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Congenital aphallia: From embryology to management - a focused minireview

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Abstract

Aphallia, or penile agenesis, is an extremely rare congenital anomaly with fewer than 100 cases reported worldwide. It results from failed development of the genital tubercle during early embryogenesis, leading to complete absence of penile structures and abnormal urethral opening. This defect is often part of a broader caudal developmental disturbance and is frequently associated with genitourinary anomalies such as urethrorectal fistula, renal agenesis, renal dysplasia, hydronephrosis, and cryptorchidism, all of which significantly influence prognosis. Diagnosis requires careful differentiation from conditions that mimic genital absence, including concealed penis, micropenis, disorders of sex development, and intrauterine penile injury. Several classification systems exist based on urethral location, severity of associated anomalies, and presence of a functional urinary meatus. Management has historically been controversial. Earlier recommendations favored feminizing genitoplasty in infancy; however, growing recognition of prenatal androgen imprinting and the risk of later gender dysphoria has shifted current practice toward male gender assignment and staged neophalloplasty. Reconstructive strategies include temporary non-microsurgical flaps in childhood and definitive microsurgical phalloplasty in adolescence or adulthood. Urethral reconstruction remains a major surgical challenge. Optimal care requires a multidisciplinary team. This review summarizes embryology, clinical spectrum, diagnosis, and evolving management of aphallia.

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Key Words: Congenital aphallia; Gender assignment; Genitourinary malformation; Neophalloplasty; Penile agenesis; Reconstructive surgery

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Core Tip: Congenital aphallia is an exceptionally rare anomaly with significant diagnostic, reconstructive and psychosocial challenges. Early recognition and differentiation from mimicking conditions are essential. The condition frequently coexists with multisystem anomalies, which largely determine prognosis. Management has evolved from routine feminizing genitoplasty to a more individualized, patient-centered approach favoring male gender assignment and staged reconstruction. Modern surgical strategies, particularly microsurgical neophalloplasty, offer improved functional and cosmetic outcomes, although challenges in urethral reconstruction persist. A multidisciplinary approach and long-term follow-up are crucial. Emerging advances in tissue engineering hold promise for future reconstructive solutions.

INTRODUCTION

Congenital aphallia, also referred to as penile agenesis, is an exceptionally rare congenital anomaly characterized by the complete absence of the penis in a genetically male individual. Fewer than 100 cases have been reported in the literature to date[1]. The anomaly arises due to disruption of early embryological development and is commonly associated with multiple congenital malformations, particularly involving the genitourinary system[1,2]. The condition poses significant challenges not only in terms of anatomical reconstruction but also with regard to urinary function, gender identity and long-term psychosocial outcomes[3]. Historically, management strategies have been controversial, especially concerning gender assignment. However, evolving understanding of sexual differentiation and advances in reconstructive surgery have led to a shift in current practices[4]. This review aims to summarize the embryology, clinical spectrum, diagnostic approach and contemporary management strategies for congenital aphallia.

SEARCH STRATEGY AND SELECTION CRITERIA

A focused literature review was conducted using electronic databases including PubMed/MEDLINE, Web of Science and Google Scholar. The search included studies

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published up to December 2024. Keywords and Medical Subject Headings terms used were “aphallia”, “penile agenesis”, “congenital absence of penis”, “genitourinary malformations”, and “neophalloplasty”, applied individually and in combination. Relevant articles were initially screened based on titles and abstracts, followed by full-text review of eligible studies. Priority was given to original research articles, systematic reviews, and key historical reports addressing embryology, clinical presentation, associated anomalies, and management. Additional studies were identified through manual cross-referencing of selected articles.

Given the rarity of the condition, no strict restrictions based on study design were applied. However, non-English publications without accessible translations and studies lacking adequate clinical detail were excluded. This review is narrative in nature and does not adhere to a formal systematic review protocol.

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HISTORICAL BACKGROUND

The earliest recorded description of aphallia dates to 1701, when the French surgeon Barthélemy Saviard reported a case of a newborn described as “a child who had no rod”. A more detailed and formal medical description was later provided by Imminger[5] in 1853. Since then, just over 100 cases have been documented in the literature, with ongoing reports continuing to expand the clinical understanding of this rare anomaly.

EMBRYOLOGY AND PATHOGENESIS

Development of the external genitalia begins during the 4th to 7th weeks of gestation with the formation of the genital tubercle, which arises from mesenchymal proliferation at the cranial aspect of the cloacal membrane. This bipotential structure serves as the precursor of the penis in males and the clitoris in females. Concurrently, the cloaca divides into the urogenital sinus and rectum through the descent of the urorectal septum, establishing the foundation of the lower urinary and gastrointestinal tracts[6,7]. Male sexual differentiation is initiated by the sex determining region Y gene on the Y chromosome, which promotes the development of Sertoli cells, followed by differentiation of Leydig

cells within the testes. Testosterone produced by Leydig cells is converted to dihydrotestosterone by 5α-reductase, which is essential for masculinization of the external genitalia. Under androgenic influence, the genital tubercle elongates to form the phallus, while the urethral folds fuse ventrally to enclose the urethral plate, forming the penile urethra in a proximal-to-distal direction. Mesoderm contributes to the formation of the corpora cavernosa and glans, endoderm forms the urethral lining and ectoderm gives rise to the penile skin and prepuce[6,7]. Figure 1 illustrates the embryological basis and proposed pathogenetic mechanisms of aphallia.

Thus, aphallia results from complete failure of development or absence of the genital tubercle, occurring early in embryogenesis. This defect is often attributed to disruption in cloacal maturation or inadequate development of caudal mesenchyme. As a consequence, the urogenital sinus fails to elongate and remains in a primitive position, leading to an ectopic urethral opening, typically in the perineum or near the anal verge[6,7].

Although the precise etiology remains uncertain, most cases appear sporadic. Experimental studies suggest that disruption of key developmental signaling pathways, including Sonic hedgehog, fibroblast growth factors and retinoic acid signaling, may impair genital tubercle formation and caudal morphogenesis[8]. Additionally, environmental influences such as poorly controlled maternal diabetes have been proposed as potential contributing factors[9].

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EPIDEMIOLOGY

Congenital aphallia is an exceptionally rare urogenital anomaly, with an estimated incidence ranging from 1 in 10 million to 1 in 30 million live births[10]. To date, fewer than 100 cases have been reported in the literature worldwide, underscoring its rarity.

Available data suggest a global distribution without a clear geographic or ethnic predilection; however, most reported cases originate from a limited number of countries. The highest proportion of cases has been reported from the United States, followed by India, with additional reports from regions including Iran, China and Europe. Overall, a

greater number of cases have been documented from Asia[1]. These observed variations are likely attributable to differences in reporting practices and healthcare accessibility rather than true differences in incidence. No consistent genetic, environmental or familial risk factors have been identified and the condition is generally considered sporadic in occurrence[2].

CLINICAL PRESENTATION

Aphallia commonly presents in the neonatal period, with diagnosis usually evident at birth. It is characterized by complete absence of the phallus and the presence of an ectopic urethral opening, most often located in the perineum or near the anal verge[4]. In most cases, the scrotum is well developed and the testes are present, although cryptorchidism or bifid scrotum may occasionally be observed. The position of the anus is frequently normal; however, associated anorectal anomalies such as anteriorly displaced anus, imperforate anus, or funnel anus may also occur[1,4]. An illustrative case by Upreti *et al*[11] is shown in Figure 2, demonstrating a neonate with absent phallus and no identifiable urethral opening in the perineum. Both testes are descended within a well-developed scrotum with a distinct median raphe. The anal opening is normally positioned but appears narrow, suggestive of anal stenosis, with passage of meconium noted on gentle probing. No evidence of a urinary fistula is observed at the anal verge.

Antenatal suspicion of aphallia may arise in fetuses presenting with oligohydramnios or anhydramnios on ultrasonography (USG). Detailed prenatal imaging can aid early detection, particularly when associated genitourinary anomalies are present. Fetal magnetic resonance imaging serves as a valuable adjunct by providing superior delineation of genitourinary anatomy and associated malformations, allowing for diagnosis in utero in selected cases and facilitating early counseling and perinatal planning[12].

Although presentation is usually at birth, occasional diagnoses have been reported in infancy or later childhood, with rare cases identified in adulthood[13]. The majority of patients have a 46 XY karyotype with normal testicular development and testosterone

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production, resulting in typical male secondary genital features, including a well-formed scrotum[14]. The condition is predominantly described in males, while reports in females (clitoral agenesis) are exceedingly rare[15]. They are likely underdiagnosed due to less conspicuous clinical features and a higher association with severe anomalies such as bladder agenesis and intrauterine fetal demise[4].

ASSOCIATED ANOMALIES

While aphallia may occur as an isolated anomaly, it is more commonly associated with other congenital malformations, reported in over 50% of cases[1,16]. These anomalies are thought to result from early disturbances in cloacal differentiation during embryogenesis, likely representing a defect in blastogenesis[17]. As this critical period coincides with the development of multiple organ systems, a wide spectrum of associated anomalies may be observed[16,17]. An early insult in cloacal maturation or defective development of the caudal mesenchyme may lead to proximal urethrorectal communication, explaining the frequent association with anorectal malformations in patients with aphallia[15].

The genitourinary system is most frequently involved, although anomalies of the gastrointestinal, cardiovascular, respiratory and musculoskeletal systems have also been described[1]. In a study by Yuri *et al*[1], involving 41 patients with aphallia, genitourinary anomalies were present in all cases, with fistulous communications being the most common finding. Fistulas were identified in 80% (n = 29) of patients, with urethrorectal fistula being the most frequent (46%, n = 19), followed by urethroperineal fistula (17%, n = 7). Renal abnormalities were observed in 63% (n = 26) of cases, most commonly hydronephrosis (34%, n = 14). Ureteric anomalies were reported in 29% (n = 12) of patients, predominantly vesicoureteral reflux (26%, n = 11). Bladder anomalies were present in 21% (n = 9), including bladder agenesis in 7% (n = 3). Urethral anomalies were also noted in 21% (n = 9), with urethral agenesis in 9% (n = 4) and posterior urethral valves in 7% (n = 3). Cryptorchidism was observed in 12% (n = 5) cases. Gastrointestinal involvement included anorectal malformations in 21% (n = 9) patients, with additional gastrointestinal abnormalities reported in three cases. Involvement of other systems was

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less frequent, with respiratory anomalies observed in 9% (n = 4) and cardiovascular anomalies in 12% (n = 5) of cases.

Aphallia may also occur as part of a broader spectrum of anomalies, particularly within the urorectal septum malformation sequence[18]. The partial form is characterized by a single perineal opening draining a common cloaca and is often associated with genitourinary, gastrointestinal and musculoskeletal anomalies. In contrast, the complete form is associated with absence of both perineal and anal openings, severe renal anomalies, oligohydramnios, pulmonary hypoplasia and is generally incompatible with postnatal survival[16,17]. Accordingly, aphallia should be regarded as a developmental field defect, reflecting a broad spectrum ranging from an isolated malformation to part of complex congenital syndromes.

CLASSIFICATION SYSTEMS

Aphallia can be classified using anatomical, prognostic and clinical criteria, each providing important insights into disease severity and outcomes. One approach considers aphallia as a disorder of sex development (DSD) of the non-hormonal and non-chromosomal type[19]. However, more widely used systems are based on anatomical and prognostic features.

Skoog and Belman[20] anatomical classification: It categorizes aphallia according to the position of the ectopic urethral opening in relation to the anal sphincter. Three types are described: (1) Post-sphincteric type: The urethral opening is located distal to the external sphincter, typically in the perineum or below the dentate line. This is the most common subtype (approximately 60%) and is associated with the best prognosis, with the lowest incidence of associated anomalies (1.2 per patient) and highest survival rates (87%); (2) Pre-sphincteric type: The urethra opens proximal to the sphincter, usually into the rectum (urethrorectal fistula). This subtype accounts for approximately 28% of cases and is associated with a higher incidence of severe anomalies and increased neonatal mortality (36%); and (3) Urethral atresia: This is the least common form (approximately 12%) and is characterized by absence of a functional urethral opening. It is associated with multiple

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severe anomalies (4 per patient) and is typically incompatible with survival (100% mortality).

This classification highlights that the more proximal the urethral opening, the greater the likelihood of associated anomalies and adverse outcomes.

Evans *et al*[16] prognostic classification is based on the presence and severity of associated anomalies: Group I (approximately 16%): Associated with severe anomalies such as renal agenesis or dysplasia and other caudal defects, with high mortality. Group II (approximately 72%): Characterized by fewer associated anomalies and relatively lower mortality. Group III (approximately 12%): Cases without a consistent pattern of associated anomalies.

Fahmy's[12] classification provides a simplified clinical framework based on urethral anatomy and associated conditions: Aphallia with urethral atresia and absent urinary meatus, aphallia with a normal urethra and external meatus, aphallia associated with other syndromes and aphallia associated with caudal regression syndrome.

Overall, these classification systems complement each other by correlating anatomical findings with prognosis and associated anomalies, thereby aiding in clinical assessment and management planning.

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DIFFERENTIAL DIAGNOSIS

Congenital aphallia must be differentiated from conditions that may clinically simulate absence of the penis which include micropenis, buried penis, DSD and intrauterine penile amputation[21]. Accurate diagnosis is essential, as management strategies and prognosis differ significantly among these entities. A comparative summary of aphallia and its key differential diagnoses is provided in Table 1.

Micropenis

It is defined as a structurally normal penis with a stretched penile length less than 2.5 standard deviations below the mean for age. Unlike aphallia, the penile shaft, corpora cavernosa and urethral meatus are present. It is often associated with endocrine

abnormalities such as hypogonadotropic hypogonadism or growth hormone deficiency. Careful measurement and hormonal evaluation help distinguish micropenis from true penile agenesis[22].

Concealed or buried penis

The penile shaft is normally developed but is hidden beneath suprapubic fat, skin or abnormal fascial attachments, usually seen in obese children. On examination, the penis can usually be palpated and exteriorized with gentle traction, confirming its presence[23].

DSD

They may present with ambiguous genitalia, making differentiation from aphallia challenging. In DSD, there is typically some degree of genital formation rather than complete absence[12]. Karyotyping, hormonal assays and imaging of internal reproductive organs are essential for accurate diagnosis.

Intrauterine penile amputation

This rare condition results from antenatal vascular compromise or amniotic band syndrome leading to loss of a previously formed penis. Unlike aphallia, remnants of penile tissue, scarring or evidence of prior development may be present. A detailed antenatal history and careful physical examination may aid in diagnosis[12]. A thorough clinical examination, supported by imaging, genetic and hormonal evaluation, is essential to differentiate these conditions from aphallia and guide appropriate management.

DIAGNOSTIC EVALUATION AND INVESTIGATIONS

The diagnosis of aphallia is primarily clinical and is usually established at birth by the complete absence of the phallus. However, a systematic evaluation is essential to identify associated anomalies, determine prognosis and guide subsequent management[1]. The diagnostic workup and evaluation algorithm are illustrated in Figure 3.

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Clinical examination

Initial evaluation at birth involves a detailed physical examination. This includes confirmation of the absence of the phallus, identification of the urethral opening (whether ectopic or absent) and careful assessment of the scrotum and testes. The position and patency of the anus should also be evaluated due to the frequent association with anorectal anomalies. In addition, it is important to distinguish aphallia from other conditions that may mimic penile absence through careful clinical examination.

Laboratory and genetic assessment

Baseline laboratory investigations should include renal function tests, as these may be abnormal due to the high incidence of associated renal and genitourinary anomalies. Karyotype analysis is recommended in all cases to confirm chromosomal sex. Hormonal evaluation, including serum testosterone, luteinizing hormone, and follicle-stimulating hormone, may be performed to assess gonadal function and to exclude DSD. Additional endocrine and genetic testing may be indicated in selected cases based on clinical findings.

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Imaging studies

Imaging plays a central role in identifying associated anomalies and delineating anatomical details. A multimodal approach is often required.

USG kidney, ureter and bladder: First-line investigation to evaluate renal morphology, ureteric anatomy, bladder presence and associated genitourinary anomalies.

Chest X-ray: To assess pulmonary anomalies such as pulmonary hypoplasia.

Two-dimensional echocardiography: Recommended to screen for associated congenital cardiac defects.

USG abdomen and pelvis: Useful for evaluating intra-abdominal and pelvic structures and identifying associated anomalies.

Voiding cystourethrogram: To assess bladder anatomy, detects vesicoureteral reflux or posterior urethral valves and helps delineate fistulous communications.

Magnetic resonance imaging abdomen/pelvis: Provides detailed visualization of pelvic anatomy, genitourinary structures and complex associated anomalies, particularly in selected cases.

Additional imaging: Computed tomography, gastrointestinal contrast studies, or nuclear scans may be performed as clinically indicated.

Endoscopic evaluation: Endoscopic procedures such as cystoscopy or genitoscopy may be required to identify the urethral tract, locate fistulous openings and assess lower urinary tract anatomy. These are particularly useful in planning reconstructive procedures.

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MANAGEMENT

Historical perspectives and evolving concepts

The management of aphallia has historically been controversial, particularly with regard to gender assignment and reconstructive options. In earlier decades, feminizing genitoplasty was widely recommended as the primary management strategy[4,10]. This approach was based on the belief that raising affected individuals as males would result in poor psychosocial outcomes and that it was preferable to assign a female gender rather than attempt reconstruction of an inadequate phallus[10]. This traditional management involved early bilateral orchidectomy in the neonatal period to prevent postnatal androgen effects, followed by creation of a neovagina and initiation of estrogen therapy at puberty. The relative technical ease of vaginal reconstruction, compared to the

complexity and limitations of penile reconstruction, further supported this approach[4,10].

However, outcomes revealed significant limitations of this strategy. Many patients assigned female gender despite having a 46 XY karyotype experienced gender dysphoria later in life[2,4]. Increasing evidence suggests that prenatal androgen exposure plays a critical role in psychosexual development, influencing gender identity, behavior and sexual orientation. Studies involving animal models, individuals exposed to exogenous hormones in utero and patients with congenital adrenal hyperplasia have demonstrated that fetal testosterone exposure contributes to male-typical behavioral patterns and gender identity[24]. Follow-up studies of individuals with DSD, including those with penile agenesis, have shown that a substantial proportion of genetically male patients raised as females later identify as male or experience gender incongruence[25,26]. These findings have led to a paradigm shift in management philosophy.

Current consensus increasingly favors male gender assignment in patients with a 46 XY karyotype, with preservation of the testes and deferral of definitive reconstructive procedures until the individual is old enough to participate in decision-making regarding gender identity. This approach aims to reduce the risk of gender dysphoria and aligns management with the individual's likely psychosexual development[4]. Nevertheless, management decisions should be individualized, taking into account the extent of associated anomalies, potential for functional reconstruction, psychosocial factors and available healthcare resources[3]. A multidisciplinary team approach is essential to ensure comprehensive evaluation and appropriate counseling of families.

Current surgical management

The surgical management is complex and best conceptualized as a staged process encompassing acute, intermediate and long-term phases. This structured approach allows prioritization of life-threatening conditions, restoration of urinary function and eventual reconstruction of a functional and cosmetically acceptable neophallus[2,4].

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Acute phase (neonatal period)

Initial management focuses on stabilization and treatment of life-threatening conditions, particularly those related to associated anomalies. Ensuring adequate urinary drainage is critical. In patients presenting with urinary obstruction, sepsis or absent urethral outlet, temporary urinary diversion - most commonly in the form of a vesicostomy - may be required to decompress the urinary tract and prevent further complications. However, diversion may not be necessary in cases where urine drainage occurs *via* a urethroperineal fistula.

Intermediate phase

This stage aims to establish a reliable route for urinary drainage and address associated fistulous communications. Procedures such as perineal urethrostomy or catheterizable vesicostomy are performed, often in conjunction with division of urethrorectal fistulas. In selected cases, construction of a temporary phallic structure (pseudophallus) using local tissue may be undertaken during early childhood. This facilitates male gender identification and supports psychosocial development prior to definitive reconstruction.

Long-term phase (definitive reconstruction)

Definitive management involves creation of a functional and aesthetically acceptable neophallus, typically deferred until adolescence or early adulthood. This delay allows for patient participation in decision-making, availability of adequate donor tissue, and improved surgical outcomes.

Reconstructive techniques

Reconstructive options for phalloplasty are broadly divided into non-microsurgical and microsurgical techniques[27].

Non-microsurgical techniques (temporary reconstruction)

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These techniques are technically less complex and are primarily used in early childhood as interim procedures. Commonly utilized flaps include scrotal, abdominal and groin flaps. The De Castro *et al*[28] abdominal flap, based on the superficial epigastric vessels, is a well described option for temporary phalloplasty. It offers the advantage of using local tissue, preserving distant donor sites for future reconstruction and has been reported to grow proportionately with the patient, with the potential for later prosthesis implantation[28,29]. However, these procedures are generally limited in functionality and often require subsequent revision or replacement with definitive reconstruction.

Microsurgical techniques (definitive reconstruction)

Definitive neophalloplasty is most commonly performed using microsurgical free flap techniques. These procedures are complex, require specialized expertise and are typically undertaken in adolescence or adulthood. The radial forearm free flap (RFFF) remains the most widely used technique due to its reliable vascularity, pliability and suitability for simultaneous urethral reconstruction using the "tube-within-a-tube" design. Other options include the anterolateral thigh flap, latissimus dorsi flap and osteocutaneous fibular flap, each with specific advantages and limitations[27].

De Castro *et al*[28] technique for non-microsurgical flap phalloplasty is the most commonly used technique with the acceptable outcome[4]. However, the gold standard technique for phalloplasty is microsurgical phalloplasty with a RFFF, which has shown good results and positive outcomes in terms of patients' self-esteem and sexual well-being[30].

Urethral reconstruction

Urethroplasty represents the most technically demanding component of reconstruction and is associated with a high rate of complications, including strictures and fistula formation. A staged approach is frequently employed. Common techniques include the use of local skin flaps for proximal urethra and buccal mucosal grafts for distal reconstruction. Despite these efforts, some patients ultimately require a continent

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catheterizable channel (Mitrofanoff procedure) to ensure effective bladder emptying and preservation of upper urinary tract function[27].

Timing of reconstruction

The timing of definitive phalloplasty remains a subject of debate. While early construction of a pseudophallus may support psychosocial development, definitive reconstruction is generally recommended around puberty (approximately 10-15 years of age). This approach allows for: (1) Use of adequately sized donor tissue; (2) Better proportional outcomes; and (3) Patient involvement in decision-making[2]. Importantly, neophalloplasty utilizes non-hormonally responsive tissue, necessitating creation of a near adult-sized phallus at the time of reconstruction[31].

Principles of neophalloplasty

The ideal neophallus should-provide both tactile and erogenous sensation, allow voiding in a standing position through a functional neourethra, permit insertion of a penile prosthesis for sexual function, achieve satisfactory cosmetic appearance with minimal donor-site morbidity and be of adequate size and proportion[12]. Despite advances, achieving all these objectives in a single procedure remains challenging.

Outcomes and considerations

Although modern techniques have improved outcomes, phalloplasty remains associated with significant morbidity, multiple staged procedures and variable functional results[32]. Patient priorities - such as urinary function, sexual capability, cosmesis and donor-site scarring - should be carefully considered during surgical planning. Given these challenges, management should be individualized and undertaken in specialized centers with multidisciplinary expertise.

SURGICAL COMPLICATIONS

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Phalloplasty in patients with aphallia is associated with a high rate of complications, particularly involving urethral reconstruction and prosthetic implantation. Urethral complications - including fistula and stricture formation - are the most frequent and have been reported in up to 40%-80% of cases across various series, often necessitating multiple revision procedures[33]. Penile prosthesis implantation, required for achieving rigidity, represents another major source of morbidity. Reported complication rates requiring revision or explanation range from approximately 40%-45%, with common issues including infection, erosion, mechanical failure and device malposition[33].

Among reconstructive techniques, RFFF phalloplasty remains widely used, with urethral complication rates reported around 40%, although fewer patients require reoperation[33]. Alternative techniques such as the anterolateral thigh flap and latissimus dorsi flap offer advantages in terms of donor-site morbidity. However, the anterolateral thigh flap may have reduced sensory outcomes compared to RFFF[34], while latissimus dorsi flap-based reconstruction has been associated with relatively lower urethral complication rates (approximately 12.5%), with a small proportion of patients requiring reoperation for fistula formation[35]. Fibula osteocutaneous flaps and staged urethroplasty approaches, including prelamination techniques, have been explored to reduce complication rates. However, reported outcomes remain variable, with urethral stricture rates of approximately 32.6% and fistula rates around 16%[36]. Despite technical advances, urethroplasty remains the most challenging aspect of reconstruction, and complication rates remain substantial, underscoring the need for staged procedures and individualized surgical planning.

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MULTIDISCIPLINARY APPROACH

The management of aphallia presents significant clinical, psychosocial and ethical challenges in both the immediate and long-term setting. Given the rarity of the condition and the complexity of reconstruction, a coordinated multidisciplinary team is essential and typically includes pediatric surgeons, pediatric urologists, plastic and reconstructive surgeons, endocrinologists, pediatricians, psychologists and social health workers[3,4].

Early multidisciplinary evaluation enables accurate diagnosis, identification of associated anomalies and planning of staged management.

Psychosocial and ethical considerations are integral to the multidisciplinary framework. Patients are at risk of long-term psychosexual challenges and decisions regarding gender assignment and timing of reconstruction must be individualized, considering functional outcomes, reproductive potential and future autonomy[3,4]. Psychologists play a key role in family counseling and long-term psychological support. Long term multidisciplinary follow-up is crucial to optimize functional outcomes, address complications, and ensure overall quality of life.

PROGNOSIS AND SURVIVAL

The prognosis in aphallia is primarily determined by the presence and severity of associated anomalies. Isolated cases generally have a favorable outcome with good long-term survival. In contrast, patients with complex multisystem involvement - particularly severe renal anomalies, oligohydramnios and pulmonary hypoplasia - are associated with significantly increased morbidity and mortality[16,17].

Survival is closely related to anatomical subtype and associated malformations. Patients with post-sphincteric variants demonstrate the best outcomes, with reported survival rates approaching 80%-90%, whereas those with pre-sphincteric variants have higher neonatal mortality (approximately 30%-40%). Urethral atresia is typically associated with near-uniform mortality due to severe associated anomalies[20]. Long-term outcomes in survivors depend on successful urinary reconstruction, preservation of renal function and psychosocial adaptation. Many patients require multiple surgical procedures and complications such as urethral strictures and fistulas may impact quality of life. With appropriate multidisciplinary care, acceptable functional outcomes - including urinary continence and satisfactory psychosocial adjustment - can be achieved in selected cases[4].

FUTURE DIRECTIONS

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Long-term outcomes in aphallia remain inadequately defined due to the rarity of the condition and limited available data, underscoring the need for lifelong multidisciplinary follow-up, particularly after puberty to evaluate functional, psychosocial and quality-of-life outcomes[1,4]. Advances in regenerative medicine offer promising avenues for future reconstruction. Experimental studies in tissue engineering have explored bioengineered corporal tissue using autologous cells, scaffold-based constructs and stem cell-derived approaches, with encouraging results in preclinical models[37,38]. Emerging technologies such as organoid systems and biomimetic scaffolds may further enhance structural and functional restoration; however, their translation to clinical practice remains limited.

Significant challenges persist, including achieving adequate vascularization, innervation, long-term tissue viability and functional urethral integration. In addition, regulatory, ethical, and cost-related considerations must be addressed before these techniques can be widely adopted. Given the ultra-rare nature of aphallia, future progress will also depend on the development of international registries and multicenter collaborative studies to generate robust longitudinal outcome data and establish standardized management protocols.

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CONCLUSION

Aphallia is a rare and complex congenital anomaly that extends beyond anatomical absence to encompass significant functional, psychological and ethical considerations. Early diagnosis, thorough evaluation for associated anomalies and accurate differentiation from similar conditions are critical for optimal management. Prognosis is largely determined by the presence and severity of associated malformations. Management strategies have undergone a paradigm shift, with increasing emphasis on individualized care, preservation of genetic sex and staged reconstructive approaches. Despite advances in microsurgical techniques, achieving an ideal functional neophallus remains challenging. A multidisciplinary approach is essential to address the diverse medical and psychosocial needs of these patients. Future innovations in regenerative

medicine and tissue engineering may significantly improve reconstructive outcomes and quality of life.

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Footnotes

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

AI contribution statement: The authors used an AI-based tool (Notebook LLM, Google) solely to assist in the preparation of one illustrative figure only (Figure 1). The conceptualization and content of the manuscript were entirely developed by the authors. No AI tools were used for manuscript writing or for creating tables/other images. All content was critically reviewed and approved by the authors, who take full responsibility for its accuracy and integrity. AI-based writing tool was not used in the preparation of the manuscript text or in drafting the response to reviewers' comments.

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Figures and Tables

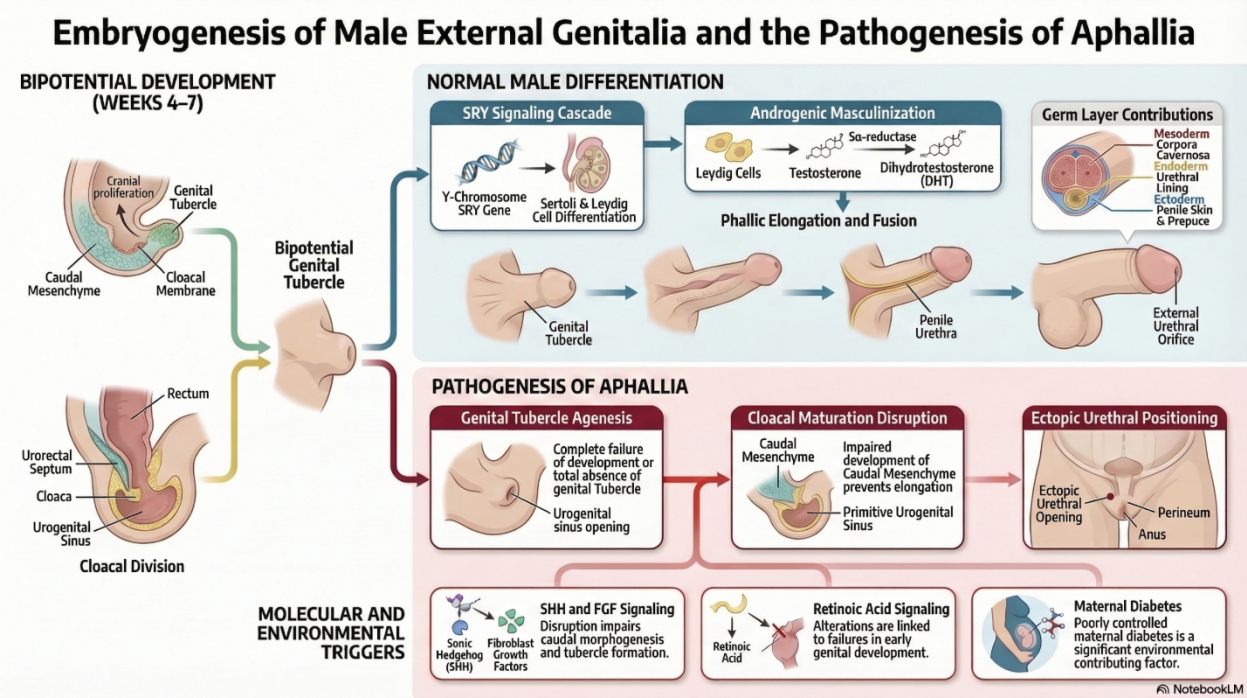


Figure 1 Embryogenesis of male external genitalia and pathogenesis of aphallia, illustrating normal genital tubercle development, androgen-driven differentiation and mechanisms leading to genital tubercle agenesis and ectopic urethral positioning. The figure layout was assisted by an artificial intelligence-based tool (NotebookLM); however, all scientific content, conceptualization, labeling and annotations were independently developed by the authors. SRY: Sex determining region Y; DHT: Dihydrotestosterone; SHH: Sonic hedgehog; FGF: Fibroblast growth factors.

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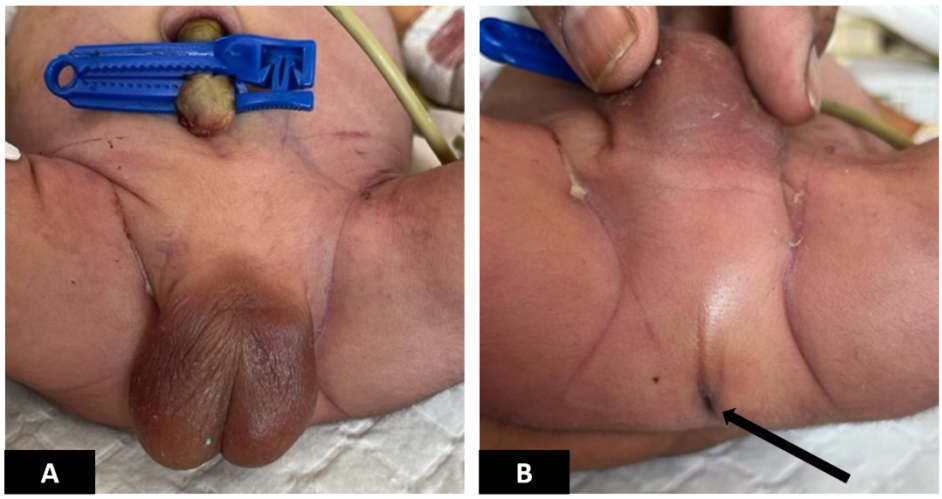


Figure 2 An illustrative case of aphallia. A: Both testes in well-developed scrotum, absent phallus and without any urinary opening or fistula; B: Narrow anal opening (black arrow marked) with no urinary fistula visualized at anal verge.

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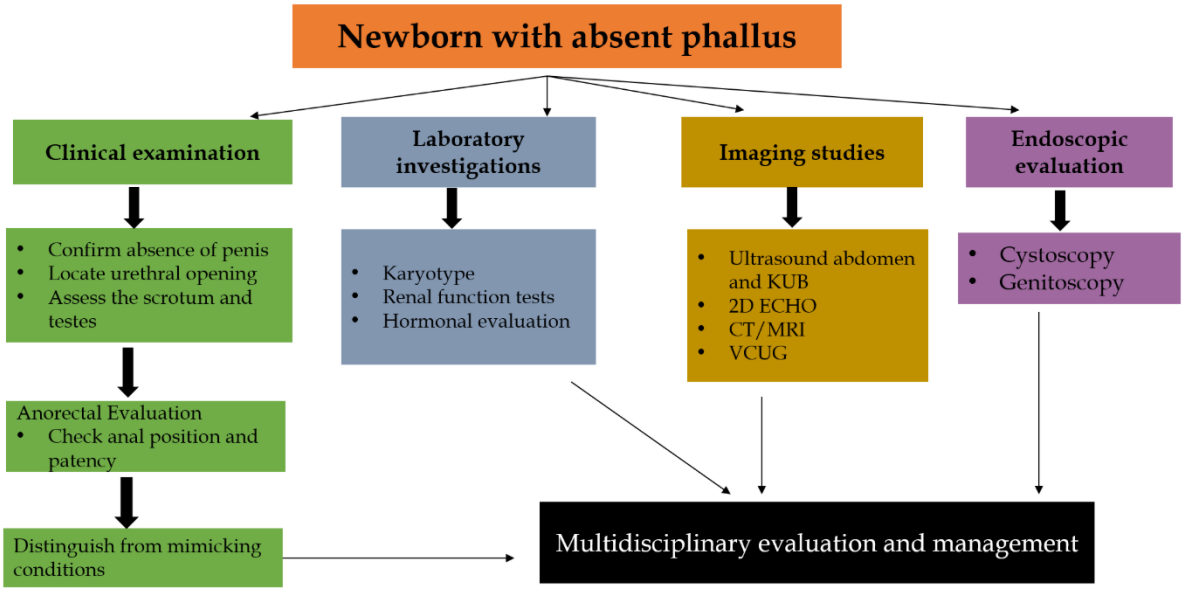


Figure 3 Diagnostic evaluation algorithm for a newborn with aphallia. Outlining stepwise clinical assessment, systemic investigations, imaging studies and endoscopic evaluation, culminating in multidisciplinary management. KUB: Kidney, ureter and bladder; 2D ECHO: 2-dimensional echocardiogram; CT: Computed tomography; MRI: Magnetic resonance imaging; VCUG: Voiding cystourethrography.

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Table 1 Comparative summary of aphallia and its differential diagnoses, highlighting differences in penile structure, urethral anatomy, associated anomalies, karyotype, and key distinguishing clinical features

Features	Aphallia	Micropenis	Concealed or buried penis	Disorders of sex development	Intrauterine penile amputation
Penile structure	Completely absent	Present but very small (< -2.5 SD)	Normal but hidden	Variable, often ambiguous	Previously formed, now absent
Corpora cavernosa	Absent	Present	Present	Usually present (variable)	May be partially present/remnants
Urethral opening	Ectopic (perineal/rectal) or absent	Normal location	Normal location	Variable/ambiguous	May be abnormal or scarred
Scrotum & testes	Usually well developed; testes present or undescended	Usually, normal	Normal	Variable (may be ambiguous)	Usually, normal
Karyotype	Typically, 46 XY	46 XY	46 XY	Variable (46 XY/46 XX/mosaic)	Usually, 46 XY
Hormonal status	Typically, normal male pattern	Often abnormal (endocrine cause)	Normal	Abnormal or discordant	Usually, normal
Associated anomalies	Common (> 50%)	May have endocrine disorders	Rare	Common (genitourinary/internal)	Usually isolated or with amniotic band defects
Key distinguishing features	Complete absence of penis	Small but present penis	Hidden but normal penis	Ambiguous genitalia	Evidence of prior penile development
Management approach	Complex reconstruction + multidisciplinary care	Hormonal therapy ± surgery	Reassurance, surgical correction (rarely)	Multidisciplinary (endocrine + surgical)	Reconstructive surgery

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