Adrenogenital syndrome: feminizing genital reconstruction

Indrė Zaparackaitė, Vidmantas Barauskas, Ole Henrik Nielsen¹, Riitta Jokela¹

Clinic of Pediatric Surgery, Kaunas University of Medicine, Lithuania
¹Department of Pediatric Surgery, Copenhagen University Hospital, Denmark

Key words: adrenogenital syndrome, urogenital sinus, genitoplasty.

Summary. Adrenogenital syndrome, or so called congenital adrenal hyperplasia, is caused by a congenital insufficiency of the enzyme 21-hydroxylase, which is responsible for converting cortisol into cholesterol. Because of virilizing effect of androgens overproduction girls develop clitoral hypertrophy and persistent urogenital sinus (common channel for urethra and vagina). Surgical treatment is recommended in order to repair those developmental faults. The aim of this study was to employ the contemporary surgical techniques and to evaluate the postoperative results.

Forty-seven patients affected by adrenogenital syndrome were investigated and treated at two institutions: Departments of Pediatric Surgery of Copenhagen University Hospital and Kaunas Medical University Hospital. Forty-three patients have been operated and underwent genitoplasty. Surgical method was chosen individually depending on the height of the urogenital sinus. In a case of low sinus a simple cut-back procedure was performed. In a case of high sinus the more complex procedure such as total urogenital mobilization or vaginal pull through would be involved. All patients underwent vaginal dilatations for 6–12 months postoperatively. Twenty-eight patients underwent clitoroplasty while the glans and the neurovascular bundle were preserved and clitoral skin used for plasty of the labia minora. Postoperatively the patients were observed for 0.5–5 years, the close results showed to be good. There were 4 cases of vaginal stenosis and 2 cases of urethrovaginal fistula (all successfully repaired later).

Early one staged genitoplasty and postoperative vaginal dilatations for the period of 6–12 months is recommended.

Introduction
The problem of ambiguous genitalia has attracted increasing attention among the medical society especially over the last 2-3 years. Several recent surveys from different medical centers have reviewed early and late postoperative results in different groups of patients. In many materials females affected by adrenogenital syndrome represent the biggest group requiring surgical genital correction (1,10,13,14,18,21).

It is recognized that the prospects for reproduction are undoubtedly better in this group of patients compared with other intersex individuals raised as females.

Adrenogenital syndrome or congenital adrenal hyperplasia represents a genetically determined enzymatic defect in the synthesis of cortisol from cholesterol. The classical virilizing adrenogenital syndrome is due to impaired steroid hydroxylation mostly caused by the deficiency of 21-hydroxylase, but there are several other types of enzymic defect. Salt wasting is another clinical manifestation and occurs in up to 75% of all cases. Adrenal androgen overproduction causes different degrees of virilization at birth in females (female pseudohermaphroditism) while some other forms may lead to sexual infantilism. The average incidence of the classical presentation is 1 in 15 000 live births. The salt wasting form is usually recognized in the neonatal period when in fact all decisions concerning gender should be made. Non-classical forms are characterized by more subtle somatic manifestations of androgen excess (11).

There is general agreement that the management should aim at creating a normal female anatomy with a minimum of complications and an improvement of life quality. The controversies among clinicians concern the timing and staging of surgical procedures.
To clarify the roles of various treatment strategies for reconstructive genital surgery we reviewed our experience combining the material from two institutions. In 1998 an intersex program was established as a joint venture between the Pediatric Surgery Clinic of Kaunas Medical University Clinics, Lithuania and the Department of Pediatric Surgery, Copenhagen University Hospital, Denmark.

Material and methods
In the period 1987-2002, 96 intersex patients raised as females were seen at the departments of Pediatric Surgery in Copenhagen and Kaunas. Forty-seven of them affected by adrenogenital syndrome are the material of the present study. Forty-three patients underwent surgical treatment. One has been managed only by vaginal dilatation. Three patients are waiting for surgery. Two 46XX individuals were raised as boys, because gender reassignment was not possible due to late diagnosis and the consequent social and psychological circumstances. They were excluded from our material.

The records of the patients from the departments of Endocrinology and Pediatric Surgery in both institutions were reviewed. The workup included clinical examination, chromosomal and hormonal status analysis, radiological bone establishment, pelvic ultrasound, cystoscopy, laparoscopy (in unclear cases) and genitograms.

The age of the patients ranged from 4 months to 21 year (mean age at the time of surgery – 6.4 years). In Copenhagen management has been consecutive. In Kaunas, because of the treatment pause from 1990, all patients were treated in 1998-99. In 10 patients from the Lithuanian group initial surgery had been done previously in Moscow in the period between 1988 and 1998. Before 1998 among Lithuanian patients the procedure of clitoral resection was quite widely applied (8 patients had the clitoris removed, 2 underwent clitoroplasty). Later it was recognized to be physiologically wrong. Since clitoral reduction was just the first stage procedure, the same patients required further surgical correction that was carried out in the frames of the international project. Clitoroplasty was performed preserving the glans and neuromuscular bundle while the skin was used for labial and introitoplasty (Fig. 2). Clitoroplasty was applied if the palpable corpora length would exceed 2.5 cm and was performed for 28 patients.

In Denmark all patients underwent clitoroplasty if needed and most of them had a one stage procedure combined with feminizing genitoplasty. The operative procedure in the frames of the international project was feminizing genitoplasty with clitoral reduction where needed. Mostly cut-back technique was applied for urogenital sinus exposing two separate openings of the vagina and the urethra (Fig. 3,4). In higher-level urethro-vaginal confluence urogenital mobilization or vaginal pull-through was used. Table 1 shows the distribution of our material according to the anatomical conditions.

Special attention was paid to postoperative vaginal dilatation. The dilatation was performed with metal Hegar dilators and each patient has followed an individual program. The older girls and the ones not feeling comfortable with metal tools were instructed

Fig. 1. Urogenital sinus: low (a), high (b)
C – clitoris; B – urinary bladder; ES – external sphincter; V – vagina; U – uterus; R – rectum
Results

The 47 patients with adrenogenital syndrome presented with a spectrum of variations in the degree of virilization. Surgically they required a differentiated management. The two main types of urogenital confluence are presented in Fig. 1. The procedures performed in our patients are listed in Table 2. In case of low urogenital sinus we would usually perform a simple cut-back procedure, in case of a high one – vaginal pull through or total urogenital mobilization.

Ten patients previously operated in Moscow in the frames of our project underwent 12 surgical procedures: 8 genitoplasties, 1 redo clitoroplasty, 1 urethroplasty, 1 was managed only with vaginal dilatation, and in 1 patient the vagina was not found.

Ten patients (previously not operated) did not need clitoroplasty since there was no obvious hypertrophy. Since the aim of this study was to evaluate close postoperative results and also for ethical reasons we did not investigate the clitoral sensitivity. At the postoperative examination in all cases there were no signs of clitoral atrophy.

Table 1. Level of urethro-vaginal confluence in patients with adrenogenital syndrome

<table>
<thead>
<tr>
<th>Confluence Level</th>
<th>Count</th>
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<tbody>
<tr>
<td>High confluence</td>
<td>6</td>
</tr>
<tr>
<td>Medium confluence</td>
<td>7</td>
</tr>
<tr>
<td>Low confluence</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
</tr>
</tbody>
</table>

Fig. 2. Clitoridectomy, preserving the glans and the neurovascular bundle (a, b) and removing the corpora cavernosa (c, d).
A – glans; B – corpora cavernosa; C – neurovascular bundle

how to perform the procedure with their own fingers increasing the size.

Fig. 3. Virilizing AGS, preoperative view

Fig. 4. Virilizing AGS, postoperative view
Operating on the introitus we have noticed that more or less pronounced scar tissue can be a problem at the site of the anastomosis. Therefore 7-14 days postoperatively we introduced the vaginal dilatation program. The program would be applied from 6 to 12 months depending on the hardness of the scar tissue and the width of the vagina itself. No fixed criteria could be applied to vaginal dilatation, such as for anal atresia. This might be due to the different plastic qualities of the tissues. An individual approach had to be used, with decreasing frequency of dilatations down to one time per month. For the last two or three months the vaginal width would stay the same, the dilatation would be done with the same caliber Hegar and would not be painful. Irreversible good results could be achieved with dilatations for an adequate time. Therefore we didn’t shorten the duration. Examination after the treatment showed good results, with satisfactory vaginal width.

Out of 43 patients 19 were operated before 3 years of age and 24 later. The results of surgical treatment are listed in table 3.

The results of genitoplasty using the same surgical approach in patients before and after 3 years of age are not equal. To confirm this hypothesis we applied the \(\chi^2\) criterion and found out that performing one-stage procedure before 3 years of age there were less complications such as vaginal stenosis or urethro-vaginal fistula and the number of surgical procedures was decreased (\(p<0.05\)).

The most common complications were vaginal stenosis (4 cases before the long-term dilatation scheme was introduced), urethro-vaginal fistula (2 cases) and in one case the vagina was not found. All mentioned complications were successfully repaired.

One patient still needs a second stage introitoplasty at puberty. She had a high pull through, with initially very narrow introitus and following dilatation problems. We also plan a perineal revision for the patient in whom the first attempt to search for the vagina was not successful, but who is having menses now via the urogenital sinus.

**Discussion**

The management of patients with genital anomalies is a complex problem, requiring an individual surgical approach depending on the anatomical conditions. The goals remain to be correction of visible anatomical anomalies, creating an appearance corresponding to the gender, and a function enabling the individual to lead a normal life, including sexual function and, if possible, reproduction. This also requires satisfaction of the individual. Many controversies about the management of genital anomalies circle around this problem.

Previously the genitoplasty was performed in 2 stages. Usually the clitoroplasty would be done first and in early childhood or later the vaginoplasty would follow. Recent reports have pointed out that a staged approach was marked by a high incidence of vaginal stenosis and the results improve with a one-stage procedure in early infancy (4,7,9,18). Depending on the anatomical conditions different techniques may be employed including cut-back, vaginal pull-through, possibly with Passerini-Glazel clitoral skin tube (17), and total urogenital mobilization, if needed using lateral skin flaps to augment the vaginal wall (10,12,15). The recommended age for a single stage procedure varies from the first 3-4 weeks of life to 12-24 months (8,9,19).

On the other hand Alizai et al claim that it is too soon to determine whether the encouraging early results of the newer techniques will be maintained through puberty (1) and Krege et al suggest that only patients graded Prader I-II° should undergo a single-

### Table 3. Clinical data revealing frequency of surgical treatment in two age groups while applying the same surgical methods.

<table>
<thead>
<tr>
<th>Age at surgery time</th>
<th>One operation</th>
<th>More than one operation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operated before 3 years</td>
<td>16</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Operated after 3 years</td>
<td>12</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>15</td>
<td>43</td>
</tr>
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</table>
stage procedure since the incidence of vaginal stenosis in different studies was reported up to 77% (13). Delayed vaginoplasty could also be recommended in case of difficult separation and limited exposure in small infants, again for fear of complications such as stricture, fistula and diverticulum formation (19).

While different authors were discussing various techniques of clitoroplasty (2,16) in 1997-1999 Diamond introduced a new attitude regarding clitoral surgery for intersex patients. He suggested that in fact there was no need for clitoral reduction at all because there was no documented proof that intersex patients would suffer from any hazards, psychological or otherwise, of having a large clitoris while the reduction procedure might cause complaints of pain or insensitivity (5,6). For the time being it is very difficult to verify any of the opposing statements because control studies (both psychological and surgical) based on statistical data are lacking.

Although the CAH patients may have various difficulties in social and physical adjustment, the favorable potential for their fertility is obvious (3,20). We find that CAH patients may benefit from early reconstructive surgery, resulting in a vaginal opening. The important point is the institution of a dilatation program. Considering the psychological peculiarities of teenagers we feel that small girls are less traumatized by prolonged postoperative dilatation. Only one of our patients experienced psychological difficulties accepting dilatation and the scheme was completed with satisfactory results.

A final judgment concerning late postoperative follow-up can be made when all patients have reached puberty. Then an estimate of the definitive need for late dilatation and/or introitoplasty can be performed.

Conclusions

Based on our experience with the present material of female genital anomalies we recommend:

1. Early one-stage reconstruction in adrenogenital syndrome (the plastic qualities of the tissue are better, there are fewer complications and there is a chance to avoid psychological problems and repeated surgery).

2. Removal of the clitoris must be considered as a damaging operation. Clitoral reduction, if necessary, should be performed with careful preservation of the neurovascular bundle and the glans. Technically it is easy to perform and it is the only way to preserve the clitoral sensitivity for the future.

3. Following procedures on the introitus in order to avoid vaginal stenosis and reduce the number of repeated surgical procedures a dilatation program should be applied for 6-12 months.

Our results are promising, but a definitive evaluation is not possible, because only few of the patients have reached puberty. This is a prospective study and the patients are going to be observed for several years.

| Adrenogenitalis sindromas: feminizuojanti genitalių plastika, pooperaciniai rezultatai |
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| **Indrė Zaparackaitė**, Vidmantas Barauskas, Ole Henrik Nielsen¹, Riitta Jokela¹ |
| Kauno medicinos universiteto Vaikų chirurgijos klinika, |
| ¹Kopenhagos universiteto ligoninės Vaikų chirurgijos klinika |

**Raktąžodžiai:** adrenogenitalinis sindromas, urogenitalinis sinusas, genitalių plastika.

**Santrauka.** Adrenogenitalinis sindromas, arba įgimta antinkščių hiperplazija, yra lemnimas genetiškai nulemtu fermento defektu, trikdančio kortizolo sintezę iš cholesterolio dėl fermento 21-hidroksilazės nepakankamumo. Dėl virilizuojančio androgenų poveikio mergaitėms atsiranda klitirio hipertrofija ir išlieka urogenitalinis sinusas (bendras šlaplės ir makšties kanalas). Šiems sklaidos trūkumams koreguoti reikalingas chirurginis gydymas. Šio darbo tikslas – pritaikyti šiuolaikinius chirurginius gydymo metodus klinikinėje praktikoje ir įvertinti gydymo rezultatus.

47 patientės, sergančios adrenogenitalinio sindromo, ištirtos ir gydytos dviejose centruose: Kopenhagos universiteto ligoninėje ir Kauno medicinos universiteto klinikose. 43 iš jų operuotos, joms daryta genitalių plastika. Operacini taktika buvo pasirenkama individualiai pagal urogenitalinio sinusu aukštį. Kai sinusas žemas, buvo atveriama jo užpakalinę silnės fiksuoju makštį prie odos. Aukštas sinusas buvo atidalytas nuo aplinkinių audinių ir makšties patraukta žemyn. Visoms operuotoms mergaitėms, praėjus 6–12 m. po operacijos, taikytas makšties dilatacijų programa. 28 patientėms atliktą klitirio plastika išsaugant jo galvutę bei neurovaskulinių


Rekomenduojama vienmomentė genitalijų plastika pacientėms iki trejų metų, po to taikant makšties dilatacijas ne trumpiau kaip 6–12 mėnesių.

References

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