTN is getting more and more attention in recent years. With the increase of obesity in the pediatric population, cases of essential hypertension increase proportionally, especially among adolescents. Nevertheless, secondary hypertension remains a diagnostic and therapeutic challenge.

In summary, renovascular HTN should be considered in every single child with high-grade HTN, symptomatic HTN (presented with hypertensive encephalopathy, cardiac failure), and difficult to control HTN (with more than two antihypertensive drugs). A clinician should keep in mind that standard imaging techniques, CT and MRI, are not fully reliable in the diagnosis of renovascular HTN, due to the inability of complete visualization of small vessels.

Ethical approval

Written informed consent was obtained from the parent of the patient for publication of the patient's clinical details and clinical images.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: KG, PS, VI; data collection: KG; analysis and interpretation of results: KG, PS, VI, BB; draft manuscript preparation: KG, VI. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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