Adrenal rest tissue in gonads of patients with classical congenital adrenal hyperplasia: Multicenter study of 45 French male patients

Inclusions intratesticulaire de tissu surrenalien chez des patients souffrant d’hyperplasie congenitale des surrenales : étude multicentrique de 45 sujets de sexe masculin

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Abstract

Objectives. – Several cases of testicular adrenal rest tumours have been reported in men with congenital adrenal hyperplasia (CAH) due to the classical form of 21-hydroxylase deficiency but the prevalence has not been established. The aims of this report were to evaluate the frequency of testicular adrenal rest tissue in this population in a retrospective multicentre study involving eight endocrinology centres, and to determine whether treatment or genetic background had an impact on the occurrence of adrenal rest tissue. Material and methods. – Testicular adrenal rest tissue (TART) was sought clinically and with ultrasound examination in forty-five males with CAH due to the classical form of 21-hydroxylase deficiency. When the diagnosis of testicular adrenal rest tumours was sought, good observance of treatment was judged on biological concentrations of 17-hydroxyprogesterone (17OHP), delta4-androstenedione, active renin and testosterone. The results of affected and non-affected subjects were compared. Results. – TART was detected in none of the 18 subjects aged 1 to 15 years but was detected in 14 of the 27 subjects aged more than 15 years. Five patients with an abnormal echography result had no clinical signs. Therapeutic control evaluated at diagnosis of TART seemed less effective when diagnosis was made in patients with adrenal rest tissue compared to TART-free subjects. Various genotypes were observed in patients with or without TART. Conclusion. – Due to the high prevalence of TART in classical CAH and the delayed clinical diagnosis, testicular ultrasonography must be performed before puberty and thereafter regularly during adulthood even if the clinical examination is normal.

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et échographique d’inclusions intratesticulaires ont été inclus. L’équilibre thérapeutique a été jugé au décours de la recherche des inclusions sur les résultats des dosages de la 17-hydroxy-progèstérone, la delta4-androsténédione, l’activité rénine plasmatique et la testostérone. Les résultats de ces paramètres ont été comparés chez les patients sans et avec inclusions.

Résultats. — Aucune inclusion n’a été trouvée parmi 18 patients âgés d’un à 15 ans mais 14 des 27 sujets de plus de 15 ans en présentent. Parmi les patients avec des inclusions à l’échographie, cinq avaient un examen clinique testiculaire normal. L’équilibre thérapeutique au diagnostic des sujets avec inclusions semblait plus mauvais que pour les patients indemnes. Sur le plan génétique, les lésions sont variées tant dans le groupe avec que sans inclusions. Conclusion. — En raison de la forte fréquence des inclusions intratesticulaires de tissu surrénalien, une échographie testiculaire doit être réalisée avant la puberté puis régulièrement à l’âge adulte même si l’examen clinique est normal.

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1. Introduction

Congénital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is one of the most frequent genetic endocrine diseases. Complete enzyme deficiency leads to the salt-wasting (SW) form and less severe deficiency to the simple virilizing (SV) form. Fertility in male patients has long been considered normal [1,2] but this opinion has recently been challenged [3–5]. Many explanations of infertility have been proposed, including central disorder of gonadotroph function and the local development of testicular adrenal rest tissue (TART). The first case of TART was reported in 1940 [6] and many case-reports have been published subsequently [7–9]. Adrenal rest tissue can affect adjacent testicular tissue function or create obstruction of the seminal tubules. Such abnormalities have also been described in patients with high ACTH levels, as observed in Addison’s disease and Nelson’s syndrome [10,11], but their development has not been fully explained to date. The clinical diagnosis of adrenal rest tissue is often late but it can be made sooner using gonad ultrasonography [12,13]. The prevalence of TART has not been clearly established [3,5,12,14]. In this study, we defined the prevalence of TART in a group of 45 men with CAH in its SW and SV forms, using systematic ultrasound examination. We evaluated the mean age at diagnosis in a retrospective descriptive multicentre study. We also investigated a relationship between adrenal rest tissue, therapeutic control and genotyping by comparing patients with and without adrenal rest tissue.

2. Material

We included patients with the SW form or the SV form of CAH with at least one ultrasound examination of the gonads. Patients were enrolled using keywords in hospital databases. We conserved only hospital centre cases if echography was performed for more than 50% of the patients followed for the SW or SV form of CAH. These endocrinology centres were located in Tours (adult–paediatric unit), Rennes (adult unit), Nantes (paediatric unit), Angers (paediatric unit), Orleans (adult, paediatric unit), and Brest (adult unit).

In the hospital centres cited above, 72.3% of the children and 87.5% of the adults with the disease had had an ultrasound examination of the gonads. Forty-seven men from these French hospital centres were included initially but two patients were subsequently excluded: one because of another severe disease associated with CAH and the other because of ectopic testes.

Ultrasonography was chosen because it is a cheap, non-invasive, easily accessible method [12,13]. Patients were classified as having the SW or SV form according to the clinical expression for the patients without available genetic analysis and according to genotype for others. The non-classical form responsible for premature pseudo puberty was not included.

3. Methods

Ultrasonography was performed in each medical centre by a senior physician. Various ultrasound scanners were used: Siemens Elegra; Aloka SSD-5500; ATL/HDI 3000; Hitachi Katana; GE LOGIQ 9; Hitachi Alpha. High frequency linear probes (7.5 MHz). US scanning was performed in longitudinal, axial and oblique views. The diagnosis of adrenal rest tissue was considered when US showed heterogeneous hypo- or hyperechogenic multifocal areas surrounding the echogenic testis mediastinum, mainly bilateral, and with well-defined margins according to Stikkelbroeck et al. [13], Willi et al. [14], Avila et al. [15,16], and Vanzulli et al. [17]. Diagnosis was only confirmed if the main author (P.P.) was in agreement by looking at images with the radiologist who had performed the examination.

Therapeutic control at diagnosis was studied on the basis of several criteria: serum 17-hydroxyprogesterone ([17OHP] normal range considered 6–30 nmol/L with conversion factor: 1 ng/mL = 3 nmol/L), delta4-androstenedione (normal range considered 1.4–12 nmol/L with conversion factor 1 ng/mL = 3.5 nmol/L), active renin (normal range considered < 40 ng/L), and testosterone (normal range considered 10–30 nmol/L with conversion factor 1 ng/mL = 3.47 nmol/L) concentrations.

We did not consider criteria of long-term hormonal control (bone age, final height, BMI) because our population was very heterogeneous (adult–children) and composed of a little number of subjects.

Doses of treatment with hydrocortisone and fludrocortisone were noted when the diagnosis of TART was made. If dexamethasone was prescribed, the dose was converted into hydrocortisone equivalent (0.75 mg dexamethasone = 20 mg hydrocortisone). Doses were expressed in hydrocortisone dose per body surface area (BSA) per day. BSA (m²) was calculated with the Mosteller formula \[ \sqrt{ (\text{Height} \text{ (cm)}) \times \text{weight} \text{ (kg)/3600})} \].

Two groups (patients older than 16 years with and without TART) were compared according to these criteria. We chose
Prevalence of testicular adrenal rest tissue (TART) with clinical exam and ultrasonography according to age and genotype.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Salt wasting (n = 31)</th>
<th>Simple virilizing (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abnormal clinical exam</td>
<td>Abnormal echography</td>
</tr>
<tr>
<td>0 to 10 (n = 10)</td>
<td>0/6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0/6</td>
</tr>
<tr>
<td>10 to 15 (n = 8)</td>
<td>0/2</td>
<td>0/2</td>
</tr>
<tr>
<td>15 to 20 (n = 9)</td>
<td>1/6</td>
<td>3/6 (50%)</td>
</tr>
<tr>
<td>Up to 20 (n = 18)</td>
<td>8/17</td>
<td>10/17 (58.8%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> 0/6 means 0 abnormal exam among six patients.

**Results**

Of the 45 male patients included, 31 had the SW type and 14 the SV type. Echography was performed when patients were aged 18 ± 9.7 years (2.2 to 40.2 years); twenty patients were adults (above 18 years). The prevalence of adrenal rest tissue evaluated by ultrasonography was 31.1% (14/45 subjects). The mean age of the patients with adrenal rest tissue was 24.5 ± 7 years (16.9 to 38.6 years). The prevalence increased with age: no case occurred in the 10 children aged less than 10 years or among the eight children aged from 10 to 15 years; three cases occurred among the patients aged from 15 to 20 years (33%) and 11 cases among patients older than 20 years (61%). The distribution of patients according to phenotype is detailed in Table 1. TART was suspected clinically before performing ultrasonography in nine males, meaning that five patients were only diagnosed by ultrasonography.

TART was bilateral in 13 of the 14 affected patients. Only one patient had a unilateral lesion. The others had multiple foci surrounding the echogenic hilum in the testicles: two lesions in eight cases, three lesions in one case and more than three lesions in four cases. These lesions were often described with ultrasonography as heterogeneous, hypoechoic areas, with the exception of one patient (the patient with the single lesion).

TART was often hypervascular (seven patients among the nine examined by colour-coded Doppler). The mean greatest diameter was 18.8 ± 11.1 mm (3 to 45 mm). If we consider only patients with abnormal testicles at clinical examination, the mean greatest diameter was 22.5 ± 10.8 mm whereas it was 11.3 ± 7.7 mm when the testicles were normal on clinical examination.

We evaluated the role of insufficient treatment in the development of adrenal rest tissue (sometimes related to poor compliance) in the two subgroups, one with adrenal rest tissue and the other without.

We took into account the doses of hydrocortisone (or equivalent) and fludrocortisone when TART was diagnosed (Table 2). There was a tendency for patients with adrenal rest tissue to be treated with higher doses of hydrocortisone (23.4 ± 8.6 mg/m²) than patients without (19.1 ± 9.4 mg/m²) but the difference was not significant. On the other hand, doses of fludrocortisone were higher in the group without (79.49 ± 40.50 µg/m²) compared to the group with adrenal rest tissue (69.49 ± 20.51 µg/m²) but again the difference was not significant.

Hydrocortisone was sometimes combined with or replaced by dexamethasone at night if patients were not well equilibrated: seven of 14 patients with adrenal rest tissue had been treated with dexamethasone, all of them with the SW form of the disease. Of the other 18 patients with the SW form (without adrenal rest tissue), only four patients had been treated with dexamethasone but 10 were observed during childhood and information was not available for three of them.

Comparison of the biological markers of the disease (17-OHP, delta4-androstenedione, testosterone and active renin) showed a tendency to better results in the group without TART (Table 2), active renin being the only significant marker.

The prevalence of TART seemed to be more frequent in the group of patients with the SW phenotype, affecting 41.9% of patients (13 cases among 31 patients). In the group of patients with the SV phenotype, only one patient of 14 (7.1%) had adrenal rest tissue. These two groups of patients also differed in mean age (20.3 ± 10.3 years in the SW group compared to 12.9 ± 6 years in the SV group). We could not compare statistically groups of clinical forms because there was not enough patients.

Molecular study results for CYP21A2 were known for 37 of 45 patients. We only report the results of patients with adrenal rest tissue (all aged over 16 years) and patients without adrenal rest tissue in the same age range (Table 3). The IVS2-13A/C>G mutation in intron 2 was the most frequent, detected in eight alleles of 22 in patients with TART. This mutation was also found

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<sup>a</sup> 0/6 means 0 abnormal exam among six patients.
in five of 18 alleles in men without adrenal rest tissue. The low number of patients did not permit statistical significance. Various other genotypes were observed.

Among 25 patients over 16 years, we know that eight among 13 wished to procreate. Seven patients are in the group with adrenal rests, one patient in the other group. We do not have this information for many patients followed outside Tours.

Result of spermogram was available for five patients among seven with adrenal rest tissue wishing to procreate. Azoospermia was found in three (all with clinically abnormal testes, TART 28 to 42 mm at the greatest diameter), two had a very low sperm count (one of whom had a normal clinical examination but adrenal rest tissue of 22 mm and the other with TART of 13 mm at the greatest diameter). Only two patients were able to procreate without difficulty (two children and 1 child, respectively). Both had normal clinical examinations and adrenal rest tissue of 26 mm and 5 mm at the greatest diameter, respectively.

5. Discussion

The prevalence of TART in this study increased with age, from 0% during childhood to 61% in adults with a prevalence of TART of 31.1% in the overall study population (1 to 40 years of age). These results were compared with available published data in Table 4. Adrenal rest tissue is more often discovered during the second decade but it has sometimes been observed before 10 years of age: one case report in a 5-year-old boy [18], four cases among nineteen 2- to 10-year-old patients [19] and eight cases among 34 patients below 18 years of age [20]. The increase in prevalence with age could partially explain the differences observed in the prevalence of TART: 21 to 94% of patients [3,13,15–17,21]. Prevalence was lower if the study cohort included only children [19,20] whereas the highest prevalence was found in studies involving only adult patients [5,13,22]. In a later work, neither the duration of the disease nor the age of the patients was found to influence the prevalence of TART but they played a role in the volume of lesions observed [23].

There was a lower prevalence of TART in our cohort of children, perhaps due to greater US resolution in the scientific articles cited above [19,20]. Furthermore, our study was retrospective, and some children in the CAH population had not been investigated by testicular ultrasound. Moreover, several radiologists were involved, and this could have been a limitation, although diagnosis is fairly easy and each image was reviewed by the main author [13–17].

The different screening methods used may also explain the differences between studies, e.g. adrenal rest tissue was found during autopsy in all patients older than 14 months [24]. On the other hand, clinical screening was not a very sensitive method: in our study, only nine of the 14 patients with adrenal rest tissue diagnosed by ultrasonography were suspected clinically despite systematic clinical screening. In the studies quoted below, the diagnosis was suspected clinically in 12.5 to 85% of patients with TART diagnosed by ultrasound [13–16,25]. Only lesions of more than 2 cm were clinically palpable [9]. Ultrasonography is thus more accurate than clinical examination and must be performed for all patients.
Table 3
Genotype of 20 patients with or without adrenal rest tissue.

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Allele 1</th>
<th>Allele 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men with adrenal rest tissue (11 among 14 patients: all older than 16 years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>SV</td>
<td>p.I172N</td>
</tr>
<tr>
<td>2</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>3</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>5</td>
<td>SW</td>
<td>Rare deletion of CYP21A2</td>
</tr>
<tr>
<td>6</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>7</td>
<td>SW</td>
<td>Deletion of 30 kb</td>
</tr>
<tr>
<td>8</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>9</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>10</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td><strong>Men without adrenal rest tissue (9 among 11 patients older than 16 years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>SW</td>
<td>p.I172N</td>
</tr>
<tr>
<td>2</td>
<td>SW</td>
<td>Deletion of 8pb ± large CYP21A2 lesion</td>
</tr>
<tr>
<td>3</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>4</td>
<td>SW</td>
<td>Large CYP21A2 lesion</td>
</tr>
<tr>
<td>5</td>
<td>SW</td>
<td>Large conversion of CYP21A2 to CYP21A1P</td>
</tr>
<tr>
<td>6</td>
<td>SW</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>7</td>
<td>SV</td>
<td>G318X mutation</td>
</tr>
<tr>
<td>8</td>
<td>SV</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
<tr>
<td>9</td>
<td>SV</td>
<td>IVS2-13A/C&gt;G</td>
</tr>
</tbody>
</table>

Another reason to explain the variable prevalence of TART may be the absence of specific diagnostic criteria. Differentiation between adrenal rest cells and Leydig cells is sometimes difficult but the context and ACTH dependence can help if the diagnosis of CAH has been established. Gonadic venous sampling to search for specific secretion from the adrenocortical gland, or in vitro study of enzyme functions are reliable but invasive and, if considered to be necessary, have to be performed in specialized units [9,26–28].

In our study, the association of 21-hydroxylase deficiency and a typical ultrasound image was considered sufficient to confirm the diagnosis of adrenal rest tissue: lesions are typically described as hypoechoic, often homogenous, with well circumscribed margins near the hilum of the testis (Fig. 1). In several studies, lesions are often bilateral (86.7%) and size varies from a few millimeters to more than 4 cm, as observed in our study [13,25].

Not all male patients with 21-hydroxylase deficiency are affected by this complication. We therefore assume that certain factors must favour the growth of adrenal rest tissue. In this study, therapeutic control evaluated when diagnosis was made was not statistically different in patients with or without TART. The biological results were not different, with the exception of active renin that was higher in the group with testicular adrenal rest tissue. The importance of controlling this hormonal parameter is well established to optimise substitutive treatment. Our small groups of patients could explain the absence of significant difference in steroid levels (mainly

![Fig. 1. Patient No. 4, Sagittal US view of the right testicle showing multifocal intratesticular, hypoechoic adrenal rest tumours with well-defined margins, the largest (arrows) measuring 50 × 25 mm with calcifications.](image-url)
Table 4
Prevalence of testicular adrenal rest tissue (TART) in published data.

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Mean Age (min–max) years</th>
<th>Clinical form of 21-OH&lt;sup&gt;−&lt;/sup&gt; deficiency</th>
<th>Frequency of adrenal rest tissue on US</th>
<th>Frequency of patients with TART &amp; abnormal clinical exam</th>
<th>Mean age (patients with adrenal rest tissue)</th>
<th>Type of CAH among patients with adrenal rest tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Willi et al., 1991 [14] (17)</td>
<td>13</td>
<td>20.4 (12.5 to 36)</td>
<td>5</td>
<td>8</td>
<td>5/13 (38.5%)</td>
<td>4/5</td>
</tr>
<tr>
<td>Vanzulli et al., 1992 [17] (16)</td>
<td>30</td>
<td>17.8 (9–32)</td>
<td>–</td>
<td>–</td>
<td>8/30 (27%)</td>
<td>2/8</td>
</tr>
<tr>
<td>Avila et al., 1996 [15] (15)</td>
<td>38</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>8/38 (21%)</td>
<td>1/8</td>
</tr>
<tr>
<td>Avila et al., 1999 [12,16] (14)</td>
<td>42</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>12/42 (28.6%)</td>
<td>2/12</td>
</tr>
<tr>
<td>Cabrera et al., 2001 [3] (2)</td>
<td>18</td>
<td>Adults (&gt; 18)</td>
<td>12</td>
<td>6</td>
<td>9/18 (50%)</td>
<td>7/9</td>
</tr>
<tr>
<td>Stikkelbroeck et al., 2001–2003 [5,13,35] (8, 18)</td>
<td>17</td>
<td>21.8 (16.6–40.8)</td>
<td>14</td>
<td>3</td>
<td>16/17 (94%)</td>
<td>6/16</td>
</tr>
<tr>
<td>Claahsen-van der Grinten et al., 2007 [20,28]</td>
<td>34</td>
<td>8.1 (2–18)</td>
<td>24</td>
<td>8</td>
<td>8/34 (24%)</td>
<td>11.3 (7.25–17)</td>
</tr>
<tr>
<td>Martinez-Aguyao et al., 2007 [19]</td>
<td>19</td>
<td>5.6 (2–10)</td>
<td>18</td>
<td>1</td>
<td>4/19 (21%)</td>
<td>3/4</td>
</tr>
<tr>
<td>Reisch et al., 2009 [22]</td>
<td>22</td>
<td>30.8 (19–48)</td>
<td>15</td>
<td>7</td>
<td>10/22 (45.4%)</td>
<td>8/10</td>
</tr>
<tr>
<td>Kang et al., 2011 [23]</td>
<td>48</td>
<td>16.3 (10.6–27.1)</td>
<td>36</td>
<td>12</td>
<td>31/48 (64.6%)</td>
<td>25/31</td>
</tr>
<tr>
<td>Falhammar et al., 2012 [34]</td>
<td>30</td>
<td>19–67</td>
<td>18</td>
<td>12</td>
<td>18/21 (85.7%)</td>
<td>2/21</td>
</tr>
<tr>
<td>Our study</td>
<td>45</td>
<td>16.2 (1–40)</td>
<td>31</td>
<td>14</td>
<td>14/45 (31.1%)</td>
<td>9/14</td>
</tr>
</tbody>
</table>

17OHP) due to insufficient statistical power. However, Reisch et al. also found no correlation between TART volume and short-term hormonal control parameters (17OHP, androstenedione, ACTH, basal LH and FSH) [22,29]. In a study involving a group of children, Martinez-Aguyao and al. found higher levels of 17OHP in patients with TART but there was no difference in testosterone, androstenedione, Dehydroepiandrosterone Sulfate, renin and LH-FSH levels [19]. In contrast, Kang et al. found an impact of long-term hormonal control, judged on BMI and final height compared to targeted height, on the occurrence of TART [23]. Steroid-producing features were studied to understand the growth of these tumours: ACTH and angiotensin II seem to be growth factors of interest [28]. A hormonal impact of ACTH during foetal life has been also suggested [30].

The duration of insufficient therapeutic control seems to be important for growth and consequently an advanced bone age has been estimated to be a better indication of the risk of developing adrenal rest tissue than any biological measurement [16]. Unfortunately, we could not verify this hypothesis because much data was missing in this retrospective study. Other studies have reported the significant role of lengthy poor therapeutic control in the occurrence of TART [17,18,25].

In our study, there was no significant difference in doses of hydrocortisone and fludrocortisone prescribed at diagnosis of TART between the groups with and without adrenal rest tissue. Similarly, some authors found no correlation between prednisone, hour of intake or number of drug administrations and growth of adrenal rest tissue [5]. Others found no correlation between hydrocortisone dosage and the prevalence of TART, but did find a correlation between TART volume and undertreatment [23]. Nevertheless, a few cases with lengthy good control developed TART [5,14,16,17].

The clinical severity of the enzyme deficiency also seems to have a role: people with TART frequently have the SW form [3,9,18,25,31]. In our study, only 1 patient out of 14 with TART had the SV form. However, there was also a difference in mean age, and this could be a confounding factor. An association between TART volume and clinical type (SW or SV) has been found in several studies: volume tends to be higher in SW [22,23,29] but the prevalence has not been found to be statistically different: 69.4% patients with SW had TART compared to 50% patients with SV [23]. TART has occasionally been reported in the non-classical form of CAH [32–34] but we did not consider exploring these patients because the diagnosis of 21-hydroxylase deficit is more difficult and some patients may be asymptomatic.

Particular genotypes could therefore be another explanation. In this study, the IVS2-13A/C mutation in intron 2 was
frequently observed in the group of males with adrenal rest tissue (Table 3) but it was also present in the group without TART. The same mutation, found in both alleles in four cases out of eight, was recently suggested by Claahsen-van der Grinter to be a risk factor for the development of an adrenal rest tumour [20] but it should be emphasized that this genetic 21-hydroxylase abnormality is the most frequently observed (28.1% in about three hundred in the general SW population of the Netherlands) [35]. Other studies have suggested that the size of adrenal rest tissue is greater when patients are homozygous or heterozygous for a deletion or conversion [3,5]. In contrast, a mutation in intron 2 could be protective but we were unable to confirm this [3].

Fertility was affected in our patients. This was similar to previous reports: spermograms were abnormal in more than 50% of patients with 21-hydroxylase deficiency, mainly if adrenal rest tumours were present [3,5]. Infertility was also explained by a Leydig cell dysfunction [3]. Endocrine and exocrine testis functions are therefore modified in CAH. As a result of these findings, we advise male subjects to have a consultation of their medical file, which could not be included because of missing data.

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Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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References


