Hypospadias

14

(Glanular Hypospadias, Proximal Hypospadias, 5α Reductase Deficiency, Midshaft Hypospadias, Megameatus Intact Prepuce, Failed Hypospadias Repair)

Felicitas López Imizcoz, Elías Ramírez Velázquez, and Imran Mushtaq

Learning Objectives

- Practical aspects of diagnosis and classification of hypospadias subtypes
- To review the evidence base for preoperative hormone treatments and potential indications
- To describe the surgical decision-making based on published outcomes
- To illustrate the challenges with DSD patients and to emphasize the importance of a multidisciplinary approach
- To discuss possible treatment options in failed hypospadias repair

14.1 Glanular Hypospadias

A 6 months old boy is referred to the urology clinic by the GP for distal hypospadias (Fig. 14.1).

1. *a. How is hypospadias classified?*
   b. What type of distal hypospadias does this baby have?
2. *What is the incidence of this condition?*
3. *What is the differential diagnosis?*
4. *Do all distal hypospadias need surgical correction?*
5. *What are the surgical options?*

F. L. Imizcoz
Hospital de Pediatría Prof. Dr. Juan P. Garrahan, Buenos Aires, Argentina

E. R. Velázquez
Hospital Star Médica HIP, México City, CDMX, Mexico

I. Mushtaq (✉)
Great Ormond Street Hospital, London, UK
e-mail: imran.mushtaq@gosh.nhs.uk

P. Godbole et al. (eds.), *Practical Pediatric Urology*,
https://doi.org/10.1007/978-3-030-54020-3_14

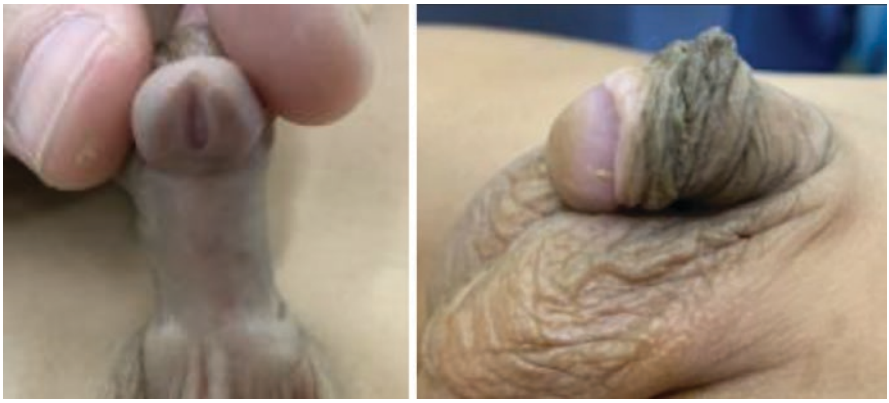

Fig. 14.1 Glanular hypospadias

1. *a.* The common classification system divides hypospadias in three different groups according to meatus position: distal-anterior hypospadias (located on the glans or distal shaft of the penis), intermediate-middle hypospadias (penile) and proximal-posterior (penoscrotal, scrotal and perineal) [1]. However, after skin release during surgery, the pathology might be different and a reclassification may need to be done. The position of the meatus alone is therefore not a reliable indicator of hypospadias severity as far as the choice of an appropriate surgical procedure is concerned [1, 2]. Several aspects should be considered such as: level of division of the corpus spongiosum, the degree of hypoplasia of the tissues forming the ventral surface, degree of curvature, urethral plate quality, penile size, glans size and shape and preputial skin availability [2]. The EUA Guidelines (2018) on Pediatric Urology suggest an alternative classification based on severity of the problem: mild hypospadias (glanular or penile isolated hypospadias without associated chordee, micropenis or scrotal anomaly); and severe hypospadias (penoscrotal, perineal hypospadias with associated chordee and scrotal anomalies) [1].
   b. This baby has a glanular hypospadias. Clinical examination alone is sufficient for the diagnosis. The clinical findings include:
   - Glanular meatus, above and distal to the coronal sulcus.
   - Good glans size and groove.
   - Hooded foreskin, deficient ventrally.
   - No curvature (chordee).
   - Both testes fully descended.
2. In newborn males, hypospadias is the second most common congenital anomaly after undescended testis [3]. Over the last 25 years, a significant increase in the incidence of hypospadias has been found which may simply reflect a more frequent or early diagnosis of minor forms of hypospadias over time, or an increasing tendency to report them to congenital-anomaly registries [4]. According to

the last EUROCAT registry-based study (from 2001 to 2010) the total prevalence of hypospadias in Europe is 18.6 new cases out of 10,000 births (5.1–36.8). The mean worldwide prevalence varies from 34.2 in North America, 5.2 in South America, 0.6–69 in Asia, 5.9 in Africa and 17.1–34.8 in Australia [1].

3. The differential diagnosis includes other forms of distal hypospadias. This is the most common type and represent 65% of all cases of hypospadias [1, 5]. They include four distinct forms: glanular 15%, coronal 50%, sub coronal 30% (distal shaft of the penis) and a fourth type mega meatus with intact prepuce (MIP) which represents 5% [5, 6].
4. The primary goal of hypospadias repair is to achieve both cosmetic and functional normality [7]. In theory therefore, penile curvature must be corrected and a neo-urethra of an adequate size with opening on the tip of the glans formed, with adequate skin coverage of the penile shaft [8]. Ironically, the very distal forms of hypospadias, are sometimes the most challenging in terms of the decision-making process, because cosmesis is often the only real indication for surgery [7]. Meatal stenosis, a ventrally deflected urine stream and parent preference are the most usual indications for surgical correction of glanular hypospadias. Increasing dissatisfaction with urethroplasty techniques, such as the Snodgrass repair, have led to many surgeons preferring more minimal procedures (circumcision, chordee correction, meatoplasty) that have minimal complications but an equal patient and parent satisfaction.

   According to a survey conducted by the European association of urology including pediatric urologists, pediatric surgeons, urologists, and plastic surgeons in 68 countries, 78% opted for a surgical management on distal hypospadias and only 12% for non-surgical approach [9]. Although the majority of pediatric urologists choose a surgical correction for distal hypospadias, conservative management is still a valid option considering there is not always functional compromise in these group of patients. Parents should be fully informed about all the different management options.
5. For children with glanular hypospadias, the need for surgery and the surgical technique to be used remain controversial. Techniques described include meatal advancement and glanuloplasty (MAGPI) [9], meatal mobilization and glanuloplasty (MMGPI) [5], glanular approximation procedure (GAP) [6], a simple modified circumcision and meatoplasty, tubularized incised plate procedure (TIP) and Mathieu flap technique. Case selection is a crucial factor influencing the complication rate. For example, the MAGPI technique is one of the most common operation for glanular and coronal hypospadias repair. Ventral glanular tilt, meatal retraction (seen in up to 22%) [10] and splaying of the urinary stream can result from performing a MAGPI in a patient with non-compliant urethra with deep grooved glans [8]. Whatever technique is used, one should expect a predictable outcome with complication rates below 10% in distal hypospadias (fistula, meatal stenosis, dehiscence, recurrent ventral curvature, and haematoma) [1].

14.2 Proximal Hypospadias

A male infant is born at 33 weeks' gestation (IVF twin pregnancy). He attends the clinic at the age of 3 months because his parents are concerned that he urinates from the base of a small penis. Both testes are palpable on the scrotum (Fig. 14.2).

1. *What is the most likely diagnosis?*
2. *What other clinical features are mandatory to examine in a boy with this diagnosis?*
3. *What are the risk factors for this condition?*
4. *Is hormone therapy recommended in this case?*
5. *What are the surgical options for this condition?*

1. The most likely diagnosis is proximal-posterior penoscrotal hypospadias.
2. The diagnostic evaluation, apart from the hypospadias clinical features, includes an assessment of associated anomalies, which are:
   - cryptorchidism (in up to 10% of cases of hypospadias);
   - patent processus vaginalis or inguinal hernia (in 9–15%) [1].

   Severe hypospadias with unilaterally or bilaterally impalpable testes, or with ambiguous genitalia, requires a complete genetic and endocrine work-up immediately after birth to exclude a disorder of sex development (DSD), especially congenital adrenal hyperplasia [1].
1. Risk factors associated with hypospadias can be genetic, placental and/or environmental (Level of Evidence: 2b) [1, 11]. In the case of this infant, prematurity, low weight at birth together with in vitro fertilization (IVF) would be identified

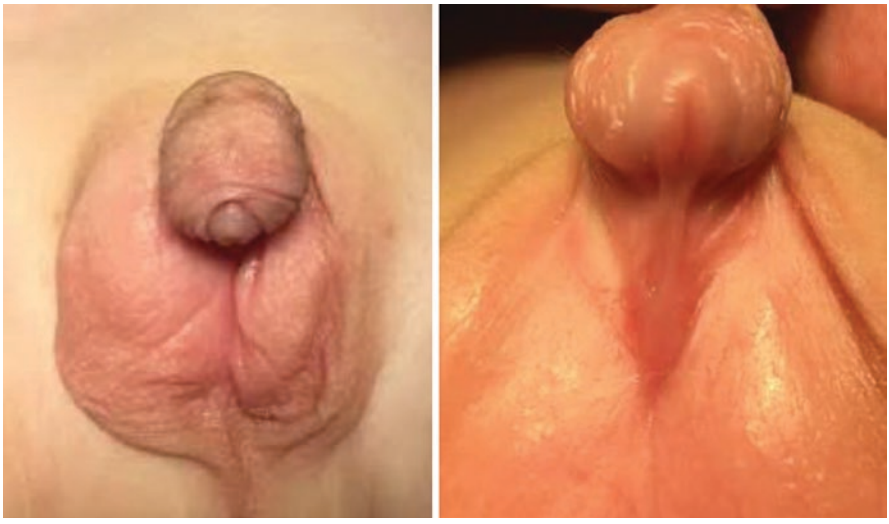

Fig. 14.2 Proximal-posterior hypospadias

as risk factors to his condition. IVF is associated to a five-fold increased risk of hypospadias, which may be related to maternal progesterone administration [12]. Parents should be counseled about this risk as well as the possibility that 7% of other family members may also be affected [1]. Interactions between genetic and environmental factors may help explain non-replication in genetic studies of hypospadias. The use of oral contraceptives prior to pregnancy has not been associated with an increased risk of hypospadias in offspring, but their use after conception increases the risk of middle and posterior hypospadias [1].

2. Pre-operative hormonal treatment may be recommended in this case due to small penile and glans size. Therapy options are local or parenteral application of testosterone, dihydrotestosterone or beta-chorionic gonadotropin. It use is limited to small appearing penis, reduced glans circumference or reduced urethral plate because it was reported to lead to significant enlargement of the glans and shaft of the penis (Level of Evidence: 1b) [13, 14]. According to expert opinion, a small penis is defined as penile length <25 mm during the first year of life and a glans with a diameter <14 mm [15].

   Moderate quality evidence from three randomized controlled studies demonstrated significantly lower rates of urethrocutaneous fistulae and reoperation rates in patients who received pre-operative hormonal treatment [16].

   Side effects such as changes in child's behavior, increased genital pigmentation, appearance of pubic hair, penile skin irritation and redness, increased erections and peri-operative bleeding have been reported, but no persistent side effects related to hormonal stimulation have been reported in the literature. There is also no evidence about possible effects on bone maturation [16–18].

3. Surgical options for this infant include either one stage repair versus a two stage repair. Considering the short urethral plate, the severe ventral curvature (more than 45°) and the proximal division of corpora spongiosum, this infant is most likely to require a two-stage repair. The decision making should be taken after assessment of the length and quality of the urethral plate and the degree of chordee once the penis has been degloved [1].

   Previously reported series of single-stage repairs for proximal defects have reported high complication rates of 20–50% [19]. Regardless of convincing results recently published [20], in the survey conducted by the European association of urology, the TIP repair in the correction of proximal hypospadias is not widely used and around 43.3–76.6% prefer a two-stage repair for these complex cases [9]. The two-stage procedure has become more popular due to lower risk of chordee recurrence and more robust long term favorable outcome [1].

   Two stage procedures include two-stage preputial flaps (Byars or Dennis Brown) or two-stage preputial graft repair (Bracka). According to Cuckow et al. [21], in a cohort of 208 pediatric patients who underwent two-stage Bracka procedure using free grafts (preputial, buccal or retro auricular), cosmetic and functional result were considered excellent in 90% of patients, good in 3.7% and 6.3% required reoperation. Complications after the second stage were: urethrocutaneous fistulae (3.4%), meatal stenosis (1.4%), and three partial glans dehiscence (1.4%).

14.3 DSD (5α Reductase Deficiency)

A new-born baby, with no antenatal history, is in NICU for respiratory distress. The neonatal team is concerned with the sex assignment due to the genital appearance, which are ambiguous with severe penoscrotal transposition, a small phallus, perineal-scrotal hypospadias, bifid scrotum and two perineal openings (Fig. 14.3). Both gonads are palpable in the genital folds.

1. *How are these group of disorders named?*
2. *How should this patient be managed?*
3. *What is the most likely diagnosis and what are the differential diagnosis?*
4. *When is the best timing for surgical repair? Is hormone therapy indicated in this case?*

1. These disorders, formerly called 'intersex disorders', are characterized by a presentation in which there is a discordance between chromosomal, gonadal, or anatomical sex [1]. They were renamed in 2005 as "disorders of sex development" (DSD), by the European Society for Paediatric Endocrinology and the Lawson Wilkins Pediatric Endocrinology Society in a document known as the Chicago Consensus Statement [22]. However, in a recent publication, Gorduza et al. suggest a new terminology to avoid the confusion and distress the terms 'disorder' or 'sex' may cause [23]. The term "anomalies of gonadal/genital development" (AGD) was proposed to outline the current surgical approach to these very distinct conditions and address the many current controversies regarding each of them. AGD can be divided into five main groups: virilized 46 XX, unvirilized 46 XY, chromosomic mosaicism or chimerism (essentially the mixed gonadal dysgenesis 45 XO/46 XY and 46 XX/46 XY), ovotesticular 46 XX and heterogeneous category including cloacal exstrophy, aphallia and some complex cloacal anomalies.
2. This baby should be referred to a DSD multidisciplinary team, comprising geneticists, pediatric urologist, gynaecologists, endocrinologists, psychologists and biochemists. The challenge during the neonatal period is to use the information available to make the most appropriate choice in order to select a gender concor-

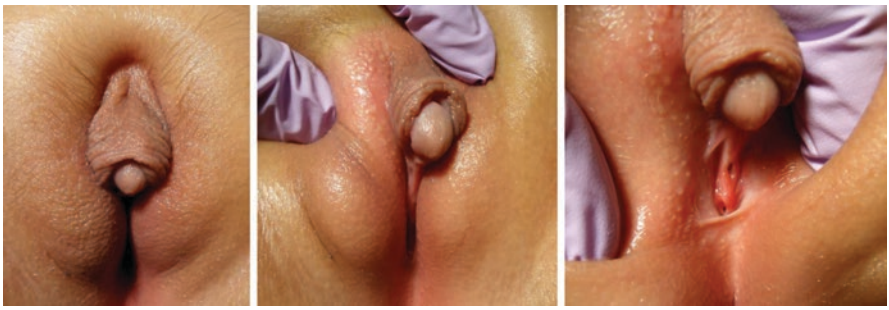

Fig. 14.3 Desorder of sex development (DSD)

dant with the individual identity of the child (which is invisible during this period), the social identity (which is the way the 'society' looks at the individual and the only tangible identity approachable after birth) and the behavioral identity, which is not yet apparent [24]. The situation should be explained to the caregivers fully and kindly. Registering the birth and naming the baby should be delayed as long as necessary [1].

A careful physical examination is mandatory evaluating pigmentation of genital and areolar area, hypospadias or urogenital sinus, size of phallus, palpable and/or symmetrical gonads and blood pressure [1]. If it is possible to palpate a gonad, it is almost certainly a testis; this clinical finding therefore virtually excludes 46XX DSD [1]. The following laboratory investigations are needed for the initial assessment: karyotype, plasma 17-hydroxyprogesterone assay and plasma electrolytes. Abdominal ultrasound to evaluate the presence of Müllerian duct structures is also recommended [1].

3. Laboratory results exclude congenital adrenal hyperplasia (CAH), which is the most frequently occurring DSD. Karyotype result is 46 XY. Abdominal US revealed no Mullerian structures. Endocrine evaluation detected elevated mean plasma testosterone but low dihydrotestosterone (DHT) levels. After hCG stimulation, the testosterone-to-DHT ratio increased to greater than 20:1. According to these results, this baby's most likely diagnosis is a 5-α-Reductase type 2 deficiency. The diagnosis is confirmed by sequencing the entire 5α-reductase type 2 *(SRD5A2)* gene [25]. It is a rare autosomal recessive sex-limited condition resulting in the inability to convert testosterone to the more physiologically active DHT. Wide range of genital ambiguity can manifest at birth and pronounced masculinization at puberty.

Differential diagnosis includes other apparent female DSD with clitoral hypertrophy, such as CAH or other under virilized 46 XY such as partial androgen insensitivity syndrome (PAIS). Genetic studies will exclude 46XX or chromosomal mosaicism. Furthermore, endocrine evaluation is crucial to determine exact entity.

4. In reference to the consensus statement [22], it is clear that the timing of surgery is nowadays much more controversial. The rationale for early surgery includes: beneficial effects of oestrogens on infant tissue; minimizing family anxiety; mitigating the risks of stigmatization and gender-identity confusion [26]. However, adverse outcomes have led to recommendations to delay unnecessary surgery to an age when the patient can give informed consent. Surgery that alters appearance is not urgent [1].

   In this case, where male assignment has been done early in life, treatment includes hormone and surgical correction of severe hypospadias. Knowing that 5-α-Reductase type 2 deficiency patients will have an acceptable physiological virilization during puberty, deferring hypospadias reconstruction may be advantageous. Although the recommended age for surgical correction of hypospadias is 6–18 (24) months [1], there is a view that this group should be the exception and hypospadias repair should be delayed until post puberty.

14.4 Midshaft Hypospadias

A year-old male infant is referred to the urology service by the GP for hypospadias. On clinical examination both testes are in the scrotum, there is some degree of chordee with a midshaft meatus and hooded foreskin. The glans is small and has no groove (Fig. 14.4).

1. What is the incidence of midshaft hypospadias?
2. Are all midshaft hypospadias treated in the same way?
3. a. What are the surgical options for this case?
   b. Is a graft needed?
4. How is the follow up of hypospadias patients?

1. Midshaft hypospadias is the least common variety, accounts for 10% of hypospadias [7].
2. Midshaft hypospadias should be reassessed after the shaft has been degloved and the degree of chordee is measured [1]. The level of division of the corpus spongiosum is the main determinant of the severity of hypospadias, as the urethral segment sitting proximal to the meatus is usually hypoplastic and deficient of spongiosum. Only then can the appropriate urethroplasty technique be chosen for each case in particular, not being able to universalize one technique [2]. Caregivers should be correctly informed about the different options before the surgery takes place.
3. a. During this baby's surgery, after shaft is degloved, mild chordee (<30°) is evident, and the urethral plate is adequate to be preserved. Chordee is corrected with a dorsal plication. Assessment of the urethral plate is crucial to determine whether it can be closed without a midline incision (Thiersch-Duplay), if a

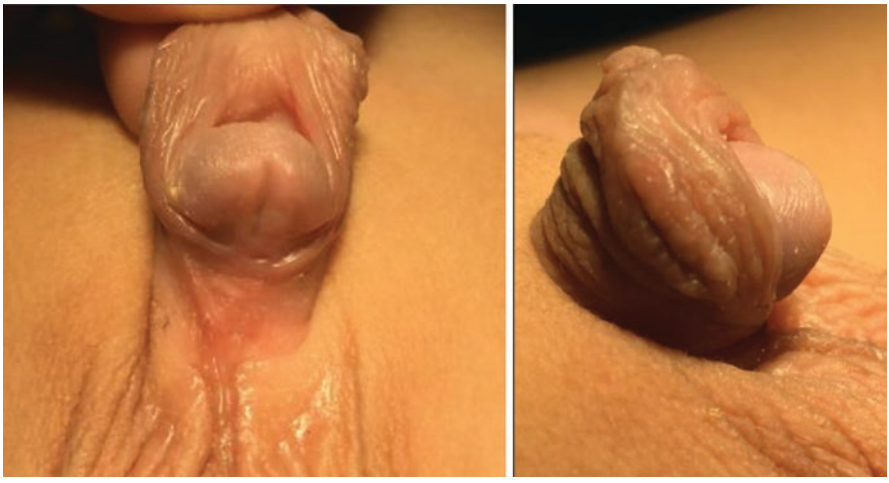

Fig. 14.4 Midshaft hypospadias

medial deep dorsal incision is required (Snodgrass TIP procedure), or if augmentation is necessary (onlay flap, Snodgraft procedure). However, this assessment is somewhat subjective [2, 15]. Mouriquand believes that length, width and thickness define the quality of the urethral plate and therefore need to be taken into account in decision making [15]. Ru W et al. highlights the value of the ratio between the urethral plate and the glans width for objectivity and accuracy in urethral plate evaluation, which in turn serves as an independent factor influencing outcomes in tubularized incised plate repair [27]. According to Seleim et al., in a recent prospective evaluation of 104 preservable narrow plate primary hypospadias repair (<8 mm), 4 mm width is the lower limit of clinical relevance that defines poor urethral plate [28].

b. In this case, an augmenting graft should be considered as a good option. In the presence of a narrow, shallow, inelastic urethral plate and conical small glans, a more substantial augmentation is required, rather than just incising the plate [7]. This can apply to distal hypospadias, but more particularly to severe penile forms where the application of an extended Snodgrass procedure may generate concerns for the long-term outcome [7]. The onlay preputial island flap, described by Duckett, is a good option. However, the more recent Snodgraft procedure could also be considered. The resulting meatus is wide and slit like. The excellent take of graft material enables a satisfactory urethra to be recessed back into the glans [29]. The Snodgraft procedure has been also utilized in redo hypospadias repair and specifically BXO cases [7].

5. EUA Guidelines strongly recommend long-term follow-up to detect urethral stricture, voiding dysfunctions, recurrent penile curvature, ejaculation dysfunction and patient satisfaction [1]. However, urethral performance after reconstruction is still difficult to assessed. Most often surgeons only rely upon the parent's or the patient's views, or the observation of the urine stream is not done in optimal conditions. Urine flow studies are not reliable as most patients who received urethral surgery have long-lasting dyssynergic voiding and because the urodynamic profile of the reconstructed urethra is abnormal even without significant urethral stricture [7]. This explains why most urine flow studies after hypospadias surgery have a flat profile despite satisfactory urethroplasty [15]. Although peak flow rates and uroflow curve rates have unclear meaning, Snodgrass recommends urethroscopy when there is a flat tracing with a flow rate less than 5 cc/s, and/or in patients with obstructive voiding symptoms [15]. The use of validated objective scoring systems to assist in evaluating the functional and cosmetic outcome should be developed [1].

14.5 Mega-Meatus Intact Prepuce (MIP)

A 2-year old boy is referred to the clinic because parents notice a wide meatus proximal to the coronal sulcus with splayed urinary stream and normal retractable prepuce (Fig. 14.5).

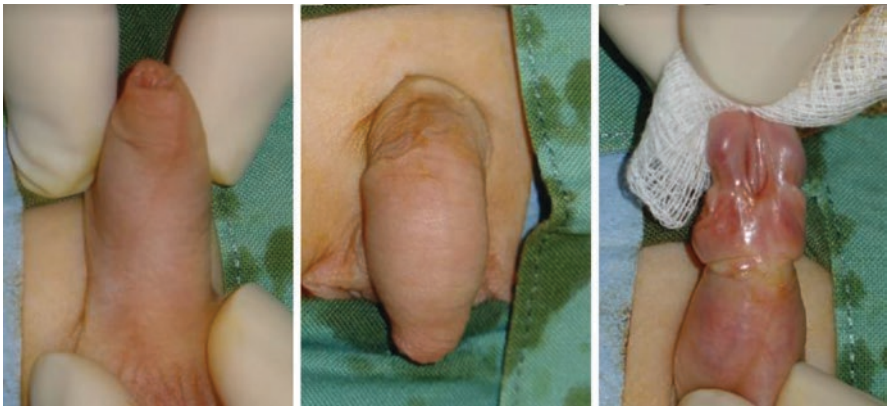

Fig. 14.5 Megameatus intact prepuce (MIP)

1. What is the most likely diagnosis?
2. What are the clinical features that characterizes this entity?
3. How is the diagnosis done? Is it the same as other type of hypospadias?
4. What is the incidence of this condition?
5. What are the different modalities of treatment?

1. The most likely diagnosis is megameatus with intact prepuce.
2. MIP is a unique anatomical variant of hypospadias characterized by a deep glanular groove, a large meatus and an intact prepuce that completely covers the glans [30].
3. Diagnosis and management of MIP can be particularly challenging [31]. Typical hypospadias diagnosis is usually straightforward, identified at birth or even antenatally [32]. However, in MIP cases, the diagnosis is often delayed either late in life in non-circumcised boys at the time of retraction of the prepuce or at the time of neonatal circumcision [30]. It was once hypothesized that the cause of the glans defect was previous surgery, however it is now understood that this is a urethral formation defect [32, 33].

   There are several differences between MIP and typical distal hypospadias. In MIP, by definition, there is a completely formed prepuce with a patulous meatus, no chordee and the frenulum is usually absent [34]. Fahmy et al. identified 15 cases of MIP, in a cohort of 12,518 boys, concluding that any deviation from normal penile medial raphe (deviation, hyperpigmentation, prominent or bifurcation) should raise suspicion about presence of MIP, with a sensitivity of 80%, a specificity 99.8% and positive predictive value of 24.4% [32].
4. The MIP is a rare variant of glanular hypospadias first described by Juskiewenski et al. in 1983 [35]. The reported prevalence is 1 of 10,000 patients, which represents an incidence of 3–6.8% of all hypospadias although its true incidence is unknown given the fact that a number of patients with MIP may not be identified [32, 36].

5. Patients diagnosed with MIP variant of hypospadias should be referred to a pediatric urologist before age 6 months [36]. Surgical repair could be offered, between the age of 6–18 months, for those patients with a large fish mouth or blunderbuss appearing meatus that opens close or at the coronal margin. When the caliber of the urethral meatus is minor, the location is close to the tip of the glans with good urinary stream, surgical repair may not be necessary [36].

   Several anatomical considerations should be taken into account during MIP reconstruction surgery. In general, the urethral plate is often irregular and may extend laterally to the level of the coronal margin making the dissection more difficult. If the lateral extent of the urethra is not recognized, injury can occur at the time of repair, making reconstruction more problematic [36].

   Numerous techniques have been described, starting by Duckett and Keating in 1989 who being dissatisfied with the results of the MAGPI and peri meatal-based flap procedure, described the "pyramid procedure" [37]. Yet another technique designed to overcome the challenges of a wide, deep glanular groove and a noncompliant fish mouth procedure is the glans approximation procedure (GAP) [6]. Tubularized incised plate urethroplasty and modified Thiersch-Duplay tubularization of the urethral plate are other techniques with excellent cosmetic and functional results [36, 38]. Cedron adapted the principle of the Mathieu procedure to the repair of MIP with the advantage of an improved visualization of the urethra during dissection and also providing healthy vascularized coverage to the reconstructed urethra [36].

   Reported complications of surgical treatment are: 0–9% rate of urethra cutaneous fistula and 0–18% rate of meatal stenosis [36, 39].

14.6 Failed Hypospadias Repair

A 12-year old boy attends with his parents to the urology clinic. They are concerned about the cosmetic appearance of his penis after three surgical procedures in another centre. He is having curved erections, and has to urinate siting down on the toilet because the urine stream flows downwards. He describes abdominal straining during micturition. On clinical examinations there is firm scar tissue in the ventral aspect of the shaft, with a narrow distal penile meatus (Fig. 14.6).

1. How should this patient be managed?
2. When is the best timing for surgery?
3. What are the surgical options in this case?
4. What grafts are there available when prepuce is absent?

1. This patient is a case of failed hypospadias repair. This group includes patients with persisting functional complications after previous hypospadias repair, that present either as recurrent stricture, urethrocutaneous fistula, glans dehiscence, urethral dehiscence, chordee, or glans deformity. In a series of 100 redo hypo-

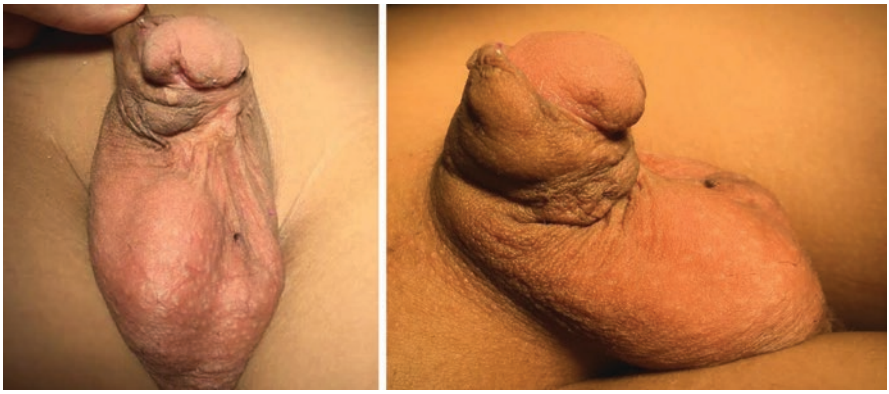

Fig. 14.6 Failed hypospadias repair

spadias surgery, BXO was found as one of the most important yet often unrecognized causes of late hypospadias failures [7].

Failed hypospadias is a complex and challenging issue [40]. Preoperative uroflowmetry and post voiding US are important to asses for any bladder or upper urinary tract compromise. The assesment should begin with a diagnostic cystoscopy to evaluate the neo-urethra and the severity of any stricture.

2. In this case, at least minimal intervention should be done as soon as possible to treat outlet obstruction. Suprapubic line or even perineal urethrostostomy should be considered as transient solution if the patient is not psychologically ready for a major reconstruction.

   Once the obstruction has been dealt with, there is controversy on the age at which to operate as well as the technique to be used. These group of patients are usually older and therefore the patient himself should play an essential role in the decision making.
3. There are no clear guidelines for the management of these types of patients [1]. Single stage repair of redo cases usually is not possible due to the lack of vascularized tissues to reconstruct the urethra, provide good skin cover and an interposing tissue layer [41]. Hence, failed hypospadias merit two-staged grafted urethroplasty [41]. Planning the surgery in a staged fashion gives the surgeon the opportunity to remove the non-vascularized tissues, address the curvature and lay down a vascularized tissue usually a graft to be utilized in a second stage for urethral reconstruction. It has been reported an overall success rate of 72% using staged graft repair [41].
4. Grafts are commonly taken from either genital or non-genital sites like inner preputial graft if the child is not circumcised, buccal mucosa graft and post auricular skin graft. Following the principles published by Cuckow et al., in the case of not having enough foreskin in proximal hypospadias, alternatives are posterior auricular Wolfe graft and / or oral mucosa [19].

However, up to 12% of patients will need a revision of the first stage because of graft retraction. Leslie et al. [42], in retrospective study on 30 children with prior failed repairs reported induration and thickening in the graft after the first stage that in their experience affected the incidence of complications in a significant way. This may support the use of corticoid betamethasone cream beginning 4 weeks after healing of the graft and thereafter for at least 6 months to prevent the occurrence of hypertrophy and induration.

References

1. *EAU Guidelines*. Edn. Presented at the EAU Annual Congress Copenhagen 2018. ISBN 978–94–92671-01-1.
2. Mouriquand P, Gorduza D, Noche ME, Targnion A. Long-term outcome of hypospadias surgery: current dilemas. Curr Opin Urol. 2011;21:465–9.
3. Bouty A, Ayers KL, Pask A, Heloury Y, Sinclair AH. The genetic and environmental factors underlying hypospadias. Sex Dev. 2015;9:239–59.
4. Dolk H. Rise in prevalence of hypospadias. Lancet. 1998;351:770.
5. Moradi M, Kazemzadeh B, Hood B, Rezaee H, Kaseb K. Meatal mobilization and Glanuloplasty: A viable option for coronal and glanular hypospadias repair. Urology. 2016;94:204–7.
6. Zaontz MR, Dean GE. Glandular hypospadias repair. Urol Clin North Am. 2002;29(2):291–298, V–VI.
7. Manzoni G, Bracka A, Palminteri, Marrocco G. Hypospadias surgery: when, what and by whom? BJU Int. 2004;94:1188–95.
8. Belman AB. Hypospadias and chordee. In: Belman AB, King LR, Kramer SA, editors. Clinical Pediatric Urology. London: Martin Dunitz; 2002.
9. Springer A, Krois W, Horcher E. Trends in hypospadias surgery: results of a worldwide survey. Eur Urol. 2011;60(6):1184–9.
10. Unluer ES, Miroglu C, Ozturk R. Long-term follow up results of the MAGPI (meatal advancement and glanuloplasty) operations in distal hypospadias. Int Urol Nephrol. 1991;23(6):581–7.
11. Morera AM, et al. A study of risk factors for hypospadias in the Rhone-Alpes region (France). J Pediatr Urol. 2006;2:169.
12. Silver RI, Rodriguez R, Chang TS, Gearhart JP. In vitro fertilization is associated with an increased risk of hypospadias. J Urol. 1999;161(6):1954–7.
13. Netto JM, et al. Hormone therapy in hypospadias surgery: a systematic review. J Pediatr Urol. 2013;9:971.
14. Malik RD, et al. Survey of pediatric urologists on the preoperative use of testosterone in the surgical correction of hypospadias. J Pediatr Urol. 2014;10(5):840–3.
15. Snodgrass W, Macedo A, Hoebeke P, Mouriquand P. Hypospadias dilemmas: A round table. J Pediatr Urol. 2011;7:145–57.
16. Chua ME, et al. Preoperative hormonal stimulation effect on hypospadias repair complications: Meta-analysis of observational versus randomized controlled studies. J Pediatr Urol. 2017;13:470.
17. Kaya C, et al. The role of pre-operative androgen stimulation in hypospadias surgery. Transl Androl Urol. 2014;3:340.
18. Wright I, et al. Effect of preoperative hormonal stimulation on postoperative complication rates after proximal hypospadias repair: a systematic review. J Urol. 2013;190:652.
19. Johal N, Nitkunan T, O'Malley K, Cuckow P. The Two-Stage Repair for Severe Primary Hypospadias. E Urol. 2000;50:366–71.

20. Snodgrass W, Bush N. Tubularized incised plate proximal hypospadias repair: continued evolution and extended applications. J Pediatr Urol. 2011;7:2–9.
21. Pfistermüller K, Manoharan S, Desai D, Cuckow P. Two-stage hypospadias repair with a free graft for severe primary and revision hypospadias: A single surgeon's experience with long-term follow-up. J Pediatr Urol. 2017;13(1):35.e1–7.
22. Lee PA, et al. Consensus statement on management of intersex disorders. International Consensus Conference on Intersex. Pediatrics. 2006;118:488.
23. Gorduza D, Quigley C, Caldamone A, Mouriquand P. Surgery of Anomalies of gonadal and genital Development in the ¨Post-Truth Era¨. Urol Clin N Am. 2018;45:659–69.
24. Vidal I, Gorduza DB, Haraux E, et al. Surgical options in disorders of sex development with ambiguous genitalia. Best Pract Res Clin Endocrinol Metab. 2010;24:311–24.
25. Wein AJ, Kavoussi LR, Partin AW, Peters CA. Campbell-Walsh Urology. 11th ed. Philadelphia, PA: Elsevier; 2016.
26. Bergman JE, et al. Epidemiology of hypospadias in Europe: a registry-based study. World J Urol. 2015;33:2159.
27. Ru W, Shen J, Tang D, Xu S, Wu D, Tao C, Chen G, Gao L, Wang X, Shen Y. Width proportion of the urethral plate to the glans can serve as an appraisal index of the urethral plate in hypospadias repair. Int J Urol. 2018;25(7):649–53.
28. Seleim HM, et al. Comprehensive evaluation of grafting the preservable plates with consideration of native plate width at primary hypospadias surgery. J Pediatr Urol. 2019; https://doi.org/10.1016/j.jpurol.2019.05.002.
29. Kolon TF, Gonzales ET Jr. The dorsal inlay graft for hypospadias repair. J Urol. 2000;163:1941–3.
30. Bhat A, Bhat M, Singh V. Results of tubularized urethral plate urethroplasty in Megameatus Intact Prepuce. Indian J Urol. 2017;33:315–8.
31. Marco C, Bulotta AL, Varetti C, et al. Ambiguous external genitalia due to defect of 5-α-reductase in seven Iraqi patients: prevalence of a novel mutation. Gene. 2013;526:490–3.
32. Fahmy M, et al. Othman D. Penile Median Raphe Anomalies as an Indicator of Megameatus Intact Prepuce Anomaly in Children Undergoing Routine Circumcision. Urology. 2018;121:164–7.
33. Peretz D, Westreich M. Pseudo-iatrogenic hypospadias: the megameatus intact-prepuce hypospadias variant. Plast Reconstr Surg. 2003;111(3):1182–5.
34. Elbatarny A, Shehata S, Ismail K. Megameatus intact prepuce variety of hypospadias: tips for repair using the modified glanular approximation procedure. Ann Pediatr Surg. 2011;7(2):1687–37.
35. Juskiewenski S, et al. Treatment of anterior hypospadias. (Balanoplasty). J Urol (Paris). 1983;89(2):153–6.
36. Cendron M. The Megameatus, Intact Prepuce Variant of Hypospadias: Use of the Inframeatal Vascularized Flap for Surgical correction. Front Pediatr. 2018;6:55.
37. Duckett J, Keating M. Technical challenge of the megameatus inctact prepuce hypospadias variant: the pyramid procedure. J Urol. 1989;141:1407–9.
38. Faasse MA, et al. Repair of megameatus: A modified approach. J Pediatr Urol. 2015; https://doi.org/10.1016/j.jpurol.2015.01.003.
39. Snodgrass WT, Khavari R. Prior circumcision does not complicate repair of hypospadias with an intact prepuce. J Urol. 2006;176:296–8.
40. Kulkarni S, Joglekar O, Alkandari M, Pankaj J. Redo hypospadias surgery: current and novel techniques. Res Repo Urol. 2018;10:117–26.
41. Badawy H, et al. Staged Repair of Redo and Crippled Hypospadias: Analysis of Outcome and Complications. J Pediatr Urol. 2019;15(2):151-1–151-10.
42. Leslie B, Lorenzo AJ, Figueroa V, Moore K, Farhat WA, Bägli DJ. Pippi Salle JL. Critical outcome analysis of staged buccal mucosa graft urethroplasty for prior failed hypospadias repair in children. J Urol. 2011;185(3):1077–82.