



Fig. 1. Pathway for adrenal hormone synthesis demonstrating the 21-hydroxylase and the 17,20-desmolase deficiencies. A deficiency of the 21-hydroxylase enzyme normally leads to an increase in DHEA since 17-hydroxyprogesterone increases and can only be shunted to the reticularis since it is required for the final products in both the fasciculata and the glomerulosa. A concomitant deficiency of 17,20-desmolase prevents the increase in DHEA and thus partially protects from effects of increased androgens.

Virilizing congenital adrenal hyperplasia with normal dehydroepiandrosterone sulfate

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The most common cause of congenital adrenal hyperplasia is the 21-hydroxylase deficiency. It is characterized by excessive secretion of both 17 α -hydroxyprogesterone and dehydroepiandrosterone (DHEA). The patients frequently present with clitoromegaly, ambiguous genitalia, and hirsutism.

The patient described below presented with classical symptoms and signs of congenital adrenal hyperplasia with a very elevated level of 17-hydroxyprogesterone. However, the DHEA sulfate level was in the low normal range. This case thus represents the second reported case of a 21-hydroxylase deficiency with an associated 17,20-desmolase deficiency and the first one with virilization.¹

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The patient presented at age 12 with the complaint of mild hirsutism. Pelvic examination disclosed clitoromegaly and partial fusion of the labia. Height was 63 inches, and she gave a history of being taller than her peers as a preteen but seemingly stopped active growing by age 11. Complete general examination was negative except for mild facial hirsutism with a tendency toward a male-type escutcheon and acne.

The 17 α -hydroxyprogesterone level was markedly elevated at 8,720 ng/dl (normal = 15-90). However, the DHEA sulfate level was normal at 118 and, on repeat, 85 μ g/dl (normal = 60 to 300 μ g/dl). The androstenedione level was increased at 643 ng/dl (normal = 20 to 250 ng/dl) and the testosterone level was increased at 120 ng/dl (normal = 30 to 95). A 24-hour urine sample for measurement of 17-ketosteroids contained 9.5 mg/gm of creatinine, and the sample for measurement of 17-hydroxycorticosteroids contained 1.5 mg/gm of creatinine (normal, >6.5 mg/gm of creatinine).

She was given an oral contraceptive (Demulen), and both the androstenedione and testosterone levels were suppressed to well within the normal range: Androstenedione = 85 ng/dl (normal = 20 to 250 ng/dl) and testosterone = 35 ng/dl (normal = 30 to 95 ng/dl).

The patient then underwent corrective plastic surgery (clitoridectomy and vulvoplasty) and was treated with hydrocortisone (20 mg at bedtime and 10 mg in the morning).

This case demonstrates congenital adrenal hyperplasia associated with both a 21-hydroxylase deficiency and a concomitant 17,20-desmolase deficiency. This is only the second time this association has ever been reported. Thus, in contrast to the mother and daughter reported in the German article,¹ in whom phenotypes were perfectly normal, this patient did present with many of the classic features of the 21-hydroxylase deficiency type of congenital adrenal hyperplasia.¹

The presence of a markedly elevated 17-hydroxyprogesterone level with a normal DHEA sulfate level proves the deficiency of the concomitant 17,20-desmolase deficiency as evidenced in Fig. 1. Normally, the marked elevation in 17-hydroxyprogesterone would be metabolized further in the reticularis to both andro-

stenedione and DHEA sulfate, the latter being a specific marker for an adrenal rather than an ovarian source. The presence of some of the virilizing features of the classic 21-hydroxylase type of congenital adrenal hyperplasia in our case is related to the severity of the 21-hydroxylase deficiency in view of the marked elevation of the 17-hydroxyprogesterone level. Although protected by the failure to be converted to DHEA and androstenedione, the levels in utero were probably sufficient to cause mild virilization. This contrasts with the reported case of the German mother and daughter with baseline pregnanetriol (urinary excretory product of serum 17-hydroxyprogesterone) levels that were only slightly elevated. This would explain their normal phenotypic appearance. It is possible that a good part of the adult hirsutism was related to associated polycystic ovarian syndrome since testosterone and androstenedione levels, which were slightly elevated, were suppressed to normal values with oral contraceptives.

An elevated testosterone level is generally indicative of an ovarian source of male hormone, whereas an increase in DHEA sulfate generally pinpoints the problem to the adrenal. There have been only a few rare cases reported of testosterone secretion from an adrenal neoplasm.² This case demonstrates the exception to the rule that a normal DHEA sulfate level rules out an adrenal source of androgens.

REFERENCES

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