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Mid aortic syndrome : An unusual cause of childhood hypertension

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Mid aortic syndrome (MAS) is characterized by an extensive narrowing of the abdominal aorta, with involvement of the renal and visceral arterial branches. Angiography is the gold standard for the diagnosis of MAS. However, computed tomography angiography (CTA) can effectively determine the location and the extent of the stenosis. Medical management of MAS generally means a lifelong, combination of multiple classes of antihypertensive medications. Surgical correction such as aortoaortic bypass with renal revascularization remains the definitive treatment of the idiopathic MAS. Moreover, the surgery can provide tissues for histological examination to arrive at the definite diagnosis of MAS. We reported a case of MAS in a child with discrepancy of the blood pressure in the upper and lower extremities along with abdominal bruits. The diagnosis of MAS was confirmed by the CTA. Her blood pressure was controlled with 6 antihypertensive drugs with no serious side effects observed.

Keywords: *Mid aortic syndrome (MAS), renovascular hypertension, children.*

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อังคนีย์ ชะนะกุล, พรพิมล เรียนถาวร. ภาวะความดันโลหิตสูงในเด็กที่เกิดจากความผิดปกติของหลอดเลือด. จุฬาลงกรณ์เวชสาร 2553 ก.ย. – ต.ค.; 54(5): 479 – 85

Mid aortic syndrome (MAS) เกิดจากการตีบแคบของหลอดเลือด aorta ในบริเวณ ช่องท้อง และหลอดเลือดสาขาต่างๆ เช่น renal arteries หรือหลอดเลือดที่ไปเลี้ยงอวัยวะภายในช่องท้องอื่นๆ อาการแสดงอย่างหนึ่งของภาวะ MAS คือ ความดันโลหิตสูง ภาวะ MAS สามารถวินิจฉัยได้โดยการทำ computed tomography angiography (CTA) การรักษา MAS มีทั้งการใช้ยาลดความดันและการผ่าตัด ความดันโลหิตสูงใน MAS มักต้องอาศัยยาลดความดันหลายๆ ตัวร่วมกันและจะต้องรับประทานยาไปตลอดชีวิต การผ่าตัดแก้ไขหลอดเลือดตีบ เช่น aortoaortic bypass with renal revascularization นอกจากจะช่วยลดความดันแล้วยังช่วยเพิ่มปริมาณเลือดที่ไปเลี้ยงอวัยวะภายในช่องท้องต่างๆ ที่มีหลอดเลือดตีบได้ นอกจากนั้นยังสามารถเก็บเนื้อเยื่อของผนังหลอดเลือดที่ตีบได้ในระหว่างผ่าตัดมาศึกษาทางพยาธิวิทยาเพื่อให้ได้การวินิจฉัยที่แน่นอน รายงายผู้ป่วยนี้แสดงภาวะ MAS ที่ผู้ป่วยมาด้วยความดันโลหิตสูงโดยความดันที่วัดได้จากแขนสูงกว่าความดันที่วัดได้จากขาร่วมกับพบ abdominal bruits การวินิจฉัยภาวะนี้อาศัยการทำ CTA ซึ่งแสดงการตีบของหลอดเลือด aortaในระดับ L2 - 3 ร่วมไปกับการตีบของ renal arteries ทั้ง 2 ข้าง การควบคุมความดันโลหิตในผู้ป่วยรายนี้ทำได้ยาก ต้องอาศัยยาลดความดันถึง 6 ชนิดร่วมกัน

คำสำคัญ: *การตีบแคบของหลอดเลือด, ภาวะความดันโลหิตสูงในเด็ก.*

Renovascular disease is an uncommon but important cause of secondary hypertension in children. It is usually diagnosed after a long delay because blood pressure (BP) is infrequently measured in children due to difficulties in measuring and interpreting their BP findings.

Renovascular disease accounts for 8 - 10% of all childhood hypertension. [1] In 16-70% of pediatric cases of renovascular disease, hypertension is an incidental finding but can also present with severe symptoms secondary to target-organ damage, such as an acute cerebral incident (10 - 15%) or heart failure (7%).[2] The presenting BP in children with renovascular hypertension is generally very high and difficult to control with antihypertensive drugs. So the children with poorly controlled BP needing more than two drugs should undergo further investigations for renovascular hypertension.

Case Report

A 14-year-old girl was referred to King Chulalongkorn Memorial hospital for evaluation and management of refractory hypertension. Previously she was a healthy child without any significant past medical history. She was admitted to a general hospital after involving in a motor vehicle accident. She was completely asymptomatic and did not experience any insults from the accident. However, her BP was found to be markedly elevated to 210/140 mmHg (BP at the 95th percentile for her height and age = 126/82 mmHg, BP at the 99th percentile for her height and age = 133/89mmHg). Enalapril and amlodipine were started but the BP remained high. Consequently, nicardipine continuous infusion (dose titrated to 5 mcg/kg/min) and 4 mg of doxazocin oral daily were added. Enalapril was subsequently discontinued because of rising of serum creatinine from the baseline of 0.6 to 1.4 mg/dl (normal 0.5-1.20 mg/dl). Her systolic blood pressure (SBP) still ranged from 150 - 160 mmHg so she was transferred to King Chulalongkorn Memorial Hospital.

She did not have any history of urinary tract infection, hematuria or edema. She never had recurrent headaches, visual changes, vomiting or weight loss. There was no history of hypertension in the family. Other family history was noncontributory.

On physical examination, the vital signs included a body temperature of 36^{O}C, heart rate of 124/min (repeated heart rate 2 hours later was 80/min), respiratory rate of 20/min and 4-extremity BP measurement showed the following: right upper extremity: 167/91 mmHg; left upper extremity: 160/95 mmHg; right lower extremity: 101/59 mmHg; left lower extremity: 106/41 mmHg.

The cardiac examination revealed intermittent carotid bruits in her neck. There was a systolic ejection murmur grade III/VI at the left parasternal border. The abdominal examination was bilaterally positive for abdominal bruits. Extremities were warm and well-perfused with a good capillary refill. Delayed femoral and pedal pulses were noted. The rest of the physical examination was unremarkable. There were no birthmarks observed.

Laboratory studies included a urinalysis showing normal urine without any protein or red blood cells. Serum electrolytes were within normal limits. The kidney function test was normal with blood urea nitrogen (BUN) of 12 mg/dl (normal 10 - 20 mg/dl) and serum creatinine of 0.6 mg/dl (normal 0.5 - 1.2 mg/dl). Inflammatory markers were within normal limits with

ESR of 10 mm/hr (normal 0-28 mm/hr) and C-reactive protein of less than 3.19 mg/L (normal <5 mg/L). Her ANA was negative. Chest radiography showed mild cardiomegaly. Echocardiogram was otherwise unremarkable except for left ventricular hypertrophy. There was no evidence of coarctation of the aorta despite the discrepancy of the BP in the upper and lower extremities. Kidney ultrasound showed normal sized kidneys (right kidney of 9 cm and left kidney of 10 cm).

After admission, the upper extremity BP ranged from 160 - 170/90 - 100 and lower extremity BP ranged from 100 -110/40 - 60 mmHg. Antihypertensive medications were gradually introduced to her BP regimen of continuous nicardipine infusion, oral doxazocin, amlodipine, hydralazine, furosemide and metoprolol. The medications were titrated up to the maximum dosages. To prevent lower limb ischemia, the SBP in the lower extremities was kept between 90 - 100 mmHg by allowing the SBP in the upper extremities to be between 130 - 135 mmHg. Because of the history of serum creatinine rising after an exposure to an ACEI and abdominal bruits, serum renin and plasma aldosterone were obtained, showing marked elevation of serum renin of 25 ng/ml/hr (normal 0.2 - 2.8 ng/ml/hr) and plasma aldosterone of 602.5 pg/ml (normal 10 - 160 pg/ml). Doppler ultrasound of the abdominal arteries demonstrated an extensive stenosis of the infrarenal abdominal aorta. To better visualize abdominal arteries, a computed tomography angiogram (CTA) was done (Figure 1). The CTA showed a severe narrowing of the abdominal aorta at the levels of L2-3 with multiple collateral vessels to supply the distal aorta and femoral arteries. The narrowest segment was about 0.27 cm in diameter with a string-like appearance but the aortic wall at the narrowing segment was not thickened. There was severe stenosis of bilateral proximal renal arteries with multiple collateral vessels supplying right and left renal arteries. She was diagnosed with mid-aortic syndrome (MAS).

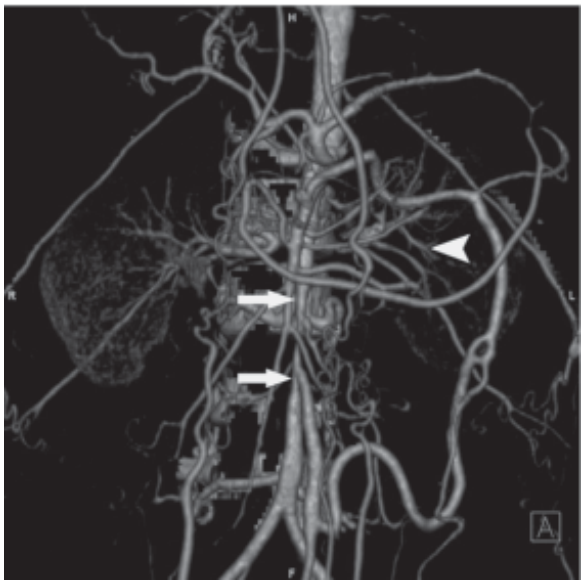

Figure 1. Computed tomogram angiography shows severe stenosis of the abdominal aorta at the levels of L2-3 and bilateral proximal renal arteries (arrows), consistent with mid aortic syndrome (MAS). There were multiple collateral vessels to supply the distal aorta, femoral arteries and renal arteries (arrowhead).

In order to wean her off continuous nicardipine infusion, minoxidil was started. nicardipine drip was discontinued after a week of admission and her BP were at the goal in both upper and lower extremities with oral amlodipine (20 mg/day), hydralazine (4 mg/kg/day), doxazocin (4 mg/day), metoprolol (200 mg/day), furosemide (1.6mg/kg/day) and minoxidil (0.2 mg/kg/day) with no serious side effects observed. Surgical correction such as the aortoaortic bypass with renal revascularization was considered to prevent the development of acute renal failure, bowel and lower limb ischemia and to reduce the side effects from exposure to multiple hypertensive drugs.

Discussion

MAS is an unusual but important cause of renovascular hypertension in children and adolescents. MAS is characterized by an extensive narrowing of the abdominal aorta, often with involvement of the renal and visceral arterial branches. [3] The majority of MAS cases are idiopathic. Other secondary causes are Takayasu arteritis, atherosclerosis, neurofibromatosis, fibromuscular dysplasia, Williams syndrome, mucopolysaccharidosis and retroperitoneal fibrosis. [4] In our patient, the cause of MAS was most likely idiopathic, given that the inflammatory markers were not elevated and she did not have any syndromic feature. However; chronic cases of Takayasu arteritis for which the only presenting symptom was severe stenosis of the aorta without elevated ESR could not be completely excluded.

The mean age at diagnosis of MAS was 14.3 year and there seems to be no sexual predilection. [5] The pathogenesis of idiopathic MAS remains inconclusive but could be attributable to: fusion failure of the two dorsal aortas during the embryonic period; rubella infection[6], or abnormal migration of the kidneys. [7] The location of the aortic lesion in idiopathic MAS is supra-renal in 11 - 40%, intra-renal in 19 - 52%, infra -renal in 19 - 25% and diffuse in 12% of the cases. [4, 7] The most common histological finding in the aorta and visceral vessels is fibroplasia of the intima and variable distortions of the intemal elastic lamina with a lack of inflammatory changes. [8,9] The hallmark presentation is previously undiagnosed hypertension, like in this patient. Further presenting features can include weak or absent femoral pulses, claudication in the lower extremities, differential BP between the upper and lower extremities, abdominal bruits, symptomatic intestinal ischemia, congestive heart failure, or cardiomyopathy. [10] Oliguric renal failure was reported in only 4% of MAS cases. The low incidence of renal failure is probably due to the occlusion of the vasculature occurs gradually, giving opportunity for the effective collateral circulation to form. [5]

Angiography is the gold standard for the diagnosis of MAS. However, CTA can effectively determine the location and the extent of the stenosis in the middle part of the aorta, its associated visceral branches and the presence of collateral circulation as well. In this patient, the CTA revealed a long narrowing segment of 3.3 cm of the aorta at the level of the renal arteries which is the most common type of idiopathic MAS. Additional evaluation for idiopathic MAS includes a renal function test, peripheral renin activity, a renal ultrasound, an echocardiography and a retinal examination. Secondary causes should be excluded by careful history taking and physical

examination to rule out syndromes mentioned above and, if at all possible, by histological examination of the walls of the aorta and its branches.

Medical management of MAS generally means a lifelong, combination of multiple classes of antihypertensive medications. The choice of antihypertensive medications is similar to other forms of renovascular hypertension. The patients should be followed up regularly for monitoring of the blood pressure, renal function and growth of the kidneys. Risks of hypertension, impairment of vascular flow to the kidneys or other organs and side effects of medications need to be weighed against the risks from surgical correction when medical treatment is employed. Surgical correction remains the definitive treatment of idiopathic MAS. Moreover, the surgery can provide tissues for histological examination to arrive at the definite diagnosis. Indications for surgery are uncontrolled hypertension, a very severe stenosis of the renal arteries, claudication, and intestinal ischemia. [11] The proper timing of surgery should be individualized and based on the severity of the symptoms, the response to medical treatment, the age and size of the patient and the consideration of surgical risks. [10, 11] In this patient, her blood pressure was controlled with 6 antihypertensive drugs. The side effects of medications and signs of end organ ischemia including claudication, abdominal angina and renal function test have been carefully and closely monitored.

In conclusion, idiopathic MAS, although rare, is an important cause of renovascular hypertension in children and should be considered in the differential diagnosis of hypertension, especially when there are differential BP, abdominal bruits, claudication or decreased femoral pulses. Secondary causes of MAS should be excluded. The diagnosis often relies on imaging studies such as renal ultrasound with Doppler, echocardiography, and CT angiography. The options for treatment of vascular causes of hypertension are medical or surgical. In general, surgery is reserved for those in whom medical controlled of blood pressure is unsatisfactory or associated with intolerable side effects.

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