Journal of Pediatric Endocrinology & Metabolism, 16, 565-570 (2003)

Monozygotic Twins with Congenital Adrenal Hyperplasia: Long-term Endocrine Evaluation and Gene Analysis

Theodore W. AvRuskin[1], Selma F. Witchel[2], Doris R. Taha[1] and Christina S. Juan[1]

[1]Department of Pediatrics, Division of Pediatric Endocrinology and Metabolism, The Brookdale University Hospital and Medical Center, State University of New York at Brooklyn, NY and [2]Department of Pediatrics, Division of Pediatric Endocrinology and Metabolism, Children's Hospital of Pittsburgh, Pittsburgh, PA, USA

ABSTRACT

Monozygotic female twins with congenital adrenal hyperplasia due to 21-hydroxylase deficiency are described and evaluated over the first 6 years of life. Despite appropriate steroids, NaCl, and fludrocortisone therapies, there was significant fluctuation in the suppression of adrenal steroid secretion. Advanced bone maturation in both was noted. For the first time, molecular genetic analysis was performed and documented that the twins were compound heterozygotes for two different mutations: the maternal allele carried the 8-bp deletion mutation, whereas the paternal allele carried the I172N missense mutation. Parental DNA samples confirmed that the mutations were on different alleles.

KEY WORDS

monozygotic twins, congenital adrenal hyperplasia, endocrine evaluation, adrenal status, gene analysis

INTRODUCTION

Congenital adrenal hyperplasia (CAH), an inborn error of metabolism of adrenocortical steroidogenesis, is inherited as an autosomal recessive trait[1]. The most severe form results in excess adrenal androgen secretion from early fetal life producing virilization of the external genitalia of affected female fetuses from the time of sexual differentiation, which occurs between 6-13 weeks of gestation[2,3]. This disorder is due to mutations in the 21-hydroxylase (*CYP21*) gene[4,5]. Human 21-hydroxylase deficiency is the leading cause of impaired cortisol synthesis in CAH[6,7]. The incidence of classic 21-hydroxylase deficiency (21OHD) is 1:5,000-15,000 live births, whereas a milder non-classical form of the disease occurs in 0.3% of Caucasians and in 1-3% of European Jews. The molecular genetics have been reviewed[8-10]. To date, 49 mutations have been reported causing 21OHD[10].

Twins with CAH are rarely reported. Identical twins with this disorder have been reported slightly more frequently[11-17] than dizygotic twins[18-20]. However, in none of these reports has there been an identification of the gene mutation, nor an evaluation of adrenal gland function throughout childhood. This present report describes the adrenal defect and documents adrenal gland response to steroid therapy from the time of diagnosis to 6 years in monozygotic twins with 21OHD.

PATIENT REPORTS

The twins were products of a term gestation to a 31 year-old Hispanic G2P0 female (one spontaneous abortion and one ectopic pregnancy). The father, 39, and mother were from the Dominican Republic. There was no consanguinity. Both twins were delivered by Caesarian section secondary to breech presentation at term. There were no perinatal or maternal complications. Both had normal APGAR scores and weighed 2290 g.

Because of ambiguous external genitalia consisting of an enlarged phallus, increased posterior labioscrotal fusion, and an anogenital ratio >0.5[21],

Reprint address:
Theodore W. AvRuskin, M.D.
The Brookdale University Hospital and Medical Center
Aaron Suite 222
One Brookdale Plaza
Brooklyn, NY 11212-3198, USA
e-mail: tavruski@brookdale.edu