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Case Report

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Partial Androgen Insensitivity Syndrome in a 16-Year-Old Presenting with Primary Amenorrhea: A Case Report

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Abstract

Partial Androgen Insensitivity Syndrome (PAIS) is a rare X-linked recessive disorder of sex development (DSD) characterized by resistance to androgen activity, affecting the morphogenesis and differentiation of androgen-responsive tissues. Caused by X-linked mutations in the androgen receptor (AR) gene, AIS encompasses a range of phenotypes from infertile males to phenotypically female individuals. It often presents with ambiguous genitalia and primary amenorrhea in adolescence, leading to diagnostic challenges and delayed management. We report the case of a 16-year-old phenotypically female patient from Pakistan who presented with primary amenorrhea. Clinical evaluation revealed ambiguous genitalia including clitoromegaly, hypospadias, a blind vaginal pouch, and bilateral inguinal masses. Hormonal assays demonstrated elevated gonadotropins with low testosterone levels. Karyotyping confirmed a 46,XY genotype. Imaging revealed the absence of Müllerian structures and bilateral inguinal testes. The patient and her family elected to pursue male gender identity, and a multidisciplinary team coordinated bilateral orchidopexy and excision of the vaginal sinus. This case underscores the importance of early recognition and comprehensive evaluation of primary amenorrhea, particularly in resource-limited settings. Timely diagnosis of PAIS allows for appropriate gender-affirming decisions, surgical management, and long-term hormonal therapy. Psychological support and family counselling are critical in optimizing patient outcomes.

Keywords:- Androgen Insensitivity Syndrome, Primary Amenorrhea, Disorders of Sex Development, Partial AIS, Orchidopexy.

INTRODUCTION

Androgen Insensitivity Syndrome, also known as testicular feminization syndrome, is a spectrum of disorders arising from varying degrees of androgen receptor (AR) resistance.[1] This results in an XY individual exhibiting a female or ambiguous phenotype, as androgens are critical for male sexual differentiation both prenatally and at puberty.[2] Partial AIS (PAIS) is the third most common cause of primary amenorrhea, following gonadal dysgenesis and Müllerian agenesis.[3]

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PAIS is graded based on genital phenotype[4]

1. Normal female genitalia with androgen-dependent hair development at puberty
2. Female phenotype with mild clitoromegaly or posterior labial fusion
3. Intermediate external genitalia with perineal urogenital sinus and labioscrotal folds
4. Predominantly male phenotype with perineal hypospadias, cryptorchidism, or bifid scrotum
5. Mild phenotype with isolated hypospadias and/or micropenis

AIS is typically categorized into complete (CAIS), partial (PAIS), and mild (MAIS) forms, as proposed by Quigley et al.[5]

CASE REPORT

We present the case of a 16-year-old phenotypically female patient with an XY karyotype, diagnosed as partial AIS following a two-year evaluation for primary amenorrhea. Examination revealed ambiguous genitalia including a vaginal sinus, 1.5 cm phallus, hypospadias, and bilateral undescended testes. Upon the patient and family's request to raise the child as male, bilateral orchidopexy and vaginal sinus excision were performed.

The patient appeared healthy, of normal intellect, with a height of 5'7" and weight of 60 kg. No facial or chest hair was noted. Laryngoscopy indicated excessive parapharyngeal fat. She had Tanner stage 3 breast and axillary hair development and a mildly feminine voice that reportedly deepened in the past year. Genital examination showed enlarged labia, clitoromegaly (>1 cm width, >2 cm length), a 3 cm blind vaginal pouch, and bilateral inguinal masses. There was no prior history of illness or surgery. She performed well in school and had no learning difficulties. Despite occasional aggression, she maintained good social interactions, preferring indoor activities. She resided with her grandmother, while her parents and siblings lived in a rural area.

The patient was born from a consanguineous marriage and had five sisters. A younger sister (age 2) was diagnosed with a similar disorder and is undergoing evaluation for masculinizing surgery. No additional relevant family history was reported.

Investigations:

Hormone Profile:

- Elevated FSH (56.32 mIU/mL)
- Elevated LH (28.69 mIU/mL)
- Elevated Androstenedione: 4.995 → 9.35 → >10 ng/mL over a month
- Normal 17-OH progesterone (0.945 ng/mL)
- Normal DHEA-S (292 µg/dL)
- Normal progesterone (<0.1 ng/mL)
- Low testosterone: 1.0 → 0.865 → 0.939 ng/mL
- **Karyotype:** 46, XY (male)

Imaging Investigations

An ultrasound abdomen was done which showed No uterus and atrophic ovarian structures. An MRI was done to confirm the findings. MRI showed no uterus or ovaries; both testes were located in inguinal canals. The right testis measured 2.2 × 1.7 cm, while the left testis measured 1.9 × 2.2 cms. The CPT urethrogram revealed distinct and separate openings for the vagina and urethra in the perineal region. Upon introducing contrast through the vaginal opening, imaging demonstrated a small, blind-ended vaginal pouch, with no opacification of endometrial cavities or fallopian tubes, suggesting their absence. Subsequently, diluted contrast was introduced through the urethral opening, which revealed a small-calibre urethra. The opacified urethra displayed a focal dilatation in its mid-segment; however, there was no evidence of stricture, filling defect, or any obstruction. The contrast flowed freely into the urinary bladder, and no extravasation into the surrounding soft tissues was observed, indicating the integrity of the lower urinary tract.

DISCUSSION

This report aims to highlight the importance of early recognition of PAIS in cases of primary amenorrhea. Though rare—affecting 1 in 20,000 to 99,000 genetic males[6]—PAIS is often misdiagnosed until puberty.[7] Early identification can improve quality of life by aligning physical treatment with gender identity, allowing timely gonadectomy to prevent germ cell tumors[8], and initiating hormone replacement therapy to prevent

complications like osteoporosis. Prompt psychological support and education are vital for patient and family well-being.[9] Patient underwent bilateral orchidopexy 5 months apart. Thereafter vaginal sinus excision was also done

CONCLUSION:-

The patient's findings confirmed a diagnosis of PAIS. In alignment with the patient's and family's wishes to transition to male gender identity, surgical interventions were undertaken. Further management included plans for hormone replacement therapy, hypospadias repair, and penile lengthening, coordinated with endocrinology, urology, and plastic surgery departments.

Conflict of interest

None

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