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Abstract Topic: - Clinical Genetics

Abstract Title: - Case report: 17 Alpha Hydroxylase Deficiency - A rare form of Congenital Adrenal Hyperplasia

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Aims: - CAH is AR disorder of cortisol biosynthesis. Cortisol deficiency leads to high ACTH which causes adrenocortical hyperplasia and excess of intermediate metabolites. Depends on enzyme deficiency sign, symptoms and Lab findings seen for mineralocorticoid deficiency or excess, incomplete virilisation or precocious puberty in affected male, virilisation or sexual infantilism in affected females. We present a case of 17-alpha hydroxylase deficiency is a rare cause of CAH found in less than 1% of cases and incidence is about 1 in 50,000. The consequent defects in the synthesis of cortisol leads to high ACTH which stimulate a large quantity of 11-deoxycorticosterone (DOC) and corticosterone. High concentrations of DOC (potent mineralocorticoid) lead to hypertension, hypokalemia, suppresses renin-angiotensin system and low plasma aldosterone concentration. In gonads, the absence of 17, 20-lyase activity prohibits the synthesis of androgens, which causes pseudo hermaphroditism in males and sexual infantilism with primary hypogonadism in females.

Methods: - 12 year female with uneventful birth history brought for acute gastroenteritis. Detected hypertension, hypokalemia and mild metabolic acidosis. Low appetite and headache since few days. On examination Pigmentation of skin around nail beds, nipples, linea Alba and oral mucosa, no breast development, no pubic or axillary hair. No dysmorphism. USG abdomen showed enlarged right suprarenal gland, only small uterine ridge seen and no ovary seen. Renal Doppler study was normal. Potassium was persistently low with low cortisol, high ACTH, very low Estradiol, Suppressed plasma renin activity and very high LH & FSH. Suspected 17 alpha hydroxylase deficiency sent investigation for Genetic confirmation. Started antihypertensive and steroid (Hydrocortisone) and improvement seen in potassium level and hypertension both.

Results: - Chromosome analysis revealed the presence of an additional marker from an unknown origin. Karyotype was 47, XX, +mar. Whole Exome sequencing Genetic mutations have been found consistent with 17 alpha hydroxylase /17, 20 lyase deficiency. The CYP17A1 c.286C>T (p.Arg96Trp) variant has been reported in homozygous state. When electrolyte imbalance and fluid retention recovered started on low dose Estrogen which is being gradually increased. Weight and height improved, pigmentation got better and breast development started.

Conclusions: - For hypertension in children Renal causes and essential hypertension are most common but rare endocrine causes should be kept in mind particularly associated with electrolyte imbalance, hypoglycemia and sign of cortisol deficiency

Keywords: - Chromosome analysis revealed the presence of an additional marker from an unknown origin. Karyotype was 47, XX, +mar. Whole Exome sequencing Genetic mutations have been found consistent with 17 alpha hydroxylase /17, 20 lyase deficiency. The CYP17A1 c.286C>T (p.Arg96Trp) variant has been reported in homozygous state. When electrolyte imbalance and fluid retention recovered started on low dose Estrogen which is being gradually increased. Weight and height improved, pigmentation got better and breast development started.