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Complete Androgen Insensitivity Syndrome Diagnosed in Infancy: A Case Report

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ABSTRACT

Complete androgen insensitivity syndrome (CAIS) is a rare X-linked disorder characterized by a 46 XY karyotype and phenotypically female external genitalia due to complete end-organ resistance to androgens. Most cases are diagnosed in adolescence during evaluation of primary amenorrhea. Diagnosis in infancy is less common and usually occurs when inguinal masses or hernias are evaluated. We report the case of a 6-month-old infant with CAIS who presented with female-like external genitalia and inguinal swelling, highlighting the diagnostic approach, differential diagnoses, and clinical management considerations.

Keywords: Androgen insensitivity syndrome, 46 XY DSD, inguinal hernia, karyotype

INTRODUCTION

Disorders of sex development (DSD) encompass a spectrum of congenital conditions in which chromosomal, gonadal, or anatomical sex is atypical. (1) Among these, complete androgen insensitivity syndrome (CAIS) is one of the most common causes of 46 XY DSD presenting with a female phenotype. (2) CAIS results from pathogenic variants in the androgen receptor (AR) gene located on Xq11–12, leading to a complete inability of target tissues to respond to androgens. (3)

Individuals with CAIS typically present with normal female external genitalia, absent uterus and fallopian tubes, undescended testes, and a blind-ending vagina. (4) The gonads are often located intra-abdominally or in the inguinal canal and are at increased risk of malignant transformation after puberty. (5) Most cases are identified during adolescence because of primary amenorrhea, but diagnosis in infancy can occur when inguinal swellings are investigated, particularly in phenotypic females. (6)

We present the case of a 6-month-old infant with a 46 XY karyotype, reared as female, who was diagnosed with CAIS following evaluation of inguinal swelling.

CASE PRESENTATION

A 6-month-old infant reared as a girl was brought by her parents to our hospital with the complaint of a globular swelling in the right inguinal region noted since the age of 1 month. The child was born to a non-consanguineous couple as the second child, at term by lower segment cesarean section. She cried immediately after birth and was assigned female gender based on external

genitalia with no atypical genital features observed at that time.

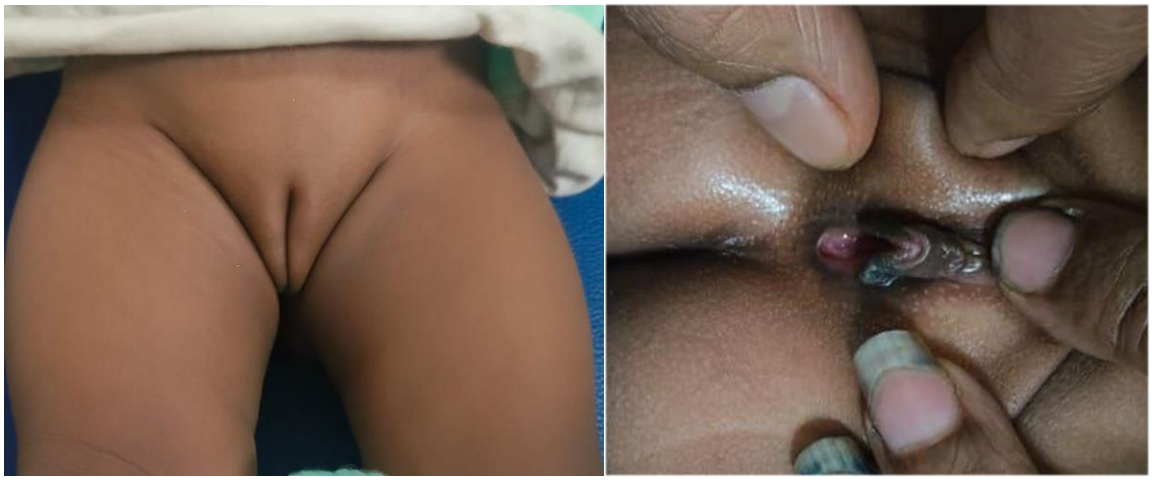
There were no perinatal complications such as poor feeding, vomiting, or hypoglycemia. At 1 month of age, parents noticed swelling in the right inguinal region, more prominent when the infant was crying. Developmental milestones were appropriate for age, and the infant was exclusively breastfed. There was no family history of infertility, atypical genitalia.

On general examination, the infant was active, with stable vital signs: BP (Right Upper Limb) 87/62 mmHg, PR 120/min, RR 40/min. Anthropometry revealed a length of 61 cm (−2.09 SDS) and a weight of 5.6 kg (−2.19 SDS).

External genital examination showed:(Figure 1A, 1B)

- Female-like external genitalia
- Two perineal openings
- Completely unfused labioscrotal folds
- Phallus length of 1 cm
- Bilateral palpable gonads in the inguinal region (~1 mL each), with no palpable groove.

The External Masculinization Score (EMS) was 2/12, and the External Genitalia Score (EGS) was 2/12. Systemic examination was unremarkable.



(Figure 1a: complete female-like genitalia, Figure 1b: two urogenital openings with completely unfused labioscrotal folds)

Investigations

Karyotype was 46 XY, Ultrasonography of the pelvis showed bilateral testes present in the inguinal region, MRI abdomen and pelvis showed bilateral undescended testis-like structures near the external inguinal ring (right 9 × 7.3 × 6 mm; left 9.7 × 10 × 5 mm), right inguinal hernia containing mesentery and bowel loops, absent uterus, ovaries, prostate, and seminal vesicles.

Table 1: Hormonal profile at 5 months of age.

Parameter	Result	Reference Range
LH	6.8 IU/L	0.8 – 7.6 IU/L
FSH	2.8 IU/L	0.7- 11.1 IU/L
Testosterone	25 ng/dL	Male minipuberty peak: up to 250 ng/dL
17-OH Progesterone	0.37 ng/mL	(<2ng/ml)
8 am Cortisol	10.9 µg/dL	5–25 µg/dL
ACTH	26 pg/mL	< 46 pg/mL
Sodium/Potassium	135 / 5.17 mmol/L	130-140 / 3.5-5.5 mmol/L
Progesterone	< 0.5 ng/mL	Normal

Whole-exome sequencing identified a likely pathogenic variant in the androgen receptor, causing androgen insensitivity syndrome. (Figure 2) The final diagnosis was CAIS.

Gene (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
***AR* (+)** (ENST00000374690.9)	Exon 6	c.2338C>T **(p.Arg780Trp)**	Homozygous	Androgen insensitivity syndrome (OMIM#300068) / Partial androgen insensitivity with or without breast cancer (OMIM#312300)	X-linked recessive	Likely Pathogenic **(PM1, PM2, PP3, PP5)**

(Figure 2: Whole exome sequencing)

DISCUSSION

CAIS is an X-linked recessive disorder with an estimated incidence of 1 in 20,000 to 1 in 100,000 genetic males. (7) Mutations in the androgen receptor gene lead to complete resistance of target tissues to androgens. (8) Despite normal or even elevated androgen levels, the absence of receptor function results in female external genitalia development, because external genitalia in the fetus are determined by androgen action rather than karyotype. (9)

Affected individuals typically present during adolescence with primary amenorrhea and normal breast development but sparse or absent pubic and axillary hair. (10) However, in some cases — like the present one — the diagnosis is made in infancy when inguinal swellings (testes) are evaluated in phenotypic girls. (11) Our patient presented similarly, with inguinal swelling. In the hormonal profile during infancy, testosterone levels may show a "minipuberty" surge in typical male infants, which may be blunted or normal in CAIS. (12) In our patient, testosterone was low-normal for male minipuberty, and LH was on the higher side, compatible with androgen resistance.

The differentials of CAIS could be due to 17β-HSD3 deficiency, leading to impaired testosterone biosynthesis, typically with female like genitalia at birth and virilization at puberty (13), 17α-hydroxylase deficiency, characterized by female like genitalia, hypertension, and hypokalemia (14), 3β-HSD deficiency, usually presents with salt-wasting, pigmenatation and undervirilization (15), Gonadal dysgenesis, associated with dysgenetic gonads and presence of Müllerian structures. (16)

In our case, the absence of a uterus, normal electrolyte levels, and normal cortisol ruled out adrenal causes. Genetic confirmation of an Androgen receptor mutation established CAIS.

Management of CAIS requires a multidisciplinary approach involving endocrinologists, geneticists, surgeons, and psychologists. (17) Key aspects include:

1. **Gender assignment:** Most CAIS patients are raised as females due to the normal female phenotype and gender identity. In our case, we advised the same to continue raising as a female.
2. **Gonadectomy:** Testes are often retained until after puberty to allow for spontaneous breast development via aromatization of androgens. Gonadectomy is then recommended due to the risk of gonadoblastoma or seminoma (2–5% risk in adolescence, increasing with age). (18) The same has been planned in our case as well.
3. **Hormone replacement therapy:** Estrogen replacement is initiated after gonadectomy to maintain secondary sexual characteristics and bone health. (19)
4. **Psychological support and genetic counseling:** Families should receive appropriate counseling regarding the nature of the condition, fertility options, and long-term care. (20)

CONCLUSION

CAIS should be considered in any phenotypic female presenting with an

inguinal hernia or palpable gonads. Early recognition and diagnosis through appropriate imaging, hormonal evaluation, and genetic testing enable optimal clinical management and informed decision-making. A multidisciplinary approach is essential for gender assignment, gonadal management, hormone replacement therapy, and psychosocial support.

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REFERENCES

1. Hughes IA, Houk C, Ahmed SF, Lee PA. Consensus statement on management of intersex disorders. Arch Dis Child. 2006;91(7):554–63.
2. Ahmed SF, Achermann JC, Arlt W, Balen AH, Conway G, Edwards Z, et al. UK guidance on management of disorders of sex development. Clin Endocrinol (Oxf). 2016;84(5):771–88.
3. Audi L, Fernández-Cancio M, Carrascosa A. Androgen insensitivity syndrome: clinical features and molecular basis. Horm Res Paediatr. 2010;73(2):81–92.
4. Melo KFS, Mendonca BB, Billerbeck AEC, Costa EMF, Inácio M, Silva FA, et al. Clinical, hormonal, behavioral, and genetic characteristics of androgen insensitivity syndrome. J Clin Endocrinol Metab. 2003;88(7):3241–50.
5. Deans R, Creighton SM, Liao LM, Conway GS. Timing of gonadectomy in CAIS: patient preferences. J Sex Med. 2012;9(2):585–9.
6. Qiao Y, Han B, Wang X, Zhang H, Chen J, Wang Y. Clinical characteristics of androgen insensitivity syndrome in infancy and childhood. Horm Res Paediatr. 2020;93(3):181–8.
7. Boehmer AL, Brinkmann AO, Sandkuijl LA, Halley DJJ, Niermeijer MF, Andersson S, et al. 46 XY DSD due to androgen insensitivity syndrome: frequency, clinical presentation, and molecular defects. J Clin Endocrinol Metab. 2001;86(8):4151–60.
8. Gottlieb B, Beitel LK, Nadarajah A, Paliouras M, Trifiro M. The androgen receptor gene mutations database (ARDB). Hum Mutat. 2012;33(1):87–97.
9. Hughes IA. Androgen insensitivity syndrome. J Med Genet. 2002;39(9):499–507.
10. van der Zwan YG, Callens N, van Kuppenveld JH, Drop SL, Wolffenbuttel KP, Cools M. Disorders of sex development: etiology and clinical management. Horm Res Paediatr. 2013;79(3):137–48.
11. Kuttenn F, Mowszowicz I, Wright F, Mauvais-Jarvis P. Complete androgen insensitivity syndrome in infancy. J Clin Endocrinol Metab. 1985;61(5):1003–8.
12. Kuiri-Hänninen T, Sankilampi U, Dunkel L. Activation of the hypothalamic-pituitary-gonadal axis in infancy. Horm Res Paediatr. 2014;82(2):73–80.
13. Mendonca BB, Gomes NL, Costa EMF, Inácio M, Belgorosky A, Rivarola MA, et al. 17β-HSD3 deficiency in 46 XY DSD: diagnosis and management. J Clin Endocrinol Metab. 2000;85(7):2660–7.
14. Zachmann M, Prader A, Kind HP, Häfliger H, Budliger H. 17α-hydroxylase deficiency: a rare form of congenital adrenal hyperplasia. J Pediatr. 1969;75(6):1027–37.
15. Moisan AM, Ricketts ML, Tardy V, Desrochers M, Sanchez R, Collu R, et al. New insight into the molecular basis of 3β-hydroxysteroid dehydrogenase deficiency. J Clin Endocrinol Metab. 1999;84(12):4410–6.
16. McCann-Crosby B, Sutton VR. Gonadal dysgenesis. Semin Reprod Med. 2012;30(5): 339–52.
17. Lee PA, Houk CP, Ahmed SF, Hughes IA. Consensus statement on management of intersex disorders. Pediatrics. 2006; 118(2):e488–500.
18. Cools M, Looijenga LHJ, Wolffenbuttel KP, Drop SL. Gonadal development and tumor formation at the crossroads of male and female sex determination. Sex Dev. 2011;5(4):167–80.
19. Wisniewski AB, Migeon CJ. Long-term outcomes in women with complete androgen insensitivity syndrome. Fertil Steril. 2002; 77(4):735–42.
20. Wisniewski AB, Mazur T. 46 XY DSD with androgen insensitivity syndrome: review and clinical management. Pediatr Endocrinol Rev. 2009;6(4):456–61.

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