Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive diseases caused by inactivating mutations in genes involved in the cortisol biosynthesis. More than 90% of CAH cases are due to steroid 11β-hydroxylase deficiency. Steroid 11β-hydroxylase is encoded by CYP11B1 and its deficiency is the second most common cause of CAH. At an incidence of one in 15,000 live births, it accounts for about 5 to 8% of cases of adrenogenital defects [1,2]. There is lack of DCO production and subsequently aldosterone, causing renal salt-wasting in most of the patients [3].

The excessive steroid precursors are shunted into the adrenocortical synthesis pathway, resulting in virilization and ambiguous genitalia of genetically female infants [3-6]. The CYP11B1 gene is localized on chromosome 8q21, approximately 40 kb from the paralog CYP11B2 gene which encodes aldosterone synthase; based on HGD database, there are 109 different mutations reported in the literature [7-10]. Although hypertension is common in steroidal 11β-hydroxylase deficiency, cardiomyopathy due to long standing uncontrolled hypertension has less frequently been reported. Only three adults [11, 12] and two children [13, 14] have been reported in the literature. In the present study, we reported three additional cases and characterized the underlying genetic defect.

**Objectives**

The aim of the study was to identify the molecular defect causing steroid 11β-hydroxylase deficiency in two patients from a Saudi family. The mutation c.780 G>A created a premature stop codon at amino acid 260 (p.W260*), resulting in a truncated protein devoid of steroid 11β-hydroxylase activity. Interestingly, a somatic mutation at the same codon (c.779 G>A, p.W260*) was reported in a patient with papillary thyroid cancer (COSMIC data base). Clinically, both patients were diagnosed with pseudo-hyperaldosteronism but no hypertension and no signs of virilization; both patients were treated with hydrocortisone and anti-hypertensive medication. Both patients’ routine follow-up was consistent with normal blood pressure and height.

**Materials and Methods**

Steroid 11β-hydroxylase deficient congenital adrenal hyperplasia was confirmed in two unrelated patients of Saudi Arabian origin, by screening for mutations in CYP11B1 gene. Genomic DNA from peripheral blood leukocytes of patients was isolated using the QIAamp DNA Blood Midi kit (Qiagen Corp., CA) and evaluation was performed by Sanger sequencing. A 21-month-old boy was admitted to the emergency department with bronchopneumonia. He had history of typical clinical presentation and lab data for 18 months. His elder brother died 13 years ago at age of 30 months old with similar clinical presentation. His single younger brother had been referred for evaluation at the local hospital and the patients developed dilated cardiomyopathy due to hypertension. This could result in misdiagnosis and delay in early treatment.

**Results**

Conclusions

Steroid 11β-hydroxylase deficient congenital adrenal hyperplasia was confirmed in two unrelated patients of Saudi Arabian origin, by screening for mutations in CYP11B1 gene. Genomic DNA from peripheral blood leukocytes of patients was isolated using the QIAamp DNA Blood Midi kit and evaluation was performed by Sanger sequencing. A 21-month-old boy was admitted to the emergency department with bronchopneumonia. He had history of typical clinical presentation and lab data for 18 months. His elder brother died 13 years ago at age of 30 months old with similar clinical presentation. His single younger brother had been referred for evaluation at the local hospital and the patients developed dilated cardiomyopathy due to hypertension. This could result in misdiagnosis and delay in early treatment. The clinical presentation and laboratory data are consistent with classic steroid 11β-hydroxylase deficiency due to p.W260* mutation. The nonsense mutation described in our patient has not been described in the literature. The mutated transcripts may be translated to a truncated protein or are degraded via nonsense-mediated decay RNA surveillance pathway. The nonsense-mediated decay RNA surveillance pathway.

**References**


2. Saudia Arabia.


5. Portrat S, Mulatero P, Curnow KM, Chaussain JL, Morel Y, Pascoe L: Congenital adrenal hyperplasia due to steroid 11beta-hydroxylase deficiency due to partial 11beta-hydroxylase deficiency from non-consanguineous parents. Their diagnosis was made based on their clinical and biochemical features. Both patients had characteristic features of classic steroid 11β-hydroxylase deficiency: accelerated growth, dilated cardiomyopathy, pubertal precocious puberty, hypertension, elevated serum levels of DOC, 17-OHP and aldosterone, and low serum levels of cortisol and deoxycorticosterone. The initial presentation of the patients was cardiac decompensation due to hypertension, which could result in misdiagnosis and early treatment opportunities. Some patients die before heart failure. Hypertension with virilization and pseudoaldosteronism should be alerted for the diagnosis of classical 11β-hydroxylase deficiency.


