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(CASE REPORT)

MRI Evaluation of a 46, XX Disorder of Sex Development Due to Classical 21-Hydroxylase Deficiency Congenital Adrenal Hyperplasia in a 6-Month-Old Infant: A Case Report

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Abstract

Background: Classical congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is the most common cause of 46,XX disorders of sex development (DSD), resulting in androgenic virilization of the female external genitalia. Magnetic resonance imaging (MRI) plays a central and increasingly indispensable role in the non-invasive characterization of internal genitourinary anatomy and in guiding multidisciplinary management.

Case Presentation: We report a 6-month-old infant registered as male at birth, followed for classical CAH due to 21-hydroxylase deficiency with bilateral adrenal hyperplasia on imaging, subsequently found to have a 46,XX karyotype on genetic testing. Clinical examination revealed pseudo-masculine external genitalia with Prader stage IV–V virilization and bilaterally non-palpable gonads. Biochemical workup confirmed markedly elevated 17-hydroxyprogesterone (17-OHP) and adrenal androgens. Pelvic MRI demonstrated probable clitoromegaly, an identifiable urogenital sinus with a vaginal component, a small median uterus with visible endometrium, bilateral hypoplastic ovarian structures, absence of any male gonadal structure, and left adrenal gland enlargement — consistent with 46,XX DSD with advanced virilization.

Conclusion: MRI is a valuable, non-irradiating modality for the comprehensive evaluation of internal genitourinary anatomy in 46,XX DSD secondary to CAH, providing essential information for sex assignment, surgical planning, and multidisciplinary management decisions.

Keywords: Congenital Adrenal Hyperplasia; Disorders of Sex Development; MRI; Prader Classification; Urogenital Sinus; Female Pseudohermaphroditism

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1. Introduction

Disorders of sex development (DSD) are congenital conditions defined by atypical chromosomal, gonadal, or anatomic sex differentiation, classified since 2006 into three karyotypic categories: 46,XX DSD, 46,XY DSD, and sex chromosome DSD [1,3]. Among these, classical CAH due to 21-hydroxylase deficiency is the leading cause of 46,XX DSD, accounting for ~95% of CAH cases [2,8]. Deficiency of the *CYP21A2*-encoded enzyme impairs cortisol and aldosterone synthesis, driving compensatory ACTH hypersecretion, bilateral adrenocortical hyperplasia, and shunting of 17-hydroxyprogesterone (17-OHP) and androstenedione into androgens [2,9]. In 46,XX fetuses, this androgen excess during the urogenital sinus development window (8–12 weeks of gestation) induces progressive external genital virilization — graded I to V on the Prader scale — while Müllerian structures remain intact given the absence of anti-Müllerian hormone (AMH) from fetal ovaries [2,3,9]. At Prader stage IV–V, the genitalia may be indistinguishable from a cryptorchid male, leading to male sex registration at birth and delayed diagnosis, with risk of life-threatening neonatal salt-wasting crises [2,6,9].

Imaging is central to the evaluation of DSD, particularly for localizing gonads, characterizing Müllerian structures, and defining urogenital sinus anatomy [3,5,10]. Ultrasonography (US) is the first-line modality in neonates, while MRI — offering superior soft-tissue contrast and multiplanar capability without ionizing radiation — is increasingly recognized as the reference standard for comprehensive internal anatomy characterization in complex DSD [3,10]. We report a 6-month-old infant with classical CAH and a 46,XX karyotype presenting with Prader stage IV–V virilization, in whom pelvic MRI was decisive for diagnosis and multidisciplinary management.

2. Case Presentation

A 6-month-old infant registered as male at birth was referred to the CHU Hassan II of Fès for evaluation of congenital adrenal hyperplasia with ambiguous external genitalia. Born at full term to non-consanguineous parents with no familial history of DSD, the infant presented in the neonatal period with a classical salt-wasting crisis (serum Na^+ 122 mEq/L; K^+ 6.8 mEq/L; hypoglycaemia) requiring emergency parenteral hydrocortisone, intravenous saline, and intensive resuscitation. Hormonal investigations revealed markedly elevated 17-OHP (210 ng/mL; normal <2 ng/mL) and ACTH (182 pg/mL; normal <46 pg/mL), confirming classical CAH due to 21-hydroxylase deficiency. Karyotyping returned 46,XX, establishing 46,XX DSD. Medical treatment with hydrocortisone (15 mg/m^2/day), fludrocortisone (0.1 mg/day), and sodium chloride supplementation was initiated.

At 6 months, physical examination revealed pseudo-masculine external genitalia with a prominent subpubic tubular structure resembling a penis — surrounded by significant perineal subcutaneous fat hypertrophy and terminating in a glans-like formation — along with fused labioscrotal folds mimicking an empty scrotum, and non-palpable gonads bilaterally, consistent with Prader stage IV–V virilization. No dysmorphic features or systemic anomalies were identified. Biochemical parameters at imaging are summarised in Table 1.

Table 1 Biochemical, hormonal, and genetic results. Abbreviations: 17-OHP, 17-hydroxyprogesterone; ACTH, adrenocorticotropic hormone; F, female.

Parameter	Result	Reference Range	Interpretation
17-OHP	210 ng/mL (neonatal) 85 ng/mL (at 6 months)	< 2 ng/mL	Markedly elevated — diagnostic
ACTH (08h00)	182 pg/mL (neonatal) 145 pg/mL (at 6 months)	< 46 pg/mL	Elevated
Cortisol (08h00)	3.2 µg/dL	6.2–19.4 µg/dL	Low
Testosterone	0.75 ng/mL	< 0.1 ng/mL (F, <6 mo)	Elevated
Sodium (neonatal nadir)	122 mEq/L	135–145 mEq/L	Severe hyponatraemia
Potassium (neonatal)	6.8 mEq/L	3.5–5.0 mEq/L	Hyperkalaemia
Karyotype	46,XX	—	Female genotype confirmed

Pelvic ultrasonography confirmed bilateral absence of scrotal or inguinal gonads, non-visualization of the ovaries, and suspected bilateral adrenal gland enlargement with cerebriform echotexture. Pelvic MRI (T2-weighted three-plane sequences and T1-weighted axial plane, 22/04/2026) was subsequently performed to provide comprehensive evaluation of internal genitourinary anatomy.

MRI Findings: The examination revealed:

- **External genitalia:** A tubular subpubic median structure resembling a penis, surrounded by significant perineal subcutaneous fat hypertrophy, opening anteriorly via a glans-like formation — consistent with clitoromegaly rather than a true penis (Figure 2a).
- **Urogenital sinus:** A median oblongue inter-vesico-rectal conduit with T2-hyperintense, T1-hypointense fluid retention, consistent with a vaginal component within a common urogenital sinus (Figure 2b).
- **Uterus:** A small median uterus measuring 17.3 × 5.6 mm on sagittal section, with an endometrial thickness of 1.5 mm — hypoplastic but morphologically identifiable (Figure 2b–c).
- **Ovaries:** Two small latero-uterine structures at the ovarian fossettes — 7 × 3 mm (right) and 7.2 × 3.3 mm (left) — non-follicular, consistent with bilateral hypoplastic ovaries (Figure 2c).
- **Absence of male structures:** Complete absence of scrotal tunics, epididymo-testicular complexes, and spermatic cords.
- **Adrenal glands:** Hypertrophy of the left adrenal gland, consistent with CAH-related bilateral adrenocortical hyperplasia (Figure 1). Semi-full bladder with thin walls and liquid content.

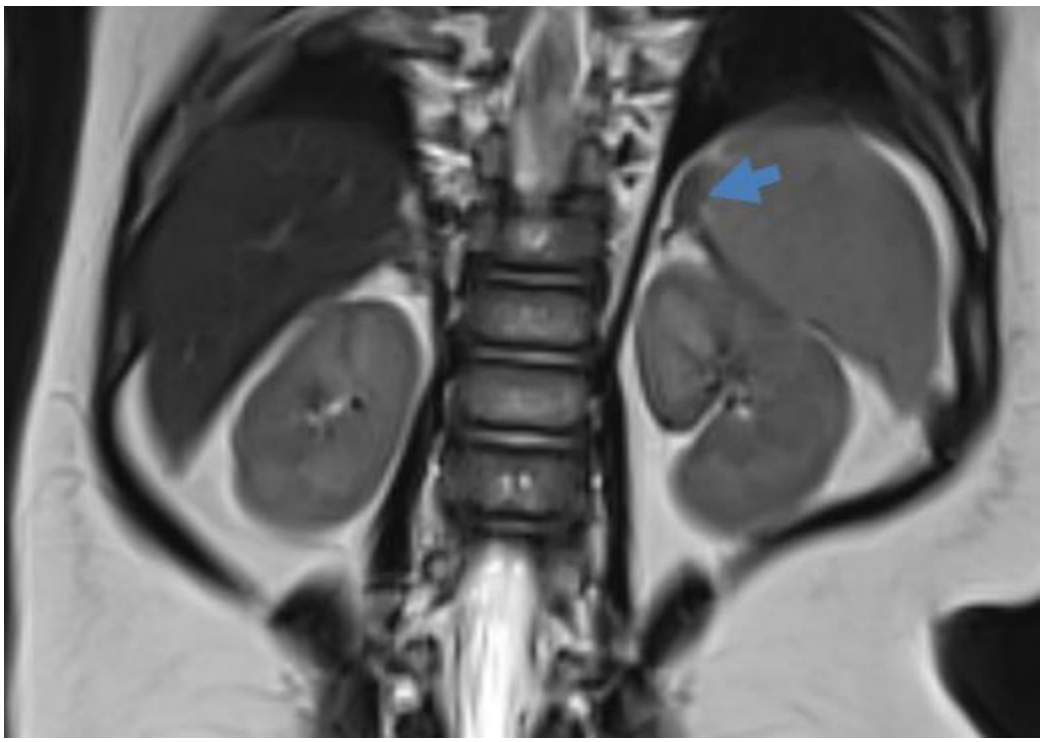

Figure 1 Adrenal MRI findings. Axial T2-weighted image demonstrating hypertrophy of the left adrenal gland (arrow), consistent with ACTH-driven bilateral adrenocortical hyperplasia in classical 21-hydroxylase deficiency CAH. The adrenal gland is enlarged and retains its adreniform shape.

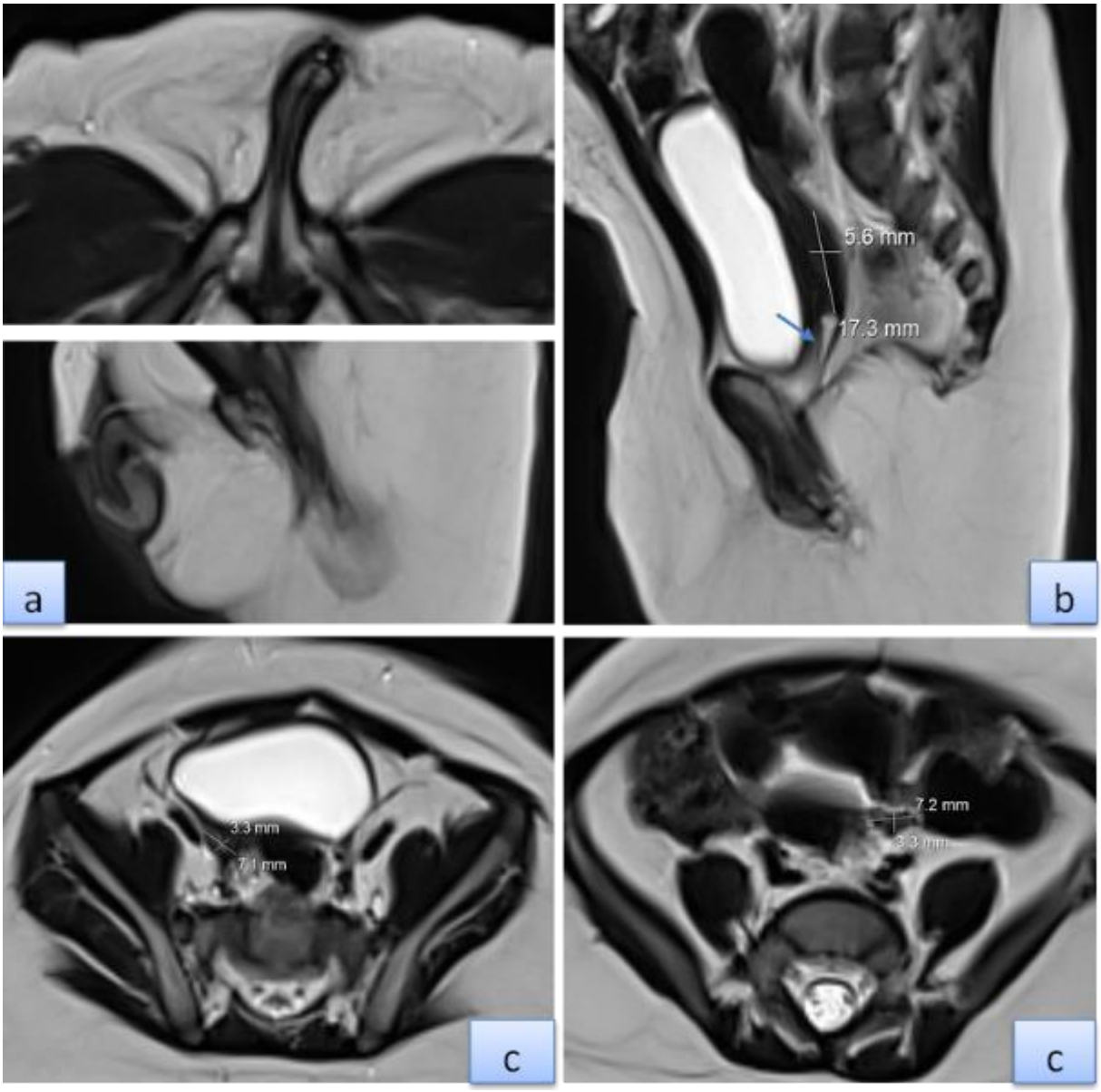

Figure 2 Pelvic MRI findings. (a) Subpubic median tubular structure with perineal subcutaneous fat hypertrophy and glans-like formation — clitoromegaly rather than a true penis. (b) Sagittal T2-weighted image showing the oblongue inter-vesico-rectal conduit (urogenital sinus, arrow) with T2-hyperintense fluid retention consistent with a vaginal component, and the small median uterus (arrowhead, 17.3 × 5.6 mm, endometrium 1.5 mm). (c) Axial T2-weighted image demonstrating two non-follicular latero-uterine structures at the ovarian fossettes (arrows) — 7 × 3 mm right, 7.2 × 3.3 mm left — consistent with bilateral hypoplastic ovaries. Absence of scrotal tunics, epididymo-testicular complexes, and spermatic cords is noted throughout.

The overall MRI conclusion was consistent with 46,XX DSD (female pseudohermaphroditism) with advanced virilization at Prader stage IV–V: probable clitoromegaly, urogenital sinus with vaginal component, hypoplastic uterus with visible endometrium, bilateral ovarian-type gonads, and complete absence of male gonadal structures.

The case was reviewed by a multidisciplinary team (endocrinology, radiology, pediatric surgery, genetics, psychology). Female sex assignment was confirmed, consistent with the 46,XX karyotype, preserved Müllerian structures, bilateral ovarian morphology, and absence of testicular elements. Hormonal optimisation was continued, and feminizing genitoplasty (clitoroplasty with neurovascular bundle preservation and vaginoplasty) was planned for a later stage.

3. Discussion

3.1. Pathophysiology of Virilization in 46,XX CAH

In 46,XX CAH due to 21-hydroxylase deficiency, impaired cortisol synthesis triggers ACTH-driven adrenal androgen excess, virilizing the female urogenital sinus at 8–12 weeks of gestation while Müllerian structures remain intact due to the absence of ovarian AMH [2,3,9]. Virilization severity follows the Prader grading : at stage IV–V, genitalia are indistinguishable from a cryptorchid male, leading to male sex registration at birth, delayed diagnosis, and risk of life-threatening adrenal crises [2,6,9].

3.2. Role of Imaging in 46,XX DSD

Imaging is central to DSD evaluation, aiming to localize gonads, characterize Müllerian and Wolffian structures, define urogenital sinus anatomy, and assess adrenal morphology [3,5,10]. US remains the first-line modality in neonates, where the characteristic cerebriform adrenal echotexture is highly specific for CAH [4,5,12]. Identification of the uterus and ovaries in an infant with non-palpable gonads strongly supports 46,XX DSD [5]. However, as in the present case, hypoplastic ovaries and small internal structures may not be visualized on US due to operator-dependent limitations [4].

MRI addresses these limitations through superior soft-tissue contrast resolution and multiplanar capability without ionizing radiation, and is increasingly considered the reference standard for comprehensive internal genitourinary anatomy characterization in complex DSD [3,10]. In the present case, MRI was decisive where US had been inconclusive, providing an exhaustive anatomical map: the nature of the external genital structure (clitoromegaly versus true penis), urogenital sinus anatomy with level and length of the urethrovaginal confluence — critical for surgical vaginoplasty planning — the uterus with visible endometrial stripe confirming Müllerian preservation and fertility potential, the bilateral ovarian-type gonads, and the complete absence of testicular tissue [3,5,10,11]. Adrenal MRI corroborated the diagnosis by demonstrating left adrenal hypertrophy with preserved adreniform shape, consistent with ACTH-driven cortical hyperplasia [4].

3.3. Sex Assignment and Multidisciplinary Management

Female sex assignment is recommended for 46,XX CAH individuals by the 2006 Chicago Consensus, given intact fertility potential, preserved Müllerian structures, and predominantly female gender identity in long-term follow-up [1,3]. MRI confirmed all anatomical criteria in our case: 46,XX karyotype, hypoplastic but intact uterus, bilateral ovarian-type gonads, and complete absence of testicular elements. Medical management (hydrocortisone and fludrocortisone) targets ACTH suppression [2,8,9]; feminizing genitoplasty (clitoroplasty and vaginoplasty) was deferred, consistent with current guidelines favouring individualized, staged approaches with emphasis on functional outcomes [1,3].

3.4. Diagnostic Challenges and Late Presentation

Male sex registration at birth due to Prader stage IV–V virilization — as in our patient — is a recognized diagnostic pitfall in 46,XX CAH, documented in multiple published cases [6,7]. These cases collectively underscore the critical importance of systematic neonatal screening programs based on 17-OHP measurement in dried blood spots, which remain the most effective strategy for early diagnosis, prevention of adrenal crises, and timely management [2,8,9].

4. Conclusion

This case of classical 21-hydroxylase deficiency CAH with Prader stage IV–V virilization in a 6-month-old 46,XX infant illustrates the indispensable role of pelvic MRI in the evaluation of severe 46,XX DSD. By simultaneously demonstrating clitoromegaly, a urogenital sinus with vaginal component, a hypoplastic uterus with endometrial stripe, bilateral ovarian-type gonads, and complete absence of male gonadal structures, MRI provided the comprehensive non-irradiating anatomical characterisation decisive for sex assignment, surgical planning, and multidisciplinary counselling. A systematic multidisciplinary approach — combining endocrine, genetic, radiological, surgical, and psychological expertise — remains essential in the management of these complex conditions.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no competing interests.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans

Statement of informed consent

Written informed consent was obtained from the patient's parents/legal guardians for publication of this case report and any accompanying radiological images. The patient's identity has been fully anonymized and no identifying information is disclosed.

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During the preparation of this manuscript, the authors used an AI language model to assist with language editing and drafting. All content was reviewed, edited, and validated by the authors, who take full responsibility for the accuracy and integrity of the published work.

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