5 Alpha Reductase deficiency; an important cause of 46 XY DSD: report of 3 cases within a family.

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August 29, 2022

Abstract

5 α reductase deficiency is a genetic disorder causing 46 XY disorder of sex development (DSD). Typical clinical feature is a male with female external genitalia or undervirilization at birth. Here we report 3 cases of this disorder within a family

Case Report

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Abstract: 5 α reductase deficiency is a genetic disorder causing 46 XY disorder of sex development (DSD). Typical clinical feature is a male with female external genitalia or undervirilization at birth. Here we report 3 cases of this disorder within a family.

Key Words: disorder of sex development, dehydrotestestrone, 5 alpha reductase deficiency

Introduction: 5α reductase is an enzyme responsible for conversion of testosterone to dehydrotestestrone in androgen target tissues. Deficiency of this enzyme results in abnormal male sexual development before birth and also during puberty[1]. This is a rare genetic condition with autosomal recessive inheritance[2]. Affected males are born with undervirilization of the external genitals or 46,XY disorder of sexual development (DSD). Individuals with this disorder have impaired virilization during the embryonal period. The wolffian structures exist and are normally differentiated but the appearance of the external genitals may range from normal female to undervirilized male at birth[5]. Children with this condition are usually raised as female and during puberty they develop some male sex characteristics like voice changes and increased muscle mass.

Most cases of this condition are reported from countries with high rates of consanguine marriages like: papua new guina, duminican republic, turkey and lebenon[3]. The prevalence of this condition in the general population is not known[4] and we don't have data about its prevalence in Iran.

Here we report 3 cases of 5α reductase deficiency in a family in Iran. Written informed consent was obtained from the patients or their guardian to publish this report.

Case Report:

A six month old baby was referred to the endocrine clinic of Imam Reza hospital, Mashhad,Iran, because of clitoromegaly and palpation of a mass in the inguinal area. The mother had noticed this mass recently. Because, female external genitalia was present at birth she was assigned as female. She was the second baby of a consanguine marriage (parents were cousins) and the first child was a normal 6 years old boy.

On physical examination, a mass was palpated in the right inguinal area and a blind vaginal pouch was detected.

Ultrasound of the abdomen and pelvis showed that there was no ovaries and uterus. Testis was detected in the left side and also in the right inguinal canal. Chromosomal analysis revealed 46xy pattern. Serum testostrone :15ng/dl, DHT:21pg/ml, FSH:2.8 miu/ml, LH: 2.4ng/dl.

Homozygote mutation of the SRD5A2 was confirmed and a diagnosis 0f 5 alpha reductase deficiency was made. After psychological counseling and because gender identity was not still established she underwent a surgery and hypospadias was corrected, orchiopexy performed and an acceptable male external genital was made for the patient (figure1).

On follow up he is a normal boy with normal physical growth and normal male gender identity and behavior.

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The second case is this patient's aunt who is 35 years old. Third child of a consanguine marriage. She was assigned as female because of the appearance of the external genitals and she went undiagnosed until puberty when she developed clitromegally and increased muscle mass and voice change. Breast development and menarche did not appear. She had been investigated and 5 alpha reductase deficiency confirmed. Patient was counseled but because she was brought up as female, a decision to perform orchidectomy was made and correction surgery of the external genitals was performed. She is now a female with strong physics and acts in contact sports professionally.

The third case of this family is the first patient's mother cousin. He is now 27 years old. He was also assigned as female but with the onset of puberty and appearance of clitromegaly and voice changes he was investigated and a diagnosis of 5 alpha reductase deficiency was made. Psychological counseling was performed and he was sex changed to male. He is now a normal male with normal male behaviors. He has married and has a normal child.

Discussion:

In this report we presented three patients with 5 alpha reductase deficiency who were relatives. Their clinical characteristics were reported and were those typically presented in the literature.

Infants whose external genitals are not typically male or female or their genital appearance is not compatible with their chromosomal sex are considered to have disorder of sex development or DSD[1]. XY DSD occurs due to insufficient androgen action. 5α reductase deficiency is one of the causes of XY DSD. This is a condition with autosomal recessive inheritance[2]. 5α reductase is the enzyme responsible for the conversion of testosterone to dihydrotestostrone (DHT).

Typical clinical feature of this disorder is a 46xy male with female appearance of the external genitals at birth. However, it may present as varying degrees of undervirilization in a male infant.[6,7]. The internal genital structures are male and mullerian structures are absent because anti mullerian hormones do act normally[8]. Most children with this condition are diagnosed at birth due to the atypical appearance of their external genitals but in cases that go underdiagnosed because of the typical female appearance of their genitals, the diagnosis is always made at puberty while the secondary male sexual characteristics like increased muscle mass and voice changes ensue[9].

Biochemical findings that support the diagnosis of 5 α reductase deficiency are that of a normal serum testosterone value and increased ratio of serum testosterone to DHT[10]. Definitive diagnosis is made via DNA mutation analysis[11,12].

Treatment of children with 5 α reductase deficiency depends on many factors. The most important factor is the patient's phenotype and gender assignment at the time of diagnosis[13].

Multidisciplinary team with good expertise in disorders of sex development is needed for the best management of these patients[14]. Issues like sex assignment and psychosocial condition of the patients and their families

must be all considered. Patients who are diagnosed in the newborn period should be raised as male, because with the onset of puberty virilization will occure[15]. For children who are diagnosed later the condition is complex and the choice of sex assignment must be made in consultation with the child and his family[14]. If the decision is made that the child be raised as female then gonadectomy must be performed to minimize the risk of tumors in the testis and also prevent virilisation[16]and the external genitalia should be corrected surgically. Estrogen therapy for the induction of breast development and also prevention of osteoporosis is indicated in these cases.

For subjects who are raised as male or have changed their sex into male, supplemental androgen therapy is needed to improve virilization and phallic growth[17.]

Conclusion:

5 alpha reductase deficiency should be considered in the differential diagnosis of children with 46xy DSD and treatment of these patients is best performed in centers with multidisciplinary teams with expertise in the management of DSDs. with proper management, both scenarios regarding sexual identity can have splendid

outcome as seen in our report

conflicts of interest: none

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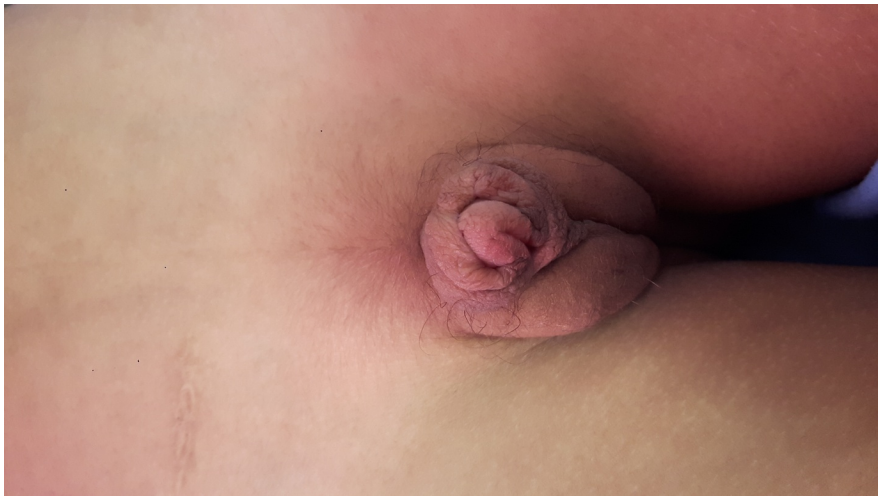
Figure 1. Patient's external genital after reconstruction surgery.



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