Chapter 20
Disorders of Sex Development (DSD) and Laparoscopy

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Abstract DSD represents a spectrum of disorders. In the most common variant 46 xx DSD, laparoscopy is rarely if ever indicated. However, in other diagnoses, laparoscopy may be performed both for diagnostic and therapeutic indications. These include ovotesticular DSD, presence of a gonad with malignant potential, and the persistence of Mullerian structures, and in those with complex morphological abnormalities. Complications are those that are generally associated with any open laparoscopic procedure of the abdomen and pelvis but with the potential for damage to the gonads and internal genital tracts. Proper patient selection is important in order to minimize the risk of complication.

Keywords Intersex • Disorders of sexual development • Malignant • Gonads • Dysgenetic

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Table 20.1 Insufficient virilization

1. Genetic male 46XY with defect androgen synthesis and/or action
2. Biosynthetic defects
3. Androgen resistance (mutation in androgen receptor and/or transport)
4. Gonadal differentiation defects (i.e., streak gonads or dysplastic testes, mixed development chromosomal defects with gonadal asymmetry):
(a) Mixed chromosome DSD with mixed gonadal dysgenesis (45XY/45XO)
(b) Ovotesticular DSD 46XY, 46XX

Significant intersex anomalies occur in up to 1 in 5,000 live born infants. These anomalies are caused by the following factors [1, 2]:

1. Anomalies predictable by endocrine principles and these include defects in:
   (a) Genetic sexual determination
   (b) Gonadal differentiation
   (c) Hormonal production and action
2. Anomalies not predictable by endocrine principles:
   (a) Morphological disorders of the perineum

A child's gender is decided by its endocrine status, its morphological status including the possibility of fertility, and the prognosis for sexual function. In addition, the child's mental status and the likely gender behavior must be considered. These decisions are complex, individualized, and changing constantly with social expectations. Laparoscopy may have a role in aiding diagnosis in areas of insufficient virilization or mixed development (see Table 20.1).

Indications

Laparoscopy has a role in DSD in several areas. In the initial assessment period, it may significantly aid diagnosis by determining the internal genital structures and gonadal type. This may ultimately influence the decision of gender assignment and the prognosis given to the parents regarding fertility. Laparoscopy is also used for surgical resection of internal structures, including Mullerian remnants, utriculi, and incompletely virilized structures. It is also useful for assessment and management of the gonad, in particular the removal of streak gonads or dysgenetic intra-abdominal ovotestes [3, 4].

Many straightforward DSD do not require laparoscopy. These include complete androgen insensitivity, congenital adrenal hyperplasia, and some partial androgen insensitivities. These conditions are easily evaluated by thorough endocrine and radiological workup and rarely require surgical intervention.

The indications can be summarized as follows [5]:

1. Laparoscopy may often have a role in ovotesticular DSD, where the external genitalia are asymmetrical. Of these patients, 20 % have specific lateral disease with a testis generally present on the right-hand side and the ovary on the left. In up to 30 % of cases, the disease has bilateral ovotestes. The remaining 50 % of patients have unilateral disease with a solitary ovotestis and a normal ovary or a testis on the contralateral side. Ovotesticular DSD often requires accurate gonadal assessment and biopsy.
2. Laparoscopy also aids in removing highly potentially malignant gonads. In mixed chromosomal DSD with mixed gonadal dysgenesis, 25 % of testes with a Y cell line will have evidence of carcinoma in situ. Half of the carcinoma in situ gonads will go on to develop a complete germ cell tumor. Laparoscopy is often worthwhile in the removal of these gonads.
3. Multiple conditions can result in persistence of Mullerian duct remnants, and enlarged utriculi are often found behind the bladder associated with severe hypospadias. Small utricular remnants are often asymptomatic and do not require any surgical treatment. Some of these young males ultimately develop recurrent utriculus infections that are worse following hypospadias repair. In these patients, laparoscopic resection of the utriculus is indicated.
4. Finally, children with complex morphological development anomalies exhibit abnormal perinea, bifid or rudimentary uteri, and dysplastic gonads. Ultrasound and MRI imaging is often unreliable in this group. Evaluation of the pelvic structures is often best achieved with laparoscopy. Preoperative patient preparation with infants with DSD requires a multidisciplinary team that includes geneticists, endocrinologists, counselors, pediatric urologists, and pediatric surgeons. A baby born with an indetermined sex is best transferred urgently to a center with appropriate expertise, so that life-threatening conditions can be excluded and laparoscopy only performed if deemed appropriate.

Preoperative Investigations

Standard preoperative investigations of a child with an indeterminate DSD include a thorough clinical assessment, ultrasonography of the perineum and pelvis, and contrast study of urogenital sinuses. Karyotyping and a comprehensive endocrine evaluation are done, including adrenal sex steroid concentrations and a hormone-binding globulin test for androgen sensitivity. Molecular genetic analysis is used to look at the androgen receptor gene and the 5-alpha reductase gene. Many of these investigations can be completed in a 48-h neonatal period, and laparoscopy is rarely required. There are several infants where the diagnosis and internal assessment still remains in doubt and the picture is mixed. In this case, laparoscopic evaluation of the pelvic contents and gonadal biopsy is indicated in the neonatal period.

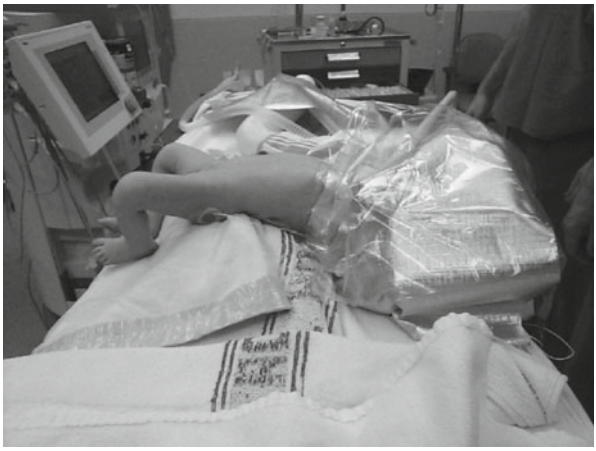

Fig. 20.1 Patient position for neonatal DSD case

Operative Technique

Procedure 1: Evaluation of Pelvic Structures for Indeterminant Gender in the Neonate

The patient is placed transversely on the operating table with the surgeons standing at the child's head and a small towel placed under the buttock to elevate the pelvis and expose the external genitalia (Figs. 20.1 and 20.2). A urethroscopy/cystoscopy/vaginoscopy is often performed prior to the laparoscopy. A 3 or 5 mm port is placed in the supra-umbilical region via an open technique. This gives an appropriate operating angle and allows adequate insufflation. The pelvis is insufflated and the intestines displaced cranially so that a clear view can be obtained. A spinal needle is introduced through the left iliac fossa under direct vision. This blunted needle is very useful for manipulation of organ structures in the neonate and allows excellent visualization. Very rarely is a second port actually required. The spinal needle is used to trace out any uterine or Mullerian structures and identify the gonads. Biopsies are rarely required at this stage but can be achieved by either directly introducing a 3 mm biopsy forceps or a Tru-Cut biopsy needle. All ligamentous and/or vasal structures are traced into the inguinal area. Any open internal inguinal ring must be explored. A gonad is often located within the inguinal canal and can be reduced into the abdomen by concomitant pressure on the groin. Each gonad in turn must be examined completely for elements of ovotestis. A full media recording should be made of the whole procedure to allow peer review and subsequent opinion over the next few days. Accurate assessment of a neonatal uterus, associated tubes, and gonads is easily undertaken by this technique.

Procedure 2: Laparoscopic Gonadal Excision

This is generally accomplished via a three-port approach with an umbilical optic port (5 mm) and two working ports (Fig. 20.3). Streak gonads are relatively easily

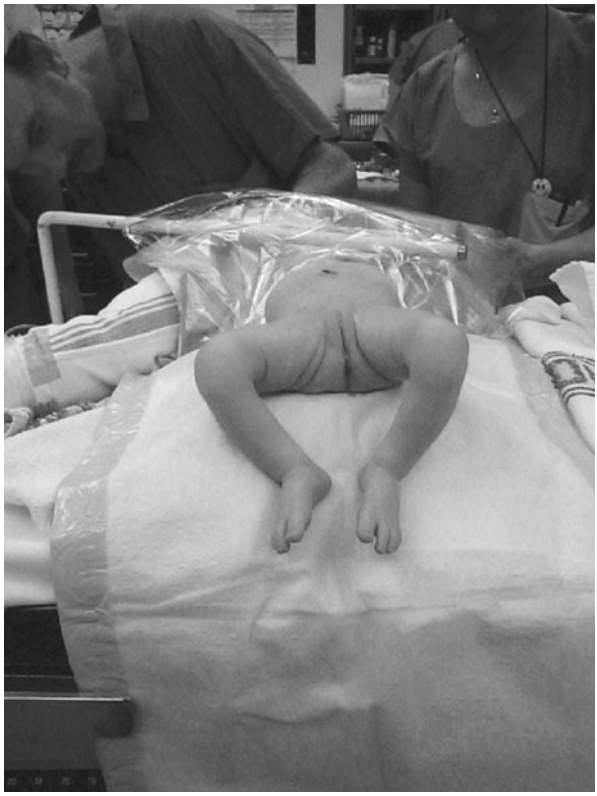

Fig. 20.2 Surgeon position for neonatal laparoscopy

identified and are best removed by preserving the fallopian tube for use in assisted reproductive techniques in the future. Simple hook diathermy or ultrasonic dissection is required to remove streak gonads. Intra-abdominal testes are easily removed in a similar fashion.

Procedure 3: Removal of Persistent Mullerian Duct Structures

An initial cystoscopy and placement of a urethral catheter with or without a ureteric catheter in the remnant is performed. A similar three-port orientation is used, but a single bladder hitch stitch is placed in the posterior bladder wall to elevate the pelvic structures. This stitch is held externally with mosquito forceps. The peritoneal reflection is opened, and midline blunt dissection occurs until a utriculus is encountered and traction on this structure allows continued dissection down into the area of the prostate.

When the utriculus enters the prostate, significant thickening of tissue occurs with some bleeding. The distal utriculus is either endolooped or suture ligated. Direct sealing with ultrasonic dissectors is not recommended. A urethral catheter is required during the procedure to avoid any inadvertent urethral tightening. Many of these procedures on children are day case procedures. I generally leave a urethral catheter in for 3–4 days, but this is not essential.

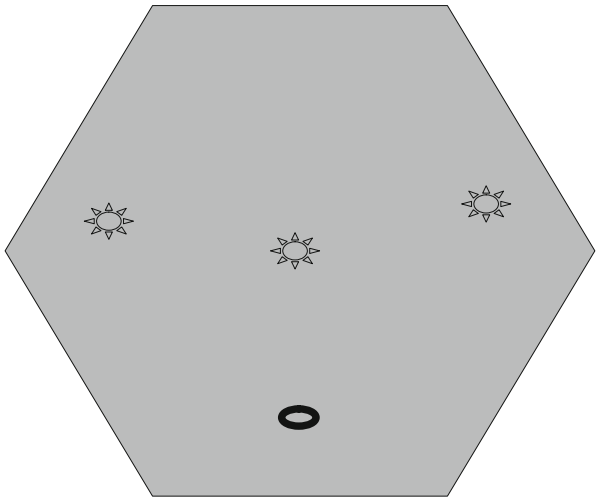

Fig. 20.3 Standard laparoscopic DSD position with three 5 mm ports and hitch stitch

Complications

Most of the techniques in laparoscopy for DSD are simple and straightforward. The major difficulties occur in the clinical decision making, particularly in mixed phenotypes such as mixed gonadal dysgenesis or ovotestis. Many errors can be made in the visual inspection of the indeterminant gonad. A thorough examination of each gonad is required. Ovarian tissue can often appear to be deperitonealized (or detunicalized) within a testes. Incomplete excision can result in inappropriate hormone production and subsequent long-term risk of malignancy.

Poor positioning of the endoloop or suture ligature on the utriculus can result in urethral stricture (too tight) or a recurrent utriculus (inadequate dissection). This can result in recurrent pelvic sepsis and subsequent frozen pelvis. Optimal care must be taken to ensure that dissection has been adequate and the clipped ligature has been placed close to the urethra without excessively tightening this structure.

Conclusion

Laparoscopy has a major role to play in many DSD. It may be useful in determining the sex of rearing and providing some prognostic indicators for fertility. The neonatal laparoscopy is reserved for accurate assessment in the rare and complex anomaly. Removal of gonadal tissue and Mullerian remnants are reasonably straightforward procedures. Careful case selection and close team coordination with the intersex team will minimize major complications and ensure appropriate case selection.

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