Clinical Case Report

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Congenital absence of the penis (aphallia)

A rare case report

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Abstract

Rationale: Absence of the penis, known as aphallia, is a very rare congenital anomaly. It is believed to be a result of either the absence of the genital tubercle or its failure to fully develop and is associated with the level of hormones and chromosomal rearrangements. The failure of the genital tubercle influences the development of the penis and partly depends upon testosterone secreted by Leydig cells of the testis. Chromosomal polymorphisms may affect the functions of protection and regulation, potentially leading to susceptibility to congenital diseases. Herein, an extremely rare case of a congenital absence of the penis is described.

Patient concerns: A 3-month-old was brought to the OPD by his parents with complaints of absence of penis since birth and urine being passed rectally. When he was born, he was registered as a boy because his chromosomes were 46XY but with 9qh+. Local examination revealed the total absence of the penis. The scrotum was well developed. The testes were palpable bilaterally. The anal opening was located normally. No urethral orifice could be identified. However, his parents had not yet decided whether to accept treatment. The child has been lost to follow up.

Diagnosis: Congenital absence of the penis (aphallia) (46 XY normal male karyotype).

Interventions: We explained the nature of the abnormality and management options to the parents. However, it was much regretted that the patient was too young to make a decision and that his parents had not made a decision yet. They left without any further contact.

Outcome: Because the parents left our hospital without any contact, it has not been possible to develop a follow-up plan.

Lessons: In consideration of the rarity and devastating psychosocial consequences of this case, we accordingly call for active cooperation with doctors to minimize the negative impact of this malformation. Early assignment of gender avoids confusion and contradiction. Parental confidence solidifies the child's own confidence in his or her gender.

Abbreviations: ASD = atrial septal defect, CHD = congenital heart disease, CT-DSA = computed tomography-digital subtraction angiography, CUF = congenital urethrorectal fistula, DHT = dihydrotestosterone, FSH = follicle-stimulating hormone, GnRH = gonadotropin-releasing hormone, HCG = human chorionic gonadotropin, HPG = hypothalamus pituitary gonad, LH = luteinizing hormone, PDA = patent ductus arteriosus, SD = disorders of sex development.

Keywords: aphallia, congenital anomaly, penis agenesis

1. Introduction

Agenesis of the penis is an extremely rare genitourinary occurring about once in 30 million births.[1] It was originally described by Imminger in 1853, and at this time, fewer than 100 cases have been reported worldwide.[2] Aphallia is caused by the failure of the genital tubercle to form or to fully develop. Clinical presentation is diagnostic; associated congenital anomalies involving both the genitourinary and other major organ systems are common. Both immediate and long-term management of aphallia patients pose a great dilemma. Herein, we describe a case of total absence of the penis and discuss briefly the dilemmas associated with the management of such patients.

2. Ethical statement and consent

The institutional review board and ethic committee of Plastic Surgery Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College approved the ethical, methodological, and protocol aspects of this investigation. The ethical approval number was 2019.05. We confirm that all methods in the present study were carried out in accordance with the relevant guidelines and regulations. Informed written consent was obtained from the patient for publication of this case report and accompanying images.

3. Case presentation

A 3-month-old was brought to our hospital by his parents with the complaints of an absence of penis since birth and urine being passed rectally. When he was born, he was registered as a boy due to his chromosomes being 46XY, although he had 9qh+. At local

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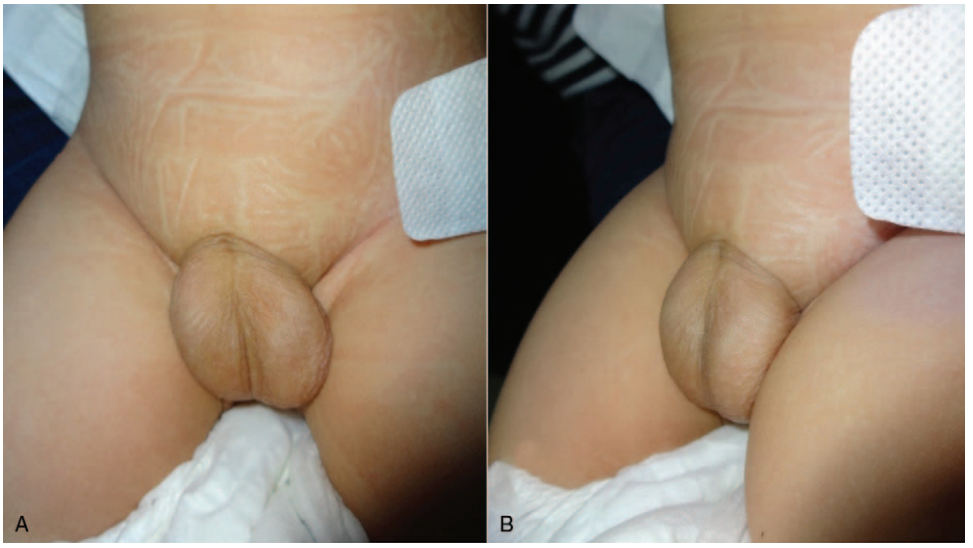

Figure 1. (A) Frontal; (B) Lateral. Absence of phallus with well-developed scrotum and fully descended testes.

examination, there was a total absence of the penis; however, the scrotum was well developed, and the testes were palpable bilaterally (Fig. 1). The anal opening was located normally, and no urethral orifice could be identified (Fig. 2). There was no other identifiable external anomaly. Analysis of the chromosomal karyotype of this family showed 46,XX with 320 to 400 bands without any abnormality (mother) (Fig. 3) and 46,XY,9qh+ (father and son) (Fig. 4). Echocardiographic assessment of the child revealed that he also suffered from patent ductus arteriosus (PDA), tricuspid regurgitation, pulmonary hypertension, and atrial septal defect (ASD). Ultrasound of the scrotum showed the presence of 2 normal testes and epididymes. Instillation of contrast into the rectum and examination by abdominal computed tomography-digital subtraction angiography (CT-DSA) demonstrated a thin tract opening in the rectum, suggesting a urethrorectal fistula. We explained the nature of the abnormality and management options to the parents. However, they did not decide whether to accept treatment and left our hospital without any further contact. The child has been lost to follow up.

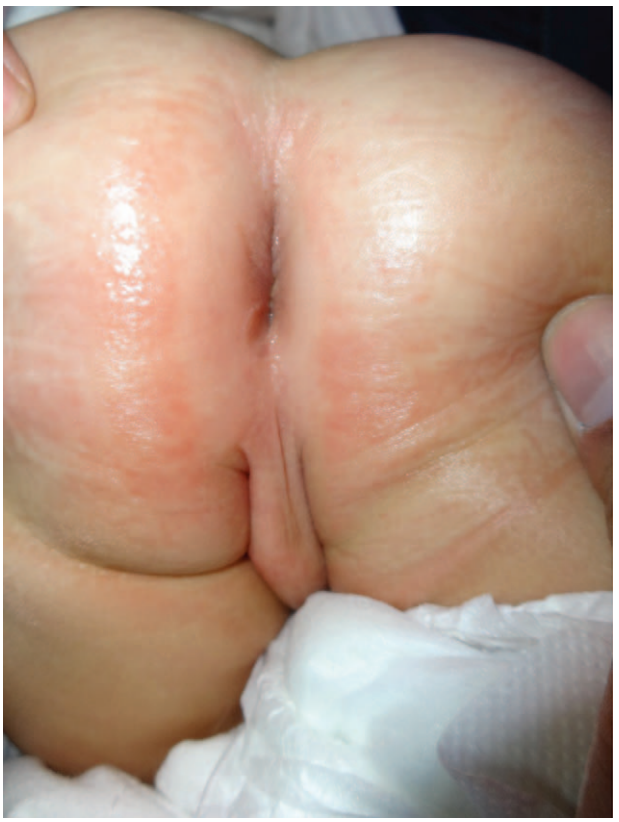

Figure 2. The anal opening is located normally, no urethral orifice could be identified.

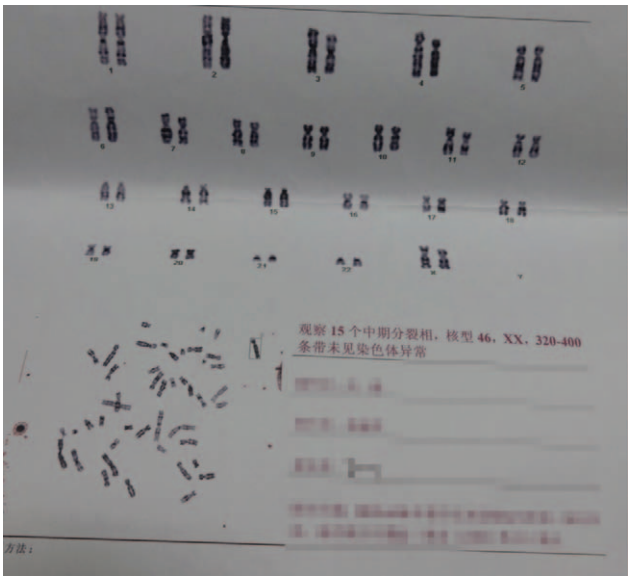

Figure 3. Analysis of chromosomal karyotype of mother showed 46,XX, 320–400 bands without abnormality.

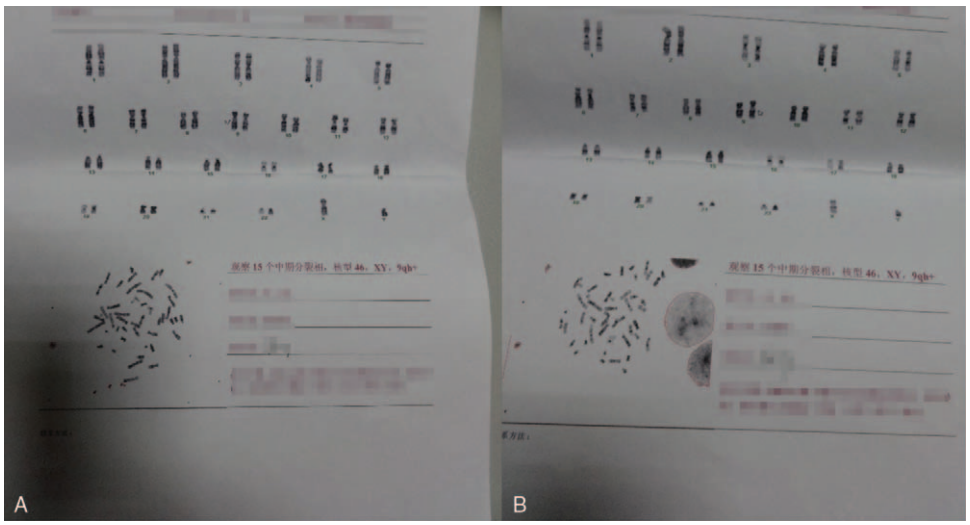

Figure 4. (A) Father; (B) Son. Analysis of chromosomal karyotype of father and son showed 46, XY,9qh+.

4. Discussion

From the 8th week of gestation, maternal placental chorionic gonadotropin begins to stimulate Leydig cells to secrete testosterone, which is converted into dihydrotestosterone (DHT) that regulates differentiation and growth of the penis.[3,4] Penis differentiation finishes at the 12th week of gestation. During that time, the genital tubercle differentiates into glans, the genital fold turns into the scapus penis, and the genital sac moves to the midline and becomes the scrotum.[5] Penile agenesis has been said to result from either the absence of formation of the genital tubercle or its failure to develop.[6] Penis growth during mid to late gestation occurs with the influence of androgens. The development of the penis mainly depends on testosterone secreted by Leydig cells of the testis, which is converted into DHT by 5α-reductase, targeting androgen receptors.[7] Human chorionic gonadotropin (HCG) secreted by the placenta at 12th week of gestation stimulates differentiation of Leydig cells and secretes testosterone.[8] By week 12, the hypothalamus and pituitary reach maturity. The gonadotropin-releasing hormone (GnRH) produced by the hypothalamus stimulates the anterior pituitary to secrete gonadotropins, including luteinizing hormone (LH) and follicle-stimulating hormone (FSH), both of which work with HCG to stimulate testosterone secretion by Leydig cells of testis and its conversion to DHT, which combine with receptors on target cells to regulate penile development and maturation.[9] Therefore, any abnormalities in the hypothalamus-pituitary-gonad axis (HPG axis) would impair development of the penis. In our case, there may be a disturbed signal transduction system during gestation. However, Joshi et al[10] holds that, in most instances, the karyotype is 46,XY with a normal constellation of sex hormones, as the pituitary gonadal axis is intact. Cases of ectopic urethral openings were thought to represent the total absence of the genital tubercle.[11] In the present case, a thin tract opening was found within the rectal wall and would, according to the aforementioned reasoning, represent the absence of the genital tubercle.

Heterochromatin is a term to describe chromosomal region that cannot be decondensed at anaphase of mitosis. It exists in all eukaryotic chromosomes and is usually located in chromosomal regions where there are less genes, such as around centromeres.[12] Initially, researchers believed that heterochromatin participated in chromosomal movement during mitosis and meiosis with certain structural functions but without gene activity. However, studies in recent years have suggested that heterochromatin may play an important role in protecting and regulating the expression of some structural genes.[13] Secondary constriction polymorphisms of the long arm of a chromosome (qh+) are the most common chromosomal polymorphisms, which when it occurs in chromosome 9 heterochromatin is called 9qh+. Both father and son in the presented case possessed 9qh+. Chromosomal polymorphisms follow Mendelian law with an incidence of 2.6%.[14] Research indicates that 9qh+ itself would not affect the health, but it may affect protecting and regulating functions that could lead to hereditary diseases or susceptibility to congenital disease.[15] The above abnormities may account for the congenital absence of the penis, congenital heart disease (CHD), and congenital urethrorectal fistula (CUF) of the patient. Because there were no other data of gene or hormone levels, we could not make an exact judgment about this patient.

Aphallia should be differentiated from concealed penis, epispadias, hypospadias, micropenis, rudimentary penis, intrauterine amputation of penis, and disorders of sexual development.[11] In the 1970 edition of Urology by Campbell and Harrison, Bunge[16] pointed out in the chapter titled Intersexuality: "We are not born with an innate attitude of identity, and how we think of ourselves is a reflection of what our parents thought we were and how we were reared." Sex identity begins at birth with the assignment of sex, and the attitudes of others by daily acts create and reinforce who we are in the ensuing months. Current thinking does not predicate the final labeling, and the morphology of the external genitalia will assume the most important feature and might be contradictory to gonadal or genetic sex.[10] Earlier reports concerning the management of aphallia had advocated phalloplasty; however, the majority of authors recommend unequivocal assignment of the female gender at birth.[17]

The patient in our study was too young to make a decision, and his parents had not yet decided whether to accept treatment and left our hospital without further contact. Thus, it is difficult to track him for follow-up planning. For this case, generally

speaking, apart from treating of CHD and CUF, the important issue is sex determination, which includes chromosomal sex; sex of the gonads; and the genital, hormonal, psychological, and social genders. The team should include a pediatrician, a urologist, a geneticist, an endocrinologist, and a mental health expert. To determine the sex requires weighing the pros and cons and proceeding to a comprehensive consideration as to whether to deliver a phalloplasty or vaginoplasty. Parents should be informed about the devastating outcomes of this anomaly and invited to regular follow-up visits with the urologist.

5. Conclusion

This case demonstrates a patient who suffered from the congenital absence of the penis, which, because of its rarity, must be considered exceptional. Follow-up treatment and psychological care are both important. Treatment of aphallia presents many challenges, and it involves a multidisciplinary approach. Early assignment of gender avoids confusion and contradiction. Parental confidence solidifies the child's own confidence in his or her gender.

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Author contributions

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Writing – original draft: Shuai Qiang.
Writing – review and editing: Shuai Qiang.

References

[1] Kessler WO, McLaughlin AP3rd. Agenesis of penis. Embryology and management. Urology 1973;1:226–9.
[2] Rattan KN, Kajal P, Pathak M, et al. Aphallia: experience with 3 cases. J Pediatr Surg 2010;45:e13–6.
[3] Traishab AM, Kim NN. Testosterone and erectile function: from basic research to a new clinical paradigm for managing men with androgen insufficiency and erectile dysfunction. Eur Urol 2007;52:54–70.
[4] Venkatesh T, Suresh PS, Tsutsumi R. New insights into the genetic basis of infertility. Appl Clin Genet 2014;2014:235–43.
[5] Yaron Z, Ronni G, Shlomo M, et al. The development of the fetal thymus: an in utero sonographic evaluation. Ultrasound Obstet Gynecol 2001;22:129–31.
[6] Gillies H. Congenital absence of the penis. Br J Plast Surg 1948;1:8–28.
[7] Imperato-McGinley J, Guerrero L, Gautier T, et al. Steroid 5 (-reductase deficiency in man: an inherited form of male pseudohermaphroditism. Science 1974;186:1213–5.
[8] Wen Q, Cheng CY, Liu Y-X. Development, function and fate of fetal Leydig cells. Semin Cell Dev Biol 2016;59:89–98.
[9] Roberts KP, Pryor JL. Anatomy and physiology of the male reproductive system. Male Infertility and Sexual Dysfunction 1997; Springer, 1–21.
[10] Joshi A, Gross J, Thomalla JV. Congenital aphallia: review of pathogenesis and current treatment guidelines. Urology 2015;86:384–7.
[11] Roth JKJr, Marshall RH, Angel JR, et al. Congenital absence of penis. Urology 1981;17:579–83.
[12] Horvath JE, Schwartz S, Eichler EEJGR. The mosaic structure of human pericentromeric DNA: a strategy for characterizing complex regions of the human genome. Genome Res 2000;10:839–52.
[13] Misteli TJS. Protein dynamics: implications for nuclear architecture and gene expression. Science 2001;291:843–7.
[14] Suganthi R, Vijesh VV, Vandana N, Fathima Ali Benazir J. Y chromosomal microdeletion screening in the workup of male infertility and its current status in India. Int J Fertil Steril 2014;7:253–66.
[15] Grewal SI, Elgin SC. Heterochromat: new possibilities for the inheritance of structure. Curr Opin Genet Dev 2002;12:178–87.
[16] Bunge RE. Campbell MF, Harrison JH. Intersexuality. Urology 3rd ed. Philadelphia, PA: WB Saunders Company; 1970;1685–7.
[17] Young HH, Cockett A, Stoller R, et al. The management of agenesis of the phallus. Pediatrics 1971;47:81–7.