Surgical aspects of ambiguous genitalia associated with congenital adrenal hyperplasia

Abdulraouf Y. Lamoshi and Bashir El-Gharmooll

Aim **The aim of the study was to review the current approach to manage ambiguous genitalia caused by CAH.**

Methods **This was a retrospective study of 30 patients with CAH and ambiguous genitalia treated over 10 years. Age at presentation, degree of verilization, preoperative diagnostic studies, operative technique, blood loss, outcome, and follow-up period were the studied variables.**

Results **The older 19 patients underwent single-stage feminizing genitoplasty and the younger 11 patients underwent a multiple-stage procedure. All patients had undergone clitoroplasty, clitoral recession, or resection. Postoperative complications documented in 23% of the patients included atrophy of the clitoris, flaps complication, and vaginal stenosis. The anatomic and cosmetic outcomes were considered good or satisfactory in 70% and 20% of cases, respectively, and poor in 10% of cases.**

Conclusion **One-stage or multiple-stage feminizing genitoplasty gives a high percentage of satisfactory cosmetic outcomes. TUM can be implemented to achieve excellent results for complex genitourinary anomalies.** ***Ann Pediatr Surg*** **11:226–230 © 2015 Annals of Pediatric Surgery.**

Annals of Pediatric Surgery 2015, **11**:226–230

Keywords: adrenal hyperplasia, congenital, genitoplasty, intersex

Department of Pediatric Surgery, Tripoli Medical Centre, Tripoli, Libya

Correspondence to Abdulraouf Y. Lamoshi, MBBCh, ABPS, MPH, MS CTS, Department of Pediatric Surgery, Tripoli Medical Centre, PO Box 7425, Tripoli, Libya
Tel: +218 92522 3706; fax: +218214625615; e-mail: raofdr@yahoo.com

Received 11 March 2015 **accepted** 27 August 2015

Introduction

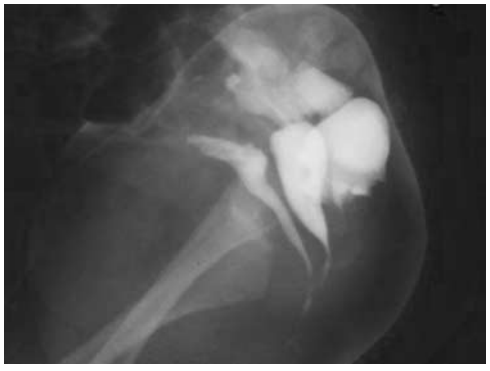
Congenital adrenal hyperplasia (CAH) is a leading cause of intersex in newborns, and the overall incidence worldwide is one in 14 000 live births [1]. The majority or three quarters of cases involve salt-losing metabolic disturbances [2]. In CAH, the urogenital sinus (UGS) is usually elongated and abnormally opens in the perineum, with an enlarged clitoris and labioscrotal folds fusion, which result in ambiguity of the genitalia; the urethra and vagina open into the UGS instead of having independent orifices on the perineum [3]. The main goal of surgical reconstruction is to allow for normal micturition by separating the genital and urinary tracts, reconstruction of sufficient vagina opening to the perineum, and achieving a near-normal appearance of external genitalia [4]. These goals can be achieved by reducing the size of the clitoris, which involves resection of corporal bodies, leaving the glans with the neurovascular bundle if the size is too large or performing clitoral recession if it is not large enough, reconstruction of labia minora from skin flaps of the phallic skin, and vaginoplasty using perineal skin flaps [5]. Reconstructive surgery used to involve multiple-stage procedures, but a single-stage procedure is feasible where clitoral reduction, vaginoplasty, and labioplasty are all performed in the same setting [5–7]. The timing of surgery is controversial; many surgeons prefer to perform corrective feminizing genitoplasty early, whereas others prefer to wait till the patient is old enough to provide consent for the procedure [7–9]. The purpose of this study is to review the outcome of our diagnostic and surgical approach of ambiguous genitalia, whether single-stage feminizing genitoplasty or a multiple-stage procedure, at various ages.

Patients and methods

Retrospectively, we studied the medical records of 30 patients with ambiguous genitalia because of CAH who were referred to the Department of Pediatric Surgery, Tripoli Medical Centre during the period from 1997 to 2007 for surgical reconstruction. The main investigations were chromosomal studies and serum electrolytes (high levels of potassium and low levels of serum sodium were considered salt-losing type). All patients underwent abdominal and pelvic ultrasound (U/S); a retrograde flush genitogram was performed by placing a Foley's catheter into the external orifice of UGS, followed by a water-soluble contrast injection under low pressure with the patient in the lateral position under fluoroscopy. This will determine the length of the UGS and the confluence of the urethra and vagina, and also enable measurement of the size of the vagina. Figure 1 shows the genitogram.

All patients underwent eua-pancysto-vaginoscopy to evaluate the length of UGS. UGS examination of the external genitalia was performed to determine the degree

Fig. 1



Genitogram showed the location of the urethra and vagina confluence and the urogenital sinus.

1687-4137 © 2015 Annals of Pediatric Surgery DOI: 10.1097/01.XPS.0000471678.25559.d5

Table 1 Age of the patients at the time of surgery

Age	Number of cases [*n* (%)]
<12 months	5 (16.66)
12–24 months	5 (16.66)
2–5 years	8 (26.66)
5–13 years	8 (26.66)
>16 years	4 (13.33)

of virilization. Mild virilization was described as partial labial fusion, UGS orifice between the labia majora, and slight clitoral enlargement; moderate virilization was described as full labial fusion, UGS orifice near the pubic end of the phallus, and moderate clitoral enlargement; and severe virilization was defined as full labial fusion. UGS opens close to or at the tip of phallus with a marked clitoral enlargement. Laparoscopy was performed in two cases.

Surgical techniques included one-stage genitoplasty or multiple-stage genitoplasty (clitoroplasty, vaginoplasty, and labioplasty). Intraoperative blood loss was assessed by counting the number of 4×4 blood-soaked gauzes with an average amount of 10 ml. The postoperative aesthetic and structural outcomes were evaluated on the basis of Creighton *et al.* [9] and Lean *et al.* [8] scores for genital proportion regularity, clitoral mass and location, vaginal introitus, and labial look. The aesthetic results were then categorized as good (standard genital appearance, not likely to be considered abnormal by a nonmedically qualified individual), satisfactory (one to two abnormalities unnoticed by a nonmedically qualified individual), or poor outcome (more than two abnormalities with abnormal-appearing genitalia) [8]. Approval was obtained from the Institutional Review Board (IRB) and permission was obtained from the patients to use their pictures, site of surgery, in this study.

Results

Thirty CAH patients underwent ambiguous genitalia surgical correction at Tripoli Medical Centre, Department of Pediatric Surgery, between 1997 and 2007. Demographically, the patients' ages ranged from infanthood to 29 years (Table 1), and all patients had 46XX chromosomal results. Eight patients (26.67%) were from the same geographical area. Mild virilization was detected in three patients (10%), 11 patients (36.67%) had moderate virilization, and 16 patients (53.33%) showed severe virilization. Metabolic assays showed that the majority of the patients were salt losers ($n = 21$, 70%) compared with nonsalt losers ($n = 9$, 30%). In terms of the enzymatic deficiency, the majority had 21-hydroxylase deficiency.

Accuracy of investigations: U/S could detect internal Müllerian structures in 70%; the sensitivity was 56.67% in neonates and young infants. In addition, retrograde genitography was 80% accurate in localizing the site of confluence of the urethra and vagina. Genitourinary cystoscopy–vaginoscopy was 100% accurate in locating the entry of the vagina into the UGS in this study. The imaging studies showed that the mean distance of vaginal insertion into the UGS was about 3 cm.

Surgical techniques included one-stage genitoplasty performed in 19 older patients and multiple-stage genitoplasty in 11 younger patients (clitoroplasty, vaginoplasty, and labioplasty). The dissection was technically easier in older children than small infants except for blood loss, which was more in older patients (average of 8.5 vs. 6.2 ml/kg). The mean operative time was 200 min, range 120–280 (170 min in the older group vs. 235 min in the younger group). None of the patients needed blood transfusion and the mean length of hospital stay was 7 days (5–9 days). The urination pattern did not change in any of old children (> 4 years), whereas it was difficult to assess urinary incontinence in younger children (< 4 years). One patient got married and had a child.

The rate of postoperative complications was 23.33% (seven patients) and included atrophy of the clitoris ($n = 2$, 6.67%), flaps complication (labia minora ischemia)

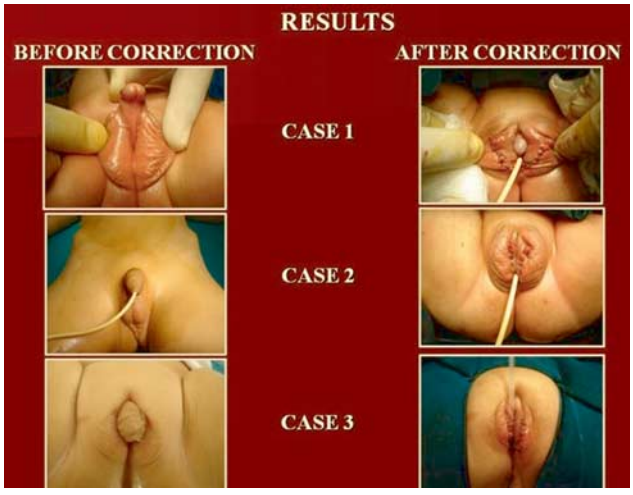
Table 2 Rate of postoperative complications and comments

Complications	Number of cases [*n* (%)]	Comments
Clitoral atrophy	2 (6.67)	Because of ischemia
Flap complications	2 (6.67)	Treated with flap refashioning
Vaginal stenosis	3 (10)	Responded to 2–3 dilatation sessions

Table 3 Overall cosmetic satisfaction results after the surgical correction

Overall cosmetic and anatomic results	Number of cases [*n* (%)]
Good	21 (70)
Satisfactory	6 (20)
Poor	3 (10)

Fig. 2



Preoperative and immediate postoperative external genitalia appearance.

Fig. 3

Preoperative and long-term postoperative external genitalia appearance.

($n = 2$, 6.67%), and vaginal stenosis ($n = 3$, 10%). The complication rate was 15.79% (three out of 19) in the older group and 36.36% in the younger group (four out of 11). The outcomes were considered good or satisfactory in 70 and 20% of cases, respectively, and poor in 10% of cases, where further reconstructive surgery will be required. Vaginal stenosis was the most reported complication in 10% ($n = 3$) of the patients who responded to repeated dilatation (Table 2).

The aesthetic and structural results were categorized as good or satisfactory in 90% of our patients (Table 3). Figures 2 and 3 show the preoperative and immediate and long-term postoperative external appearance, respectively. The case 1 picture is of less than one year old patient; the other pictures are of older patients (Figs 2 and 3).

Discussion

Numerous techniques have been reported for feminizing genitoplasty during the last few years [10–12]. A cut-back of the UGS combined with a Fortunoff inverted U-shaped perineal flap is used in cases when the urethra and the vagina share low confluence [13]. This technique is not always feasible; thus, use of the total UGS mobilization (TUM) technique, in higher confluence cases, is more appropriate where the vagina enters the UGS proximal to the external urethral sphincter [14]. The main concept of TUM involves mobilization of both the vagina and the urethra together into the vestibule [14]. This approach was reported by Levitt and Peña for intermediate-length cloaca to avoid cut-back damage to the sphincter [14]. Leslie and colleagues [15,16] reported the feasibility of performing this procedure in patients with nonanorectal malformation using a perineal approach, but they did not adopt the mobilization of UGS and fashioned an independent urethral meatus and vaginal orifice.

The proximity of the urethra to the vagina and UGS confluence is important [7]. It is generally believed that there is a correlation between the severity of virilization and the proximal migration of the vagina and the UGS confluence [4]. Jenak *et al.* [4] applied TUM technique only to reconstruct the urethra using the UGS in cases of very short urethra; in these cases damaging the sphincter is imminent and incontinence is expected (4). They also used skin flaps to form the vagina (4). However, other investigators showed that there is a change in the distance between the vaginal opening into the urethra in respect to the bladder neck irrespective of the severity of virilization [17]. In this study, we found that the TUM technique was very beneficial in severely virilized patients with expected short urethral length proximal to the confluence. We noted that the Kogan technique of clitoral reduction is a safe technique because it ensures the preservation of blood supply to the glans [18].

A planned single-stage procedure seems to yield a better result than a multistage genital procedure, with an expected 86% likelihood of achieving good cosmetic results [8]. The appropriate time for surgery is a controversial topic; most investigators suggest that the intervention should be performed early: from very early childhood till the age of 3 years [19]. The advantages of early correction are: good compliance with dilatation, parents comfort regarding the gender of their baby, and the hypothesis that the patient will not recall the surgery later in life [20]. In addition, early correction results in a low risk of genitourinary tract infection [4] and is a technically more feasible procedure during early life [21]. Lobe *et al.* reported better results in patients diagnosed and operated on during infancy [22]. Passerini-Glazel [19] reported that surgery is feasible during the first 2 months of life; however, secondary surgery might be needed later in life. In the current cohort, the technique was much easier in children older than 1 year of age compared with smaller children as evident from the shorter operative time. Moreover, the multiple-stage approach was used in our center because of the various types of anomalies across a vast range of ages (from a few weeks to adulthood). With increasing experience, we found that the single-stage approach in older children can be technically practical because tissue handling becomes easier, which is not the case for infants with delicate tissues. Furthermore, frequent surgical intervention may lead to extensive fibrosis and scarring. The other reason was the length of the UGS from the outside opening to the confluence; if it is shorter than 3 cm, one stage with flap vaginoplasty can be used, but if the confluence is near the bladder neck, the senior author prefers a multiple-staged procedure.

The potential psychological advantage of surgical correction during early childhood should be balanced with the expected need for revision later in life. In patients with abnormal-appearing genitalia, including CAH ones, early surgical correction is more beneficial than avoiding frequent dilatation later in life [19]. Delaying the definitive procedure until puberty, in particular when virilization is accompanied by a high or an intermediate vagina, is preferred by other surgeons, who report the availability of blood supply and more robust genital skin in adolescents and adults than in infants [23]. Also, vaginal dilatation, if needed, is more likely to be successful when performed regularly by motivated young women than when imposed on an incomprehensive

child [23]. In this study, we noted that the vagina was easy to handle and not thin and fragile in children older than 1 year. Similarly, postoperative regular vaginal dilation was not mandatory in every patient, especially premarital late presentation.

The late results of feminizing genitoplasty have been systematically documented in the literature [24–27]. Vaginal narrowing is the most prevalent postoperative result, which is reported in up to 78% of patients [28]. Extrinsic and intrinsic factors could play a role in vaginal stenosis. Extrinsic factors include inappropriate preparation of the anatomical field, whereas intrinsic factors mainly involve a deficient orifice or removal of the exterior fibrotic and dysplastic vaginal segment [19]. In our series, vaginal stenosis was noted only in 10% (3/30) of the patients who responded to repeated dilatation. To minimize the frequency of postoperative vaginal stenosis, Passerini-Glazel [19] and Rink and Kaefer [24] advocated deep incision of the narrow exterior segment of the vagina to reach the spacious vaginal part. A perineal reversed U-shaped Fortunoff flap is utilized to join the vaginal cavity with the perineum [21]. A number of recommendations suggest if vaginal stenosis develops, then a vaginal dilatation or surgery redo should be delayed to puberty [19,24]. This because we can benefit from the hormonal incentive and to reduce the risk of the psychological trauma due to multiple surgeries [19,24]. The two cases of complete clitoral atrophy in our series occurred after free isolation of the neurovascular bundle to the glans. Although clitoral atrophy was managed conservatively, the flap complications, labia minor ischemia, were treated by flap refashioning once and yielded good results.

Creating a normal appearance for the external genitalia is the most important aim of performing genitoplasty during early childhood, which allows the children to mature normally [21]. For this reason, evaluation of the aesthetic result is very essential for both the patients and the family. In this study, the aesthetic and structural results were categorized as good or satisfactory for 90% of our patients. Analogous to our outcome, in a group of 27 females who underwent a one-stage feminizing genitoplasty, Miranda *et al.* [21] reported outstanding cosmetic results in 63% of the patients, acceptable results in 18.5%, and unacceptable results in 18.5%. Similarly, in a cohort of 16 patients in whom the single-stage approach was used, redo surgery was required in only one patient [8]. However, another study found that personal judgment showed that 41% of the patients achieved poor aesthetic results, and in the vast majority of patients undergoing one-stage genitoplasty, an additional major corrective procedure was needed [9]. In this study, only two patients required labial refashioning as a treatment for the flap ischemia, and further interventions are unlikely; however, longer follow-up is essential.

In terms of the investigations, abdominal U/S was reported to have 100% sensitivity and specificity in the identification of female internal organs, but depends on the operators [22]. U/S also shows the ability to precisely delineate the gross structure of the vagina and UGS in more than 90% of patients [22]. In our study, the accuracy of U/S in the detection of internal Müllerian structures was only 70% and the sensitivity was lower in neonates and young infants; this could have been as result of the ultrasonographer's skills and/or the features of ultrasonography equipment [22]. In addition, retrograde genitography had 80% sensitivity in localizing the site of confluence of the urethra and the vagina. Genitourinary cystoscopy–vaginoscopy was the most accurate method to locate the entry of the vagina into the UGS in this study.

Unique characteristics

The prevalence of ambiguous genitalia was higher in certain areas in Libya; consanguinity could be the reason for the more than 10-fold higher international rate as we encountered eight cases from a particular area in the mountain with a population of 6000–7000 individuals. In patients who were older than 16 years, easy dissection was possible, but high blood loss occurred, which can be explained by the hormonal effect on the external genitalia, where the size increases with the blood supply to that area. Also, we could not conceal the phallus under the pubic arch for the same group of patients; therefore, we performed resection instead of recession. Our cohort was not in compliance with the medical treatment, which led to hypertrophied phallus and altered the external appearance of the genitalia. Our surgical technique was the same as the standard technique. In our community, this sort of surgery is very embarrassing to the patients and their parents. We noted that genitoplasty, as a one-stage operation during early infancy, was highly favored by the parents.

Conclusion

One-stage and multiple-stage genitoplasties are feasible techniques that can yield remarkable functional and cosmetic outcomes. Although the one-step approach was more suitable for older children, younger kids can also benefit from the psycho-social and less blood loss advantages of the one-step approach. Therefore, the type and time of the procedure should be tailored on the basis of the surgeon's and family's decision, considering the pros and cons of each choice. Long-term check-up is essential to evaluate the functional and psychological impacts of this procedure. TUM is a promising technique that can be used to achieve excellent results for complex genitourinary anomalies.

Acknowledgements

The authors thank all pediatric surgery and pediatric endocrinology staff who participated in this work, especially Professor Suliman Abusrewil, Professor Milad Dogga, Dr Ibtesam Hadid, and Dr Nadia Gazhere.

Conflicts of interest

There are no conflicts of interest.

References

1 Sax L. How common is intersex? A response to Anne Fausto-Sterling. *J Sex Res* 2002; **39**:174–178.
2 Merke D, Bornstein S. Congenital adrenal hyperplasia. *Lancet* 2005; **365**:2125–2136.
3 Braga LH, PS JL. Congenital adrenal hyperplasia. *Eur J Pediatr Surg* 2009; **19**:203 –210.

4 Jenak R, Ludwikowski B, Gonzalez R. Total urogenital sinus mobilization: a modified perineal approach for feminizing genitoplasty and urogenital sinus repair. *J Urol* 2001; **165** (Pt 2):2347–2349.
5 Yankovic F, Cherian A, Steven L, Mathur A, Cuckow P. Current practice in feminizing surgery for congenital adrenal hyperplasia; a specialist survey. *J Pediatr Urol* 2013; **9** (Pt B):1103–1107.
6 Gosalbez R, Castellan M, Ibrahim E, DiSandro M, Labbie A. New concepts in feminizing genitoplasty – is the Fortunoff flap obsolete? *J Urol* 2005; **174**:2350–2353. discussion 2353.
7 Miranda ML, Oliveira-Filho AG, Lemos-Marini SH, Guerra G Jr, Bustorff-Silva JM. Labioscrotal island flap in feminizing genitoplasty. *J Pediatr Surg* 2004; **39**:1030–1033.
8 Lean WL, Deshpande A, Hutson J, Grover SR. Cosmetic and anatomic outcomes after feminizing surgery for ambiguous genitalia. *J Pediatr Surg* 2005; **40**:1856–1860.
9 Creighton SM, Minto CL, Steele SJ. Objective cosmetic and anatomical outcomes at adolescence of feminizing surgery for ambiguous genitalia done in childhood. *Lancet* 2001; **358**:124–125.
10 Monstrey S, Blondeel P, Van Landuyt K, Verpaele A, Tonnard P, Matton G. The versatility of the pudendal thigh fasciocutaneous flap used as an island flap. *Plast Reconstr Surg* 2001; **107**:719–725.
11 Rink RC. Total urogenital mobilization (TUM). *Dial Pediatr Urol* 2000; **23**: 2–4.
12 Hamza AF, Soliman HA, Abdel Hay SA, Kabesh AA, Elbehery MM. Total urogenital sinus mobilization in the repair of cloacal anomalies and congenital adrenal hyperplasia. *J Pediatr Surg* 2001; **36**:1656–1658.
13 Nordenskjold A, Holmdahl G, Frisén L, Falhammar H, Filipsson H, Thorén M, *et al*. Type of mutation and surgical procedure affect long-term quality of life for women with congenital adrenal hyperplasia. *J Clin Endocrinol Metab* 2008; **93**:380–386.
14 Levitt MA, Peña A. Cloacal malformations: lessons learned from 490 cases. *Semin Pediatr Surg* 2010; **19**:128–138.
15 Leslie JA, Cain MP, Rink RC. Feminizing genital reconstruction in congenital adrenal hyperplasia. *Indian J Urol* 2009; **25**:17–26.
16 Vidal I, Gorduza DB, Haraux E, Gay C, Chatelain P, Marc Nicolino M, *et al*. Surgical options in disorders of sex development (dsd) with ambiguous genitalia Research agenda. *Best Pract Res Clin Endocrinol Metab* 2010; **24**:311–324.
17 Ganesan A, Smith GHH, Broome K, Steinberg A. Congenital adrenal hyperplasia: preliminary observation of the urethra in 9 cases. *J Urol* 2002; **167**:275–279.
18 Farkas A, Chertin B. Feminizing genitoplasty in patients with 46XX congenital adrenal hyperplasia. *J Pediatr Endocrinol Metab* 2001; **14**:713–722.
19 Passerini-Glazel G. Editorial: feminizing genitoplasty. *J Urol* 1999; **161**:1592–1593.
20 Graziano K, Teitelbaum DH, Hirschl RB, Coran AG. Vaginal reconstruction for ambigous genitalia and congenital absence of the vagina: a 27-ayear experience. *J Pediatr Surg* 2002; **37**:955–960.
21 Miranda ML, Oliveira Filho AG, Lemos-Marini SH, Bustorff-Silva JM, Guerra-Júnior G. Feminizing genitoplasty and congenital adrenal hyperplasia: analysis of anatomical results. *Arq Bras Endocrinol Metabol* 2005; **49**: 138–144.
22 Lobe TE, Woodall DL, Richards GE, *et al*. The complications of surgery for intersex: changing patterns over two decades. *J Pediatr Surg* 1987; **22**:651–652.
23 Alizai NK, Thomas DFM, Lilford RJ. Feminizing genitoplasty for CAH: what happens at puberty? *J Urol* 1999; **161**:1588–1591.
24 Rink RC, Kaefer M. Surgical management of intersexuality, cloacal malformation and other abnormalities of the genitalia in girls. In: Walsh P, Retik A, Vaughan E, *et al*, editors. *Campbell's urology*. Philadelphia: Saunders; 2002. pp. 2428–2467.
25 Al-Bassam A, Gado A. Feminizing genital reconstruction: experience with 52 cases of ambiguous genitalia. *Eur J Pediatr Surg* 2004; **14**:172–178.
26 Warne G, Grover S, Hutson J, Sinclair A, Metcalfe S, Northam E, *et al*. Long-term outcome study oo intersex conditions. *J Pediatr Endocrinol Metab* 2005; **18**:555–567.
27 Bocciardi A, Lesma A, Montorsi F, Rigatti P. Passerini-glazel feminizing genitoplasty: a long-term followup study. *J Urol* 2005; **174**:284–288. discussion 288.
28 Akbiyik F, Tiryaki T, Şenel E, Mambet E, Livanelioğlu Z, Atayurt H. Feminizing genitoplasty: an evaluation of 41 patients in 8 years. *Turk J Med Sci* 2010; **40**:813–818.