Fellow Column: Aphallia in a Neonate with Kleinfelter's Syndrome: A Case Report

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Key Words:

Aphallia
Klinefelter Syndrome
Horseshoe Kidney
Intersex
Congenital Absence of the Penis

Introduction:
Aphallia is an extremely rare congenital disorder usually recognized immediately following birth. The current estimated incidence is approximately 1 in 10-30 million births, and only about 100 cases have been reported in the literature. Given the rarity of the condition and the sizable diversity of associated genitourinary and non-genitourinary abnormalities, there is not a widely recognized standard of management of aphallia. Earlier approaches favored feminizing genitoplasty due in part to relative procedural simplicity and the prevailing philosophy that it is 'better to be incompletely female than inadequately male.' More contemporary approaches have been more often aimed at phalloplasty with the idea of surgically supporting a genetically normal male until old enough to gender self-identity. A review of the literature reveals no other reported cases of concomitant aphallia and Klinefelter syndrome, as in our patient, which complicates the selection of management.

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Due to both the intricate psychosocial elements and the unique anatomical complexities accompanying each case of aphallia, a multidisciplinary approach between the primary Neonatologist and specialists, including urology, endocrinology, and genetics, as well as psychosocial support for the family and patient, is favored. In this case report, the unique case of a neonate with aphallia and Klinefelter Syndrome will be presented along with the approach to management.

Case Presentation:

WH presented at birth with ambiguous genitalia and no clear urethral opening. He was born to a 20-year-old G1P0 mother with unremarkable prenatal workup and who denied substance use during pregnancy. His mother presented with PPROM at 29 weeks and was admitted for observation and management. A prenatal ultrasound at 33 weeks gestation was significant for a single umbilical artery, dilated large bowel, and a small left kidney with normal right kidney and bladder. The fetal echocardiogram was within normal limits. A C-Section was performed at 35w4d for anhydramnios and breech presentation. He cried spontaneously at birth, but required PPV and then NIMV for increased work of breathing and retractions. APGARs at 1 and 5 minutes were 8 and 8. Sex was unable to be determined at birth based on the external phenotype.

Urology was consulted immediately due to aphallia and concern for other urogenital anomalies (figure 1). Physical exam demonstrated palpable bilateral inguinal testes and an anteriorly displaced anus located at the base of the scrotal raphe without obvious urethral meatus. An abdominal and pelvic ultrasound were obtained on the day of birth and demonstrated bilateral inguinal testes and a horseshoe kidney. No Mullerian remnants were demonstrated, and there was no sign of obstructive uropathy. A spinal ultrasound showed no evidence of a tethered cord. Within the first 24 hours of life, he passed both stool and urine through the anteriorly displaced anus, suggesting likely pre sphincteric urethrorectal fistula (no visible meatus on the perineum (figure 2) per exam). Urology determined that there was no urgent need for surgical intervention.

Genetics was consulted and recommended obtaining a karyotype, chromosomal microarray, and chromosomal FISH. The karyotype was significant for sex chromosomes of XXY, consistent with Klinefelter Syndrome without noted mosaicism. Genetics also recommended an MRI of the abdomen and pelvis, which confirmed aphallia (as opposed to a concealed penis/rudimentary erectile tissue), horseshoe kidney, and bilateral inguinal testes. He also had a dilated colon, however, there was no evidence of Hirschsprung's disease on imaging, and he had normal stool output, so he was monitored clinically.

Endocrinology was also consulted to evaluate for possible coexisting conditions that may occur Klinefelter Syndrome in midline

Figure 2- Rash of secondary syphilis; CDC

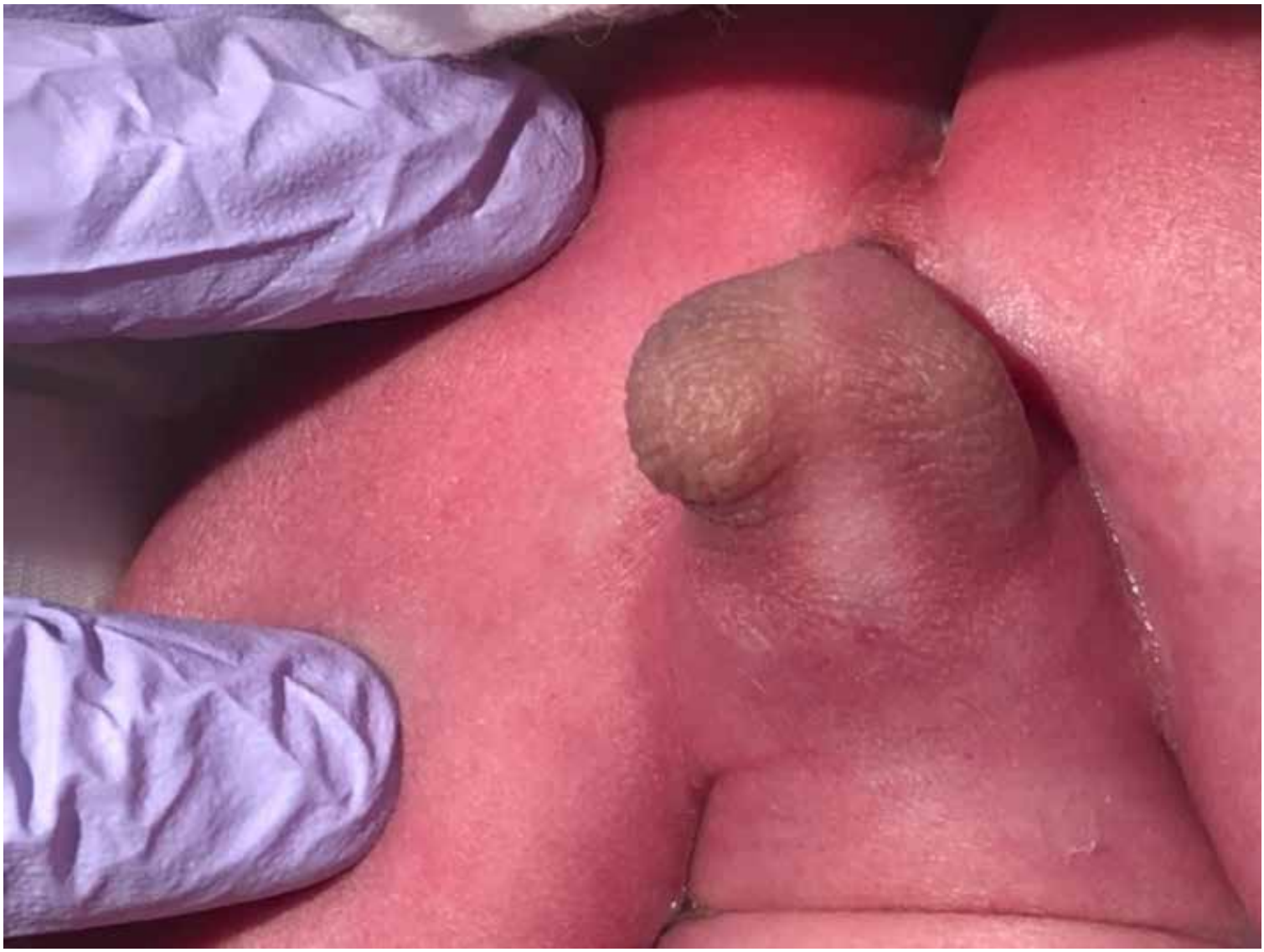

Figure 1- Morphologically normal scrotum with congenital absence of the phallus

congenital abnormalities such as aphallia, including hypopituitarism, adrenal insufficiency, and congenital adrenal hyperplasia. The initial workup done in the hospital was not concerning for congenital endocrine disorders (Additional labwork was still pending at the time of publication.).

Nephrology was also consulted due to persistently elevated serum creatinine for age with metabolic acidosis and hyperkalemia. He was diagnosed with renal tubular acidosis due to prematurity and was started on Bicitra. The RTA resolved prior to discharge, and he was weaned off Bicitra.

He initially had poor feeding requiring an NG tube, although he eventually began to nipple all his feeds without issue.

A multidisciplinary family meeting was held prior to discharge, during which a plan for future surgical intervention and management was discussed with the parents, social workers, and specialist teams. At this meeting, the parents expressed their desire to raise him as a male, which was supported by the medical team and social worker.

Management and Outcome:

Given the rarity of aphallia and the multiple associated congenital anomalies, a multidisciplinary approach to management was initiated early by involving multiple specialists, including urology, nephrology, endocrinology, and genetics. WH was treated for 22 days in the NICU. The diagnosis of aphallia was made using MRI, as physical exam alone was not sufficient to determine if any remnants of erectile tissue were present. Urology was to continue to manage the urogenital abnormalities associated with aphallia as an outpatient. Urology determined that, as he was able to stool and urinate without intervention, and there was no evidence of hydronephrosis, no immediate surgical intervention was required during his stay.

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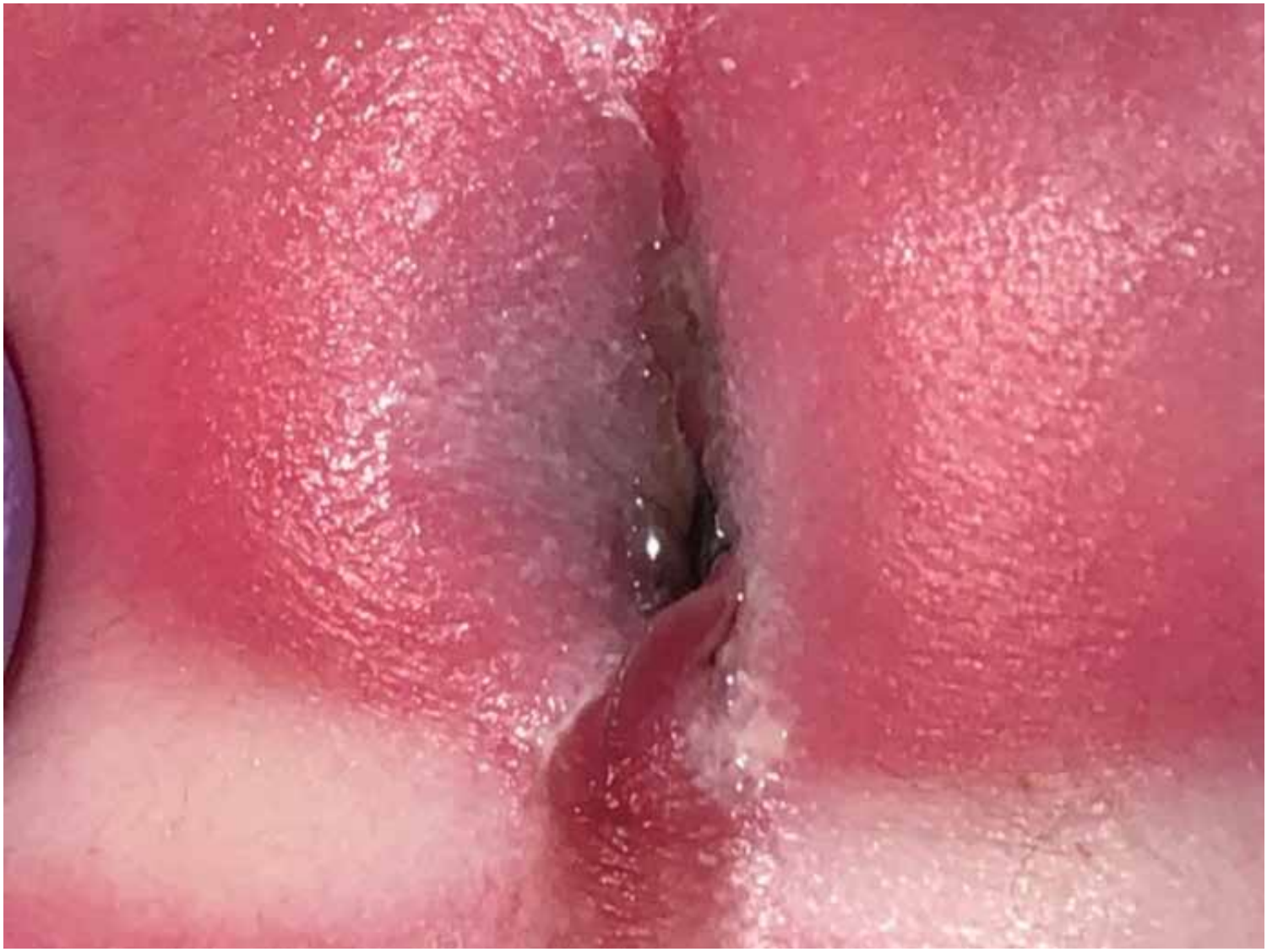

Figure 2: Perineum with anteriorly displaced anus with no visible urethral meatus, suggestive of a urethrorectal fistula

He will not require UTI prophylaxis as he has not had any UTI's, (although he is at increased risk) for UTI. The long-term plan for his management is to delay reconstructive surgery until he is post-pubertal to allow for physical and psychosocial development.

As his karyotype is significant for Klinefelter syndrome (XXY), he will continue to be followed by genetics and endocrinology. To determine if he has any other genetic abnormalities, a whole-exome sequencing sample was sent and is pending at the time of this case report. Klinefelter syndrome can have a significant impact on hormones, including hypogonadism. He will continue to be followed by endocrinology as he grows up to monitor for endocrine disorders.

Given the significant psychosocial impact aphallia can have on patients and their families, social work will also continue to follow and provide resources for the family. The family was provided resources for counseling in the future.

Discussion:

Aphallia is a rare congenital anomaly, often presenting with multiple associated abnormalities requiring a multidisciplinary approach. As defined in the literature, Aphallia is the congenital absence of the penis due to the developmental failure of the genital tubercle. The etiology of aphallia is unknown, and the incidence appears to be sporadic. Given the rarity of this condition and the wide spectrum of presentation, there has yet to be posited a definitive, standardized management strategy. Based on the Skoog's anatomical classification of the site of the urethral meatus in relation to the anus, WH has pre-sphincteric aphallia, which is also associated with increased mortality and morbidity. Based upon a

systematic review of the published literature, there are no other reports of patients with aphallia and Klinefelter syndrome. This case, therefore, presents a unique challenge, as Klinefelter syndrome is associated with multiple other abnormalities, including hypogonadism, gynecomastia, infertility, and cognitive/developmental delays. It may also suggest the implication of the sex chromosomes in the pathogenesis of aphallia, and such a case may help guide further research into the etiology of this phenomenon (just my thought, up to you guys to include or not).

Previous case studies and reviews prior to 1997 recommended early feminizing genitoplasty and raising the child as a female with female hormone replacement therapy. This was partially due to the increased difficulty of phalloplasty compared to vaginoplasty, as well as the concern for the presumed devastating psychosocial impact of being raised an aphallic male. However, follow up studies have shown that patients that underwent early feminizing genitoplasty had a high rate of gender dysphoria, most likely secondary to prenatal and early neonatal androgen imprinting prior to surgical intervention. Therefore, most surgeons and physicians recommend raising the child based upon their chromosomal sex and waiting until post-puberty for genital reconstruction surgery to allow the patient to have input on their surgical reconstruction. An endocrinologist helps manage hormone therapy in the context of pubertal changes. This patient's Klinefelter diagnosis is likely to require hormone replacement therapy due to hypogonadism; he will be followed closely by endocrinology.

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Irrespective of the patient's choice regarding genitoplasty, close follow up starting at a young age with a psychologist helps patients with aphallia navigate the significant psychosocial aspects of the condition. Klinefelter syndrome will add a layer of complexity to the already burdensome psychological impact of this condition, given it is associated with feminizing characteristics such as gynecomastia, as well as cognitive delays that may make therapy more difficult. In this case, it will be especially crucial for there to be open and active lines of communication between specialists, therapists, the patient's family, and (when he is old enough) the patient himself.

References

1. *Aslanabadi S, Zarrintan S, Abdollahi H, Rikhtegar R, Beheshtirouy S, Badebarin D, Baky Fahmy MA (2015) A rare case of aphallia with right kidney hypoplasia and left kidney dysplasia. Arch Iran Med 18(4):257–259. https://doi.org/015184/AIM.0013*
2. *Bahe P, Sharma D, Bahe A, Pandita A (2016) An infant with aphallia and its associated complication: a rare case report and review of literature. Trop Doct 46(1):51–3. https://doi.org/10.1177/0049475515576675*
3. *Friedman AA, Zelkovic PF, Reda EF, Franco I, Palmer LS (2016) Male and female aphallia associated with severe urinary tract dysplasia. J Pediatr Urol 12(4):268e1–7. https://doi.org/10.1016/jpurol.2016.04.040*
4. *Gabler, T., Charlton, R., Loveland, J., & Mapunda, E. (2018). Aphallia: a review to standardize management. Pediatric Surgery International, 34(8), 813–821. doi: 10.1007/s00383-018-4271-z*
5. *Gerard-Blanluet M, Lambert V, Khung-Savatovsky S, Perrin-Sabourin L, Passemard S (2011) Aphallia, lung agenesis and multiple defects of blastogenesis. Fetal Pediatr Pathol 30(1):22–6. https://doi.org/10.3109/15513815.2010.494698.*
6. *Gouvea JJ, Garrone G, da Cruz ML, Martins GM, Parizi JL, Oliveira DE, Ortiz V, Macedo A Jr (2015) Penile prosthesis implantation in a patient with congenital aphallia treated using the De Castro technique 10 years previously. Is it feasible? J Pediatr Urol 11(5):287–288. https://doi.org/10.1016/j.jpurol.2015.05.022*
7. *Goyal A, Bianchi A (2014) The parascrotal flap phallo-urethroplasty for aphallia reconstruction in childhood: report of a new technique. J Pediatr Urol 10(4):769–72. https://doi.org/10.1016/j.jpurol.2014.01.007*
8. *Joshi A, Gross J, Thomalla JV (2015) Congenital aphallia: review of pathogenesis and current treatment guidelines. Urology 86(2):384–387. https://doi.org/10.1016/j.urology.2015.04.031*
9. *Kane AD, Ngom G, Ndour O, Alumeti DM (2011) Aphallia: a case report and literature review. Afr J Paediatr Surg 8(3):324–325. https://doi.org/10.4103/0189-6725.91675*
10. *Macedo A Jr, da Cruz ML, Martins GM, Parizi JL, Oliveira DE, Ortiz V (2015) Neophalloplasty to congenital aphallia using two transverse skin-flaps: an alternative approach. J Pediatr Urol 11(5):289–90. https://doi.org/10.1016/j.jpurol.2015.05.025*
11. *Oliveira DEG, da Cruz ML, Luquori R, Garrone G, Leslie B, Ottoni SL, Souza GR, Ortiz V, de Castro R, Macedo A Jr (2016) Neophalloplasty in boys with aphallia: a systematic review. J Pediatr Urol 12(1):19–24. https://doi.org/10.1016/j.jpurol.2015.10.003*
12. *Rattan KN, Kajal P, Pathak M, Kadian YS, Gupta R (2010) Aphallia: experience with three cases. J Pediatr Surg 45(1):E13–E16. https://doi.org/10.1016/j.jpedsurg.2009.10.057*
13. *Skoog SJ, Belman AB (1989) Aphallia: its classification and management. J Urol 141(3):589–92. https://doi.org/10.1016/S0022-3468(89)80153-8*
14. *Willihnganz-Lawson KH, Malaeb BS, Shukla AR (2012) De Castro technique used to create neophallus: a case of aphallia. Urology 79(5):1149–1151. https://doi.org/10.1016/j.urology.2011.10.004*
15. *Hendren WH (1997) The genetic male with absent penis and urethrorectal communication: experience with 5 patients. J Urol 157(4):1469–1471. https://doi.org/10.1016/S0022-5347(01)65026-2*

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