A Novel *CYP21A2* Gene Mutation in Classic Congenital Adrenal Hyperplasia

A 3-month-old boy presented with failure to thrive since birth, and poor feeding, lethargy and vomiting for one month. He was born to consanguineous parents and weighed 3.0 kg at birth. There was no family history of previous similarly affected member or early deaths. On examination, his weight and length were 3.25 kg (-4.5 *Z*-score) and 57.0 cm (-1.35 *Z*-score), respectively. Genital hyperpigmentation was noted, but there was no ambiguity. Laboratory investigations showed low serum sodium (126 mEq/L), high serum potassium (6.7 mEq/L), and low blood pH (7.09). The 17-hydroxytprogesterone (17-OHP) level was 38.7 ng/mL. Ultrasonography showed enlarged adrenals. A diagnosis of classic Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase (21-OH) deficiency was considered and replacement steroid therapy was initiated. Synacthen test was performed in follow-up after withholding steroids. The baseline serum cortisol and 17-OHP values were 4.60 nmol/L and 22.4 ng/mL and peak stimulated values were 4.87 nmol/L and 54.7 ng/mL, respectively.

Paired-end custom amplicon Next generation sequencing (NGS) carried out on the DNA extracted from peripheral blood of the child revealed the presence of a homozygous variant c.725T>C(p.Leu242Pro) in the *CYP21A2* gene. This is a novel variant, which has never been reported in literature, including large previous Indian CAH patient cohorts [1-3]. The T>C mutation at nucleotide 725 resulting in the substitution of proline for leucine at codon 242 is predicted as pathogenic according to *in silico* mutation analysis tools (Sift, Polyphen and Mutation Taster) if clinical diagnosis of CAH is certain. However, functional characterization of mutant gene and the parents' carrier status could not be performed.

21-hydroxylase (21-OH) deficiency caused by the defective *CYP21A2* gene results in varying impairment in the secretion of cortisol and aldosterone and accounts for almost 95% of all patients with CAH [1]. The disease manifests as classic salt-wasting, classic simple virilizing and non-classic forms depending on the residual 21-OH enzymatic activity. The number of disease causing mutations in the *CYP21A2* gene has almost doubled to 212 over the past decade [1]. The identification of the mutation allows confirmation of diagnosis and early initiation of steroid therapy.

Funding: The sample was processed as part of a project funded by Department of Biotechnology, India.

Competing Interest: None stated.

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A New Interface for Better Throat Examination

Evaluation of ear, nose and throat is an integral part of physical examination of children, both in office practice and inpatient setting. A meticulous screening of these areas can give vital clues, or sometimes the diagnosis *per se*, especially in the context of a child with fever. Congested throat, follicles on the tonsils, petechiae on the palate, mucosal ulcers and quinsy are some of the common findings picked up on throat examination of a child in a tropical country where infections are common. Usually older children open their mouth on request and a good flashlight would be enough for throat examination. However, when the child is younger, he or she needs to be restrained by the caregiver and sometimes a tongue