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# Testicular adrenal-like tissue (TALT) in congenital adrenal hyperplasia: detection by ultrasonography

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**Abstract.** In a consecutive series of 15 male adolescents and young adults with congenital adrenal hyperplasia (CAH), the size, shape, firmness and echostructure of the testes were assessed. The latter was abnormal in 7 patients under long standing treatment with glucocorticoids (group I). In 8, 5 under and 3 off treatment for several years, ultrasonography (US) was normal (group II). On the basis of the US findings the patients were placed in two groups. In group I, the testes had a heterogeneous ultrasonographic pattern; clinically, most felt hard and irregular, although their volume was normal. Sperm count in 3 patients was 5.0 to $14.4 \times 10^6$/ml. Five patients have 21-hydroxylase deficiency that was diagnosed in early infancy and had salt-wasting; two have 11-beta-hydroxylase deficiency that was diagnosed late and had no salt-wasting. In group II, testicular volume, shape, firmness and echostructure were normal. All have 21-hydroxylase deficiency, no history of salt-wasting and were diagnosed late. Sperm counts in 3 patients off treatment were 10.5 to $66.0 \times 10^6$/ml. In severe cases with a history of salt loss, TALT with deficient spermiogenesis seems likely despite treatment. In mild cases, TALT is absent and spermiogenesis may be normal even without treatment. US is much more accurate in assessing the testes than palpation.

Based on autopsy studies, ectopic adrenal tissue is known to occur in numerous places in the human body. The celiac plexus and broad ligament have been systematically investigated, and a frequency of 32% and 23% respectively has been reported [1, 2]. Ectopic adrenal tissue has been found in normal fetal ovarian tissue [3], but not in normal testes [4].

In contrast, testicular adrenal like tissue (TALT) (ectopic adrenal tissue) has been repeatedly found in testes of patients with CAH [5–12]. TALT may vary from microscopic to easily palpable nodules with a diameter of 1 cm or more. Careful microscopic examination has suggested that it is present in all males with CAH [8]. Normal reproductive function is assumed when the volume, shape and firmness of the testes are normal on palpation. Sperm count and testicular histology are then likely to be normal as well. Normal endocrine function is assumed when secondary sex characteristics have developed normally and is confirmed when levels of testosterone in the plasma and/or urine are found to be normal.

In patients with CAH, however, this assumption cannot be made, since secondary sex characteristics may result from adrenal androgens. Patients who have received inadequate or no treatment, and whose bone age exceeds 13 years, usually present with small "atrophic" testes.

In some, the surface of the testicle may be nodular and the firmness increased and irregular. Such findings are suggestive of TALT. Nodules of TALT may increase testicular volume to "normal" even in the presence of severe tubular insufficiency [13]. This incorrect conclusion that the testes are normal in size may lead to the incorrect assumption of normal testicular function or even true precocious puberty in younger boys.

Since the results of palpation of these testes may be inconclusive, even by the experienced examiner, we felt that ultrasonography could make the evaluation of the testicle more accurate. We first reported ultarsonographic heterogeneity of the testes with defined areas of low echodensity in 5 of 10 patients with CAH [14]. Later, Seidenwurm et al. demonstrated similar findings in four patients with CAH [15]. We now present further data and clinical relevance.

## Patients and method

Fifteen consecutive males age 12 to 36 years had their testes examined by ultrasound. In all, the bone age exceeded 16 years at the time of the examination [16]. The clinical diagnosis of CAH had been made between 3 weeks and 7 years of age and was confirmed by steroid gas chromatography on glass capillary columns [17] and compound identification by mass spectrometry. Thirteen, among them 2 brothers (patients No. 3, 6), have 21-hydroxylase deficiency, and 2 brothers (patients Nor. 1, 5) have 11-beta-hydroxylase deficiency [18]. All but 3 patients (No. 13–15) have been receiving continuous therapy with hydrocortisone or dexamethasone. In all 15, testicular volume was measured [19] and testicular shape and firmness were

**Table 1.** Seven patients with CAH and abnormal US of the testes (group I)

| Patient number | Age at diagnosis (y/w) | Age at US (y) | Average testicular volume (ml) | Palpation | | Sperm count ($\times 10^6$/ml) | History of salt-wasting |
|---|---|---|---|---|---|---|---|
| | | | | Shape | Firmness | | |
| 1[a] | 2 y | 12 | 9 | Normal | Normal | – | – |
| 2 | 6 w | 12 1/2 | 15 | Irregular | Hard | – | + |
| 3[b] | 3 w | 17 | 15 | Irregular | Hard | – | + |
| 4 | 5 w | 17 1/2 | 12 | Irregular | Normal | – | + |
| 5[a] | 5 y | 19 | 11 | Irregular | Hard | 14.4 | – |
| 6[b] | 4 w | 23 | 11 | Irregular | Normal | 5.0 | + |
| 7 | 5 w | 27 | 15 | Normal | Hard | 5.0 | + |

[a] Brothers with 11-beta-hydroxylase deficiency; [b] Brothers with 21-hydroxylase deficiency; y, Years; w, Weeks; ml, Milliliter. The patients' numbers in table 1 and 2 do not correspond to the sequence of presentation of these patients for US

**Table 2.** Eight patients with CAH and normal US of the testes (group II)

| Patient number | Age at diagnosis (y) | Age at US (y) | Average testicular volume (ml) | Palpation | | Sperm count ($\times 10^6$/ml) | History of salt-wasting |
|---|---|---|---|---|---|---|---|
| | | | | Shape | Firmness | | |
| 8 | 7 | 12 1/2 | 18 | Normal | Normal | – | – |
| 9 | 6 | 13 1/4 | 9 | Normal | Normal | – | – |
| 10 | 5 | 14 | 6 | Normal | Hard | – | – |
| 11 | 3 | 14 3/4 | 10 | Normal | Normal | – | – |
| 12 | 5 | 15 3/4 | 9 | Normal | Normal | – | – |
| 13 | 6 | 28 | 7 | Normal | Normal | 66 | – |
| 14 | 7 | 34 | 9 | Normal | Normal | 10.5 | – |
| 15 | 6 | 36 | 10 | Normal | Normal | 20 | – |

y, Years; ml, Milliliter; –, Sperm count not done; No history of salt-wasting (same for Table 1)

assessed (Table 1, 2). In all patients, there were minimal if any differences in volume, shape and firmness between the two testicles. In 6, a sperm count was obtained (Table 1, 2). Initially, a 5 MHz compound transducer with short focus, later, a 5 or 7.5 MHz real time sector transducer with short focus were used for US.

## Results

Seven patients (No 1–7, Table 1, group 1) had either a well defined lesion of small to medium size and rather low echodensity within the testes (Fig. 1) or more extensive and rather heterogenic alterations of testicular echogenicity (Fig. 2, 3) suggesting the presence of TALT. The location of the lesions within the testes varied from patient to patient. In two patients, the extent of the lesions seemed to regress slightly on follow-up examinations. In only one patient was the volume of the testes small; in the others it was normal. In all but one, testicular shape and/or firmness were abnormal.

Patients no 5–7 had severe oligospermia, although patient no 7 in whom the sperm count averaged $5.0 \times 10^6$/ml (normal: above $20 \times 10^6$/ml) on 10 examinations has fathered a child.

In 8 other patients (no 8–15, table 2, group II), testicular structure was normal ultrasonographically. In 5 of these (patients no 9–10, 12–14), testicular volume was relatively small for bone age. Testicular shape was normal in all and firmness was increased in only one (patient no 10). Patient no 13 had a normal sperm count after therapy had been discontinued for more than 2 years [13]. Patient no 14 (who had a normal sperm count under corticoid treatment and fathered a child) became oligospermic when therapy was discontinued. Patient no 15 who has not been treated for several years has a sperm count of $20 \times 10^6$/ml. His partner became pregnant but aborted the fetus.

All 5 patients in group I with 21-hydroxylase deficiency were diagnosed in early infancy when they

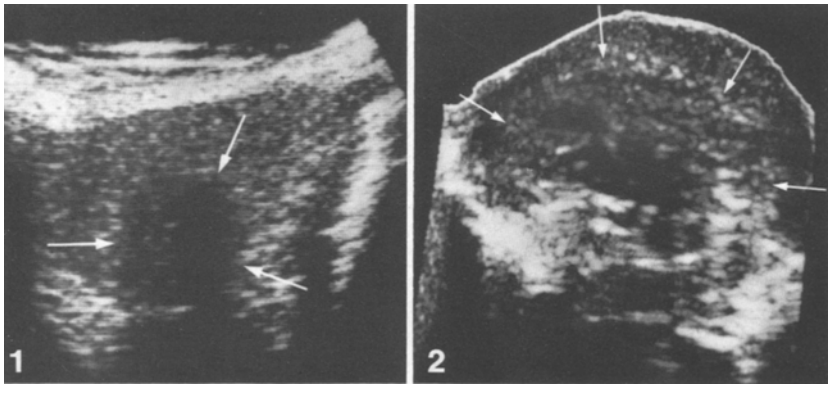


**Fig. 1.** (Patient no 2 with 21-hydroxylase deficiency) Real time longitudinal scan of right testis: well-defined hypoechoic lesion *(arrows)*: TALT

**Fig. 2.** (Patient no 3 with 21-hydroxylase deficiency) Compound longitudinal scan of right testis: TALT *(arrows)* of moderate to massive degree, heterogeneous, not well defined, surrounded by normal testicular tissue

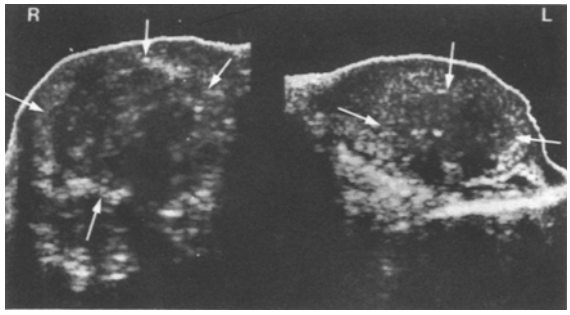


**Fig. 3.** (Patient no 5 with 11-beta-hydroxylase deficiency) Compound transverse scan of both testes: extensive alterations of both testes by TALT *(arrows)*, surrounded by normal testicular tissue

presented with symptoms and findings of salt-wasting. In contrast, none of the patients in group II had problems in infancy. All were diagnosed at age 3–7 years when precocious pubarche suggested the possibility of CAH.

## Discussion

Uni- or bilateral testicular tumors in patients with CAH have been described by several authors [5–12]. The exact histological classification is difficult, and it is not known whether these tumors represent rests of adrenal tissue or whether they originate from Leydig cells. The fact that the volume of such testes may decrease and their irregular shape and increased firmness may become normal under treatment with glucocorticoids [5, 13] suggests the presence of adrenal tissue. Since the biosynthesis of sex steroids in Leydig cells and in adrenal cells is similar, a functional study of the origin of TALT would require in vitro analysis of steroid production. In vivo, such an analysis is probably only possible after adrenalectomy. Therapy in patients with TALT is extremely difficult and almost all of them remain sterile.

Seven of our patients (group I) revealed definite structural abnormalities in both of their testes on US. In 6, these findings corresponded to the clinical impression of irregular testicular shape and/or firmness. Two of these patients have an 11-beta-hydroxylase deficiency. To our knowledge, such testicular lesions have not been described in this defect.

On the basis of the ultrasonographic findings, therapy in patient no 2 was changed from hydrocortisone to dexamethasone. This was followed by a seemingly mild reduction of TALT in the testes on US. Also, one of the 2 brothers with 11-beta-hydroxylase deficiency (patient no 5) showed an apparent partial reduction of TALT on US when the dosage of dexamethasone was increased. However, a significant reduction of TALT upon change in therapy could not be demonstrated ultrasonographically in these patients, since they were not available for a consistent protocol in treatment and follow-up monitoring.

In a previous publication, two of us (AP, MZ) reported normal spermiogenesis in 4 adult males with CAH after discontinuation of steroid therapy and referred to the rare reports of normal testicular development in untreated patients [13]. Patients no 3 and 4 in that paper are the patients no 13 and 14 in the present series. In our experience, testicular US is an important aid in both the detection of TALT and the confirmation of its clinical susspicion. In addition, our study suggests that in patients with 21-hydroxylase deficiency TALT is only seen in the severe form (i.e. patients with salt-wasting in early infancy). It is also seen in some of the patients with 11-beta-hydroxylase deficiency.

Volume of the testes is usually normal in spite of severe tubular insufficiency with oligospermia. Testicular volume may regress with more effective treatment with glucocorticoids which may also lead to normal spermiogenesis. On the other hand, in none of the patients with 21-hydroxylase deficiency who had the diagnosis of CAH made late (i.e. no salt-wasting in infancy) did US reveal TALT; almost all of them have small testes but some have normal spermiogenesis.

### *In conclusion*

Testicular US has proved to be of value in the evaluation of pubertal and adult patients with CAH. It permits the detection of abnormal testicular tissue; this tissue seems to correspond to TALT as found on histological examination. Patients with 21-hydroxylase deficiency and TALT seem to represent a more severely affected group of CAH with early clinical onset who are likely 1) to present with early symptoms of salt-wasting, 2) who later have severe disturbance of reproductive testicular function, and 3) whose treatment is particularly difficult.

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