Successful Gender Reassignment in a Young Adult with 46,XY 17-Hydroxysteroid Dehydrogenase-3 Deficiency : A Case Report

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INTRODUCTION

- 17β-hydroxysteroid dehydrogenase-3 (17BHSD-3)[17-ketosteroid reductase –(KSR)] is required for the conversion of androstenedione (A) to testosterone (T)
- Testosterone is subsequently converted to dihydrotestosterone (DHT) which facilitates development of male external genitalia.
- 17BHSD-3 deficiency is a rare autosomal recessive disorder.
- World-wide incidence around 1 in 147,000 live births.
- However, 1 in 100-300 people among the in-bred Arab Population along the Gaza Strip.
- Most severe forms in 46XY individuals are assigned female gender at birth.
- At puberty, increased androgen levels occur from action of 17β-HSD isoenzymes in the testis, liver, and adrenals.
- Gender role changes were reported in 39–64% of 46XY cases with 17β-HSD-3 previously raised as girls.

CASE DESCRIPTION

- AP, first presented at age of 12 years, with phallic enlargement at puberty,
- Raised as a female.
- Parents insisted that external genitalia was clearly female at birth
- No other significant history
- 0/E: Tanner stages breast 2, pubic hair 4, stretched phallic length (SPL) 3.2cm, Prader 3.
- Weight: 38.5kg,(btw 3rd & 10th centile) Ht: 1.465m (25th centile)
- BP : 96/70 mmHg PR: 88bpm

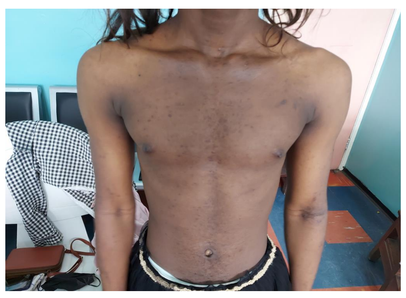
Investigations: Normal serum e/u/cr, testosterone: 11.20nmol/L↑(ref female 0.17-1.7, male : 0.34-19.0), cortisol : 210 nmol/L (240-618)
-could not afford 17hydroxyprogesterone (OHP) and karyotype then.

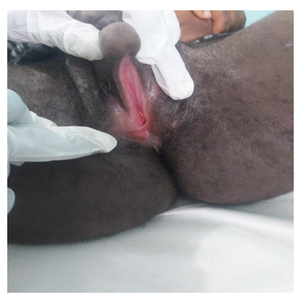
- "Pelvic USS showed uterus and ovaries".
- Presumptive diagnosis of SV CAH made and commenced on hydrocortisone tab, to expedite other investigations
- Defaulted for 4 years and then re-presented with absent female sexual characteristics and progressive masculinisation
- Karyotype : XY
- 2nd Pelvic USS : "uterine and ovarian structures, not visualised", advised MRI.
- MRI : absence of ovaries and uterus, blind ending vaginal pouch, bilateral inguinal testis and left para-testicular cyst
- HCG stimulation test: T/DHT ratio day 1: 4.95, day 4: 12.3 (<20nmol/L) and T/A ratio day 1: 0.22, day 4: 0.17 (>0.8) strongly suggestive of 17BHSD deficiency
- Laparoscopy: intra-abdominal left testis, intracanalicular right testis with normal vas deferens and pampiniform plexus bilaterally.
- Surgeons pexied gonads in scrotal sacs after biopsy
- Histology of gonadal biopsy showed germ cell aplasia.

Management

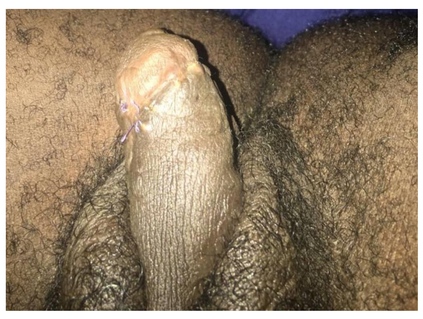
- Mental health assessment was done by the psychiatrist with a clinical interview and observation.
- Supportive psychotherapy was commenced. The pros and cons for gender reassignment were explored and options for coping identified.
- Strategies to address identified psychosocial concerns were explored.
- Without coercion requested for gender reassignment to male.
- Psychotherapy follow-up sessions continued.
- Has had orthoplasty with plans for urethroplasty after 6months
- Commenced on testosterone injections 250mg 2 weekly -for further masculinisation
- Plans on, for transition of care to the adult endo team

Before surgery (at presentation)





After Orthoplasty



DISCUSSION

- 17 BHSD deficiency was 1st characterised by *Saez et al* in mid -1970s
- Rare in Western population and even rarer in individuals of African ethnicity *(Bertelloni-2009)*
- Most common cause of 46XY DSD among the testosterone biosynthetic defects
- Prepubertal close differentials: AIS & 5ARD; At puberty: 5ARD
- Basal (puberty) or pre-pubertal HCG stimulated androgens ratios (A,T,DHT) are usually discriminatory *(Boehmer-1999,Rumsby 2019)* though pitfalls have been documented. *(Khattab-2015)*
- Molecular genetic mutation analysis gold standard for diagnosis.
- Factors contributing to gender change: body image perception, religion, family, and culture. Previous perinatal androgen exposure may also play a role. *(Khattab-2015, Cohen-Kettenis-2005)*

Limitations: *Unavailability of genetic mutation analysis*

CONCLUSION/TAKE HOME MESSAGES

- 17HSD-3 deficiency is a rare recessive disorder and important cause of 46XY DSD.
- Frequently assigned female gender at birth, but masculinisation occurs at puberty.
- The MDT needs to support the patient through the transition process if decision for gender change is made.
- Life-long care by the adult endocrinologist, surgeon and psychologist is essential especially because all the patients identified during adolescence, in literature were documented as infertile.
- Karyotyping remains an important investigation in evaluation of individuals with DSD for early diagnosis

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