A 2-year-old Boy with a Testicular Mass

Tolga Unuvar, MD; Korcan Demir, MD; Ayhan Abaci, MD; Ali Atas, MD; Handan Cakmakci, MD; and Ece Bober, MD

A 2-year-old boy was admitted to our department for a second opinion. The initial complaints were presence of pubic hair for 6 months and progressive penile enlargement. Upon laboratory studies showing elevated total testosterone, dehydroepiandrosterone sulfate (DHEAS), 17-OH progesterone levels, and ultrasonographic findings consistent with bilateral testicular mass, Leydig cell tumor (LCT) had been considered. Bilateral orchiectomy had been offered in another tertiary medical center.

His clinical history revealed a normal delivery at 37th gestational week, with a birth weight of 2,750 g, more remarkable weight and height gain compared with his peers since birth, presence of acne for 1 year, and normal motor-mental development, except delay in

Figure 1. Initial scrotal ultrasound examination revealed (a) two nodular mass lesions (arrows) within the left testis and (b) one mass lesion within the right testis (arrows).

For diagnosis, see page 473.

Editor’s note: Each month, this department features a discussion of an unusual diagnosis in genetics, radiology, or dermatology. A description and images are presented, followed by the diagnosis and an explanation of how the diagnosis was determined. As always, your comments are welcome via e-mail at pedann@slackinc.com.
language skills. There was a third-degree of consanguinity between the parents. Remaining past medical history was unremarkable.

On physical examination, the height (119.7 cm, SD score 6) and weight (26.7 kg, SD score 5) were greater than the 95th percentile. His skin was hyperpigmented, with respect to the parents. Deepening of voice was noted. Pubic hair was consistent with Tanner stage III, while axillary hair was lacking. Palpation revealed very firm testicles of 1 mL each and a soft mass of 3 mL adherent to the left testis. The penis had a pubertal appearance (12.6 cm x 2 cm). Remaining systemic examination was unremarkable.

Laboratory studies showed the following (normal values are shown in parentheses): total testosterone 242.4 ng/dL (< 10 ng/dL); DHEAS 45.8 µg/dL (< 22.2 µg/dL); 17-OH progesterone 7.6 ng/mL (< 5 ng/mL); androstenedione 3 ng/mL (0.09-0.52 ng/mL); alpha-FP 1.59 ng/mL (0.5-5.5 ng/mL); and beta-HCG < 1 IU/mL (0-5 IU/mL).

Scrotal ultrasonography revealed the dimensions of right and left testicles as 18 x 8 x 11 mm and 18 x 11 x 19 mm, respectively. There was a single hypoechoic mass of 6 mm diameter in the right testis, while multiple hypoechoic lesions (10 and 7 mm in diameter) were detected in the left (see Figure 1, page 471). If the frozen section suggested a diagnosis of LCT, incisional biopsy and testis sparing surgery were proposed after consultation with pediatric surgeons.

Before a surgical intervention, we wanted to perform further laboratory studies, particularly because of the presence of relatively hyperpigmented skin. Adrenocorticotropic hormone (ACTH) level was 900 pg/mL (normal, 0-100) and 11-deoxycorticisol > 160 ng/mL. Upon these results, his resting blood pressure was measured and found to be 135/90 mm Hg, which was above the 95th percentile for height, age, and gender (systolic 118 mm Hg, diastolic 79 mm Hg). Serum electrolytes were in normal range, and plasma renin activity was decreased (0.5 ng/mL/sec, normal range 1.7-11.2).
DISCUSSION

The main clues that could be used to establish a diagnosis at the time of admission were clinical and laboratory findings of hyperandrogenism and testicular mass, which initially raised the likelihood of an androgen secreting tumor, particularly LCT, a rare sex cord-stromal tumor most often seen between 5 and 10 years. However, there were some findings incompatible with LCT in our case. First, bilateral hypoechogenic lesions were reported to be present in fewer than 3% of the LCT patients, while only one of three Turkish cases with LCT had unilateral mass. Second, LCT did not explain the hyperpigmented skin. This finding, associated with hyperandrogenism and bilateral testicular mass, brought the mechanism of increased ACTH levels secondary to congenital adrenal hyperplasia (CAH) to mind.

Interestingly, the methods to make a differential diagnosis using clinical findings and serum markers between LCT and testicular tumor of adrenogenital syndrome are discussed in more detail in pathology literature than in surgical or pediatric literature. Young stated that testicular tumor of adrenogenital syndrome should be strongly considered when the lesion is bilateral and has any extra testicular nodularity. Ulbright stated that when ACTH is increased, the testicular abnormality may be the presentation in some cases, and bilateral involvement is invariable in testicular tumor of adrenogenital syndrome. Al-Agha and Axiotis mentioned the use of ACTH to determine adrenal hyperplasia. Rich and Keating noted the necessity of measuring 11-deoxycortisol in addition to androgens when adrenogenital syndrome is suspected in any patient with a testicular tumor. Additionally, ACTH stimulation tests were mentioned as supportive methods.

In our patient, the abovementioned clinical features suggested hyperplasia of the adrenal rest tissue, which may migrate with the descending gonads during early embryogenesis in up to 50% of newborns, due to underlying CAH. We performed further laboratory studies and found high ACTH and 11-deoxycortisol levels, indicating 11-beta-hydroxylase deficiency, which is the second most common cause of CAH and results in accumulation of a mineralocorticoid, deoxycorticosterone. Hydrocortisone treatment was started (15 mg/m²/day) to suppress ACTH. 11-deoxycortisol levels could only be normalized with a dose of 25 mg/m²/day. No testicular mass was palpable by the 15th month of treatment. Ultrasonographic hypoechogenic lesions disappeared at the third year of follow-up (see Figure 2).

In clinical experience, and unsurprisingly, there is another report of diagnostic confusion between these disorders. Ghazi et al. uncovered LCT in a boy with unilateral testicular mass who was previously diagnosed as 21-hydroxylase deficiency, depending on increased androgens without measuring ACTH or performing ACTH stimulation test and receiving hydrocortisone for nearly 1 year.

The difficulty in making a histological diagnosis of LCT or testicu-
lar tumor of adrenogenital syndrome is comparable with the problems in clinical diagnosis. If our case underwent surgery and frozen section were made, the diagnosis of testicular tumor of adrenogenital syndrome would have been more likely if broad fibrous bands, spotty nuclear atypia without mitotic activity, and cytoplasmic lipochrome pigment were found; however, individual fields would have probably been indistinguishable. The absence of Reinke crystals, which is pathognomonic for LCT, would have been suggestive of testicular tumor of adrenogenital syndrome; however, they are present only in less than half of the LCT patients. Furthermore, immunohistochemistry would not have been helpful in the distinction of these entities if the whole mass was resected. Therefore, frozen sections might have been misdiagnosed as LCT, and excision of mass and possible consequent gonadal injury or orchietomy would not have been avoided.

CONCLUSIONS
It is important to keep in mind the vital role of clinical and laboratory findings, namely blood pressure, skin pigmentation, the type of involvement, and, particularly, ACTH, in differential diagnosis of LCT and testicular tumor of adrenogenital syndrome when no endocrine disorder is previously diagnosed.

REFERENCES