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Abstract Topic:- Rare disease therapeutics

Abstract Title:- Case Report: Apparent Mineralocorticoid Excess (AME): A rare cause of monogenic hypertension

Presenting author name :- Dhrumi Thaker

Presenting author institute:- GMERS Medical College and Hospital

Co-author name:- Nilam Thaker

Co-authors institute:-Child Kidney Care Clinic

Aims:-To diagnose a rare cause of hypertension in a young child and to guide definitive management and prognostication.

Methods:- A 3 year old male child presented with the complaints of failure to thrive, polyuria, polydipsia and delayed motor milestones.

His weight (7.73 kg) and height (77.3 cm) were below third percentile. He was found to be severely hypertensive: Right UL 140/90 mm Hg, right lower limb 158/100 mm Hg, left upper limb 140/92 mm Hg and left lower limb 160/110 mm Hg. His general and systemic examination were unremarkable.

Blood workup indicated metabolic alkalosis (pH 7.57 and HCO3 31.2 mEq/L) with low serums sodium (133 mmol/L) serum potassium (2.38 mmol/L) and serum chloride (93 mmol/L). His other blood reports including Blood Urea, serum creatinine, serum calcium, serum magnesium and serum phosphorus were normal. Urine analysis showed increased excretion of sodium (77.6 mmol/L), potassium (89.77 mmol/L) and chloride (122.6 mmol/L).

USG showed normal both kidneys with bilateral faint medullary pyramidal calcification. Doppler imaging of renal vessels was unsuccessful due to lack of cooperation by child.. To rule out renovascular hypertension, CT renal angiography was performed, revealing no abnormalities, and both adrenal glands appeared to be in a healthy state. Additionally, the hormone levels were assessed, which suggested normal levels of serum 17 hydroxyprogesterone, serum cortisol and plasma ACTH. The serum aldosterone level was found to be 2.14 ng/dL (normal range for upright position: 2.52 – 39.2 ng/dL). The plasma renin activity (PRA) was also low at 0.59 ng/mL/hr (normal range is 1.6 to 7.4 ng/mL/hr). Considering all the reports, the patient's condition presented with metabolic alkalosis, hypokalemia, and low-renin low-aldosterone hypertension. Based on these findings, the likely diagnosis was suspected to be either Liddle syndrome or apparent mineralocorticoid excess (AME).

For definitive diagnosis, genetic testing in the form of clinical exome sequencing was carried out.

Results:- Clinical Exome Sequencing detected a likely pathogenic, autosomal recessive mutation: homozygous three base pair deletion in exon 5 of the HSD11B2 gene (chr16:67470698_67470700delGCT; Depth: 56x) that results in the in-frame deletion of amino acids Arginine and Tyrosine and insertion of amino acid Histidine between codons 337 and 338 (p.Arg337_Tyr338delinsHis; ENST00000326152.5). Based on these findings, final diagnosis of AME was made.

Initially, multiple anti-hypertensives were started with suboptimal control of blood pressure. Upon diagnosis of AME, tablet Spironolactone was started along with a combination of Amiloride and Hydrochlorthiazide.

Gradually, the child's blood pressure normalised and all anti-hypertensives were tapered off. His growth improved along with achievement of age appropriate motor milestones.

Conclusions:- The heterogeneity of the clinical manifestations of AME make it challenging to diagnose the disease early in its course. Genetic testing plays a pivotal role in the precise identification of AME and guides subsequent treatment to prevent target organ damage due to severe hypertension.

Keywords:- hypertension, mineralocorticoid, genetic testing, HSD11B2 gene, autosomal recessive