

## Intrauterine Growth Retardation Associated With Maternal Uniparental Disomy for Chromosome 6 Unmasked by Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia (CAH) is caused by steroid 21-hydroxylase deficiency. The gene (*CYP21*) for this enzyme is located on the short arm of chromosome 6 (6p21.3).

This enzyme deficiency leads to reduced conversion of 17-hydroxy progesterone to 11-deoxycortisol, resulting in a deficiency of cortisol and overproduction of androgens. In female newborns this disorder is associated with ambiguous genitalia. Untreated children show rapid growth, phallic enlargement, precocious pubarche, early epiphyseal closure, and short stature.

In this report, 1 female newborn with intrauterine growth retardation (IUGR) and CAH was found to be homozygous for a rare exon 4 mutation 1172N. The patient showed transient delayed mental development, evidence of early puberty, increased bone age, and accelerated growth. Genetic analysis found that only the mother was heterozygous for this mutation. Further DNA microsatellite analysis confirmed the diagnosis of uniparental disomy.

Spiro RP, et al. *Pediatr Res* 1999;46:510-513.

**Editor's comment:** *Uniparental disomy is a condition in which both copies of a chromosome segment are inherited from a single parent. There is only 1 other report of a patient with uniparental disomy of the same segment of 6p (van den Berg-Loonen EM, et al. Hum Immunol 1996;45:46-51). This patient had IUGR at birth. Clinical symptoms appear to be due to genetic imprinting or expression of recessive traits from the affected chromosome segment and not directly associated with uniparental disomy. Similar reports of uniparental disomy involving the long arm of chromosome 6 have been associated with neonatal diabetes but not IUGR. These data are suggestive that fetal growth gene(s) are located on the short arm of chromosome 6 and that genetic mutations in this particular area (6p21.3) will cause IUGR. This case study shows that a rare underlying genetic mutation can cause multiple clinical manifestations. However, the risk of recurrence of these mutations is negligible in families.*

Fima Lifshitz, MD

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