An interesting case of tetany, presenting sign of secondary hypertension in young boy.

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Abstract:
We report here a case of a 13 year old boy of takayasu arteritis of abdominal aorta andrenal arteries presented with secondary hyperaldosteronism with metabolic alkalosis and hypokalemia and tetany. This case is interesting as it is very rare presentation of takayasu arteritis.

Keyword: secondary hyperaldosteronism, takayasu arteritis, renal artery stenosis.

Introduction:
Takayasu arteritis is an important cause of secondary hypertension in young individuals. We report here a young boy presented with features of secondary hyperaldosteronism, because bilateral renal artery stenosis due to takayasu arteritis of abdominal aorta and renal artery involvement.

Clinical presentation: 13 year old boy was referred to our hospital as a case of tetany following tonsillectomy for chronic tonsillitis. Child was asymptomatic till then. There was history of fatigue arthralgia for past 6 months. There was no history of head ache, blurring of vision, claudication, arthritis, oral ulcers, hematuria, hemoptysis, hearing difficulty, ear discharge. No history of rash, exanthematous fever, skin disease. No treatment history for any illness other than upper respiratory tract infections. On examination: Patient was afebrile, Pulse rate was 82/mt, regular, all peripheral pulses are felt, no radiofemoral delay, no renal or carotid bruit. Blood pressure on both upper limbs were 160/110 mmHg in supine position, blood pressure on both lower limb was 190/120 mm Hg in supine position. Troussieusign and Chovstek sign were present. There was no palpator, jaundice, cyanosis, clubbing, lymphadenopathy. Height 137 cms, US/LS ratio normal. Mothersheight 150 cms. Scrotal rugeae present. Testes normal volume bilaterally. No axillary or pubichair. Phallus size normal according to the age. Fundus was normal. CVS, RS, GIT, CNS systemexamination were normal. ON INVESTIGATION: ECG showed LVH. RBS 109 mg/dl; Urea 30 mg/dl; Serum Creatinine 1 mg/dl; Serum Na+ 137 mEq/L; Serum K+...
2.4 mEq/L; Serum Ca++: 8.6 mEq/L; Serum Mg++: 1.4 mEq/L gm%; Serum Albumin: 4.3 gm%. Urinalysis: Specific gravity: 1.015; pH: 7; Protein: nil; Leucocytes: nil; RBC: nil; No casts; Acid Base Gas Analysis: PH: 7.6; PCO2: 28.9 mmHg; PO2: 108.6 mmHg; Na+: 138 mEq/L; K+: 2.5 mEq/L; Ca++: 0.81 mmol/L; Glucose: 122 mg/dL; Lactate: 1.17 mmol/L; Hct: 40%; C HCO3: 32.5 mmol/L; C O2: 2: 3: 4 mmol/L; BE (b): 11.9 mmol/L; BE (ecf): 11.9 mmol/L; CS O2: 99.2%; ABG Interpretation: metabolic alkalosis.

Hb: 10.4 gm/dl; TC: 6000 smear: normal; LIPID PROFILE: Serum cholesterol: 185 mg%; Serum TGL: 150 mg%; Serum HDL: 40 mg%; Serum VLDL: 54 mg%; Serum LDL: 91 mg%; c-REPI: 100 mg/L; Serum ANA: negative. cANCA & pANCA were negative. USG abdomen: Right kidney: 6.75*4.2 cm; Left kidney: 6.7*3.5 cm; Right renal artery: Resistive Index 0.5; Normal flow pattern, normal arterial wave forms; Left renal artery: Resistive Index 0.52;Normal flow pattern; Echo: Impression: normal study.

RAAS SCREENING: (blood was taken at 8 AM, with 2 hours of ambulation. Patient was put on tab. prazocin as antihypertensive before the test.); Plasma Aldosterone Concentration (PAC): 46.82 ng/dL. (normal range: 1 -16 ng/dL); Plasma Renin Activity (PRA): 12.76 ng/ml/hr. (normal range 0.15 – 2.33 ng/ml/hr). Ratio of Plasma Aldosterone Concentration to Plasma renin activity (PAC/PRA): 3.66. Impression: secondary hyperaldosteronism.

THYROID PROFILE: normal. Chest x-ray: normal. X-ray hand: pisiform formed. Bone age around 12-14 yrs. No evidence of hyperparathyroidism. 64 SLICE CT abdomen with contrast and angiography: Medial and lateral limbs of both adrenal glands are normal. No evidence of adrenal hyperplasia or SOL seen. No obvious demonstrable pathology in retroperitoneum including organ of zuckerkandl. Right kidney: supplied by single renal artery. Right Renal Artery is originating from aorta at L1 with ostial lumen diameter measuring 0.35 cm. Right renal artery shows early branches at 0.75 cm from ostia with beaded appearance and mild narrowing of upper branch. Left kidney supplied by two renal artery and drained by single renal vein. Left Renal Artery 1 (LRA1) originating from aorta at upper L1 complete occlusion of LRA with length of occlusion 1 cm and lumen before occlusion 2 mm. Post stenotic dilatation measuring 3 mm with beaded appearance. Left Renal Artery 2 (LRA2) originating from aorta at L1-L2 with ostial lumen diameter measuring 0.25 cm and shows early narrowing of proximal segment with U bent and beaded appearance with post stenotic dilatation. Lumen diameter at stenosis 0.2 cm and post stenotic segment 0.38 cm. There is short segment narrowing of renal, infra renal abdominal aorta with subtle intimal change. Lumen diameter of abdominal aorta above renal artery 1.25 cm, at the level of renal artery 0.9 cm, below renal artery 1.1 cm. IMPRESSION: TAKAYASU ARTERITIS TYPE 4 to be considered [Fig1 & 2].

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Fig:1 showing abdominal aorta involvement. Bilateral renal artery stenosis, post-stenotic dilatation. Complete occlusion of LRA1 can be seen in Fig:2 showing abdominal aorta involvement. Bilateral renal artery stenosis, post-stenotic dilatation.

MRI ABDOMEN: No mass lesion in adrenal. Liver, gallblader, spleen were normal in size and signals. No evidence of retroperitoneal mass lesion. MRI BRAIN SCREENING: normal size and signal of pituitary gland. Pituitary stalk is normal. Posterior pituitary bright spots are also observed. Other parts of brain are normal. USG OF NECK: No thyroid or parathyroid mass. MR ANGIOGRAM OF AORTIC ARCH: Diameter of ascending aorta: 1.9cm; Arch of aorta: 1.3cms; Descending aorta: 1.26cms; Impression: Ascending aorta, arch of aorta, descending aorta are normal in caliber. Branches of arch of aorta are identified normal in caliber. No evidence of branch stenosis [Fig 3].

Fig:3: MR Angiogram of Aortic Arch and major branches except infra renal abdominal aorta and both renal arteries other major branches are not involved.

DISCUSSION: This child presented with Hypertension, Hypokalemia and resultant Metabolic Alkalosis. Tetany resulted from hypocalcemia and hypomagnesemia secondary to metabolic alkalosis. This combination is suggestive of Hyperaldosteronism[2]. The sequential evaluation of a patient with otherwise unexplained hypertension and hypokalemia begins with measurement of the plasma renin activity or plasma renin concentration and aldosterone concentration[2][Fig:4].

**Plasma renin activity** — The plasma renin activity (PRA) and plasma renin concentration (PRC) are typically very low (due in part to the associated mild volume expansion) in patients with primary mineralocorticoid excess, usually less than 1 ng/mL per hour (0.2778 ng/L per sec) for PRA and usually undetectable for PRC[3]. On the other hand, increased PRA or PRC in a hypokalemic hypertensive patient is most often due to diuretic therapy, renovascular or malignant hypertension, or rarely a renin-secreting tumor.

**Plasma aldosterone to renin ratio** — The 2008 Endocrine Society guidelines recommend that the plasma aldosterone concentration to plasma renin activity (PAC/PRA) ratio can be used for case detection of primary hyperaldosteronism[4]. The following general principles apply in a hypertensive hypokalemic patient: Primary aldosteronism should be suspected when PRA is suppressed (or PRC is undetectable) and PAC is increased. Secondary hyperaldosteronism (eg,
renovascular disease) should be considered when both the PRA (or PRC) and PAC are increased and the PAC/PRA ratio is <10 (eg, renovascular disease). An alternate source of mineralocorticoid receptor stimulation (eg, hypercortisolism, licorice root ingestion) should be considered when both the PRA (or PRC) and PAC are suppressed. The test is performed by measuring a morning (preferably 8 AM), ambulatory, paired, random PAC and PRA (or PRC). An abnormal PAC/PRA ratio is laboratory dependent. In general, PRA and PRC are undetectable in patients with primary aldosteronism. Also, in most patients with primary aldosteronism, the PAC is >15 ng/dL. Most antihypertensive medications can be continued and posture stimulation is not required[5-9]. The mean value of PAC/PRA ratio in normal subjects and patients with essential hypertension is 4 to 10, compared to more than 30 to 50 in most patients with primary aldosteronism[3-10]. PRA and PRC are low in a significant number of patients with essential hypertension, but a high PAC (typically >15 ng/dL [416 pmol/L]) and a truly abnormal ratio are uncommon.

**Fig:4, Algorithm of investigation in a case of Hypertension and Hypokalemia**

Our patient’s ratio of Plasma Aldosterone Concentration to Plasma renin activity (PAC/PRA):3.6., suggestive of secondary hyperaldosteronism. Most common causes of primary hyperaldosteronisms are Aldosterone-producing adenomas, Bilateral idiopathic hyperaldosteronism (bilateral adrenal hyperplasia), Familial hyperaldosteronism type I (glucocorticoid-remediable aldosteronism) and type II (the familial occurrence of aldosterone-producing adenoma or bilateral idiopathic hyperplasia or both), Pure aldosterone-producing adrenocortical carcinomas, Ectopic aldosterone-producing tumors. These causes were ruled out by clinical examination, MRI of abdomen and pituitary. Most common causes of secondary hyperaldosteronism are Renovascular hypertension; Renin secreting tumor; Coarctation of aorta; Diuretic use and Malignant hypertension. Renin secreting tumors are ruled out by abdominal contrast CT scan. Coarctation of aorta is ruled out by clinical examination and MR angiogram. There was no history of previous diuretic use. Our patients CT angiogram of aortic arch and its branches revealed narrowing of renal and infra renal abdominal aorta with intimal narrowing and involvement of bilateral renal arterie in the form of stenosis, and post stenotic dilatation. Close differential diagnosis is Congenital Fibromuscular Dysplasia. Abdominal aortic involvement with constitutional symptoms favour takayasu arteritis Type 4. CT angiogram of aortic arch and other branches were normal. Takayasu arteritis is a chronic vasculitis of unknown etiology[1]. Women are affected in 80 to 90 percent of cases.
with an age of onset that is usually between 10 and 40 years[11,12]. Takayasu arteritis primarily affects the aorta and its primary branches[13]. The inflammation may be localized to a portion of the thoracic or abdominal aorta and branches, or may involve the entire vessel. The abdominal aorta and pulmonary arteries are involved in approximately 50 percent of patients. Active inflammation is indicated by the presence of mononuclear cells, predominantly lymphocytes, histiocytes, macrophages, and plasma cells[14]. Giant cells and granulomatous inflammation are typically found in the media[15]. Destruction of the elastic lamina and the muscular media can lead to aneurysmal dilation of the affected vessel. Alternatively, progressive inflammation and dense scarring may proceed from the adventitia leading to a compromise of the vascular lumen. Intimal proliferation may also contribute to the development of stenotic arterial lesions. If active inflammation abates, dense scar tissue remains as an indication of prior vasculitis. Systemic symptoms are common in the early phase of Takayasu arteritis, including fatigue, weight loss, and low-grade fever[16]. Vascular symptoms are rare at presentation. As the disease progresses, however, evidence of vascular involvement and insufficiency becomes clinically apparent due to dilation, narrowing, or occlusion of the proximal or distal branches of the aorta. Abdominal aorta is involved in 47% of arteriographical studies; Commonest symptoms are Abdominal pain, nausea, vomiting. Renal artery is involved in 38% of arteriographical studies; Commonest presentations are Hypertension, renal failure[1]. The early diagnosis of Takayasu arteritis may be difficult since early symptoms such as fatigue, malaise, joint aches, and low-grade fever are nonspecific. This period is sometimes called the pre pulseless phase[11]; vascular changes may not be sufficiently prominent to cause obvious extremity ischemia or arm claudication[11]. New angiographic classification of Takayasu arteritis, Takayasu conference 1994[17].

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<th>Type</th>
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<td>I</td>
<td>Branches from the aortic arch</td>
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<td>IIa</td>
<td>Ascending aorta, aortic arch and its branches</td>
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<tr>
<td>IIb</td>
<td>Ascending aorta, aortic arch and its branches, thoracic descending aorta Thoracic descending aorta, abdominal aorta, and/or renal arteries</td>
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<tr>
<td>III</td>
<td>Abdominal aorta and/or renal arteries</td>
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<td>V</td>
<td>Combined features of types IIb and IV</td>
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Renal involvement in takayasu arteritis: The ostia of the renal arteries are commonly involved, but the intrarenal vasculature and small vessels are generally normal. Renal involvement is the most common reason for hypertension[18]. Non specific ischemic glomerular lesions resulting from arterial narrowing or long-standing reno-vascular hypertension are the most common renal manifestations of TA. Primary glomerular diseases have been described rarely. Renal arterial stenosis may be bilateral and usually coexists with aortic involvement[19]. Surgical correction of renal artery stenosis is usually an effective means of decreasing or eliminating hypertension[20].
Our case presented with secondary hypertension with hypokalemia, metabolic alkalosis, and resultant hypocalcemic and hypomagnesmic tetany with constitutional symptoms. Patient developed secondary hyperaldosteronism because of bilateral renal artery stenosis. In this case diagnosis of Takayasu Arteritis type IV was made out because of involvement of abdominal aorta and both renal arteries and constitutional symptoms with elevated inflammatory markers. The case is reported because of the rarity of Takayasu arteritis in a male child presenting with features of secondary hyperaldosteronism with resultant hypocalcemic and hypomagnesmic tetany. Patient was started on immunosuppressive therapy and multiple anti-hypertensive including spironolactone. On discharge patient’s blood pressure was under control, electrolyte abnormalities were recovered. Patient is planned for interventional procedures for renal artery stenosis. In the PubMed search for similar presentation one case has been reported in similar features of Takayasu arteritis in Journal of Renal Failure in 2009.

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