Clinical, Laboratory and Molecular Genetic Findings of Patients with 17ß-Hydroxysteroid Dehydrogenase3 Deficiency

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Background: 17ß-Hydroxysteroid Dehydrogenase 3 (17ß-HSD3) deficiency is a rare autosomal recessive disorder, caused by a mutation of the *HSD17B3* gene. The phenotypic spectrum ranges from normal-appearing female external genitalia to microphallus with hypospadias and variable degrees of genital ambiguity. 17ß-HSD3 deficiency phenotype is variable, leading to misdiagnosis especially with partial androgen insensitivity syndrome and 5alfa reductase deficiency.

Aims and Objectives: We aimed to evaluate clinical and laboratory features of ten patients with *HSD17B3* mutations

Methods: Data of 10 46,XY patients with *HSD17B3* mutations were reviewed retrospectively.

Results:

- Ten patients were identified from seven pedigrees
- Range of age at presentation was 0.5-17.3 years
- Only one patient presented in early infancy
- Presenting symptoms were inguinal hernia and masses in 6 patients;hirsutism, primary amenorrhea in 3 patients; hypospadias and cryptorchidism in 1 patient
- All patients were from consanguineous families
- Six of the 9 patients had female appearance of external genitalia and 3 patients had mild cliteromegaly or a prominent clitoris and one patient had penoscrotal hypospadias and cryptorchidism at presentation

- All patients except one were raised as female
- Müllerian structures were absent in all patients
- The median testosterone/androstenedione ratio after a short hCG stimulation test was evaluated in seven patients and the ratio was <0.8 in 6 patients
- Bilateral gonadectomy was performed in all patients reared as female
- The histopathology of the gonads was consistent with testis and spermatic cord and no malignancy was seen

Mutations:

- Five of seven mutations were reported previously
- Two mutations are first time reported in this study

Table 1 Clinical, laboratory, and genetic features of patients with 17β-hydroxysteroid dehydrogenase deficiency

No	Assigned gender	Age at Presentation (yrs)	Presenting symptoms	External genitalia	Testosterone/ Androstenedione	Mutation	Reference	Current Age (yrs)	Follow-up
1	female	6.4	Inguinal masses	female	0.01	Exon 2 c.167C>T p. Ala56 Val	Novel	16.3	Continues in female gender
2	female	8.75	Inguinal masses	female	-	Exon 2 c.182G>A p.Gly61Glu	Known	19.3	Continues in female gender
3	female	6.25	Inguinal hernia and masses	female	-	Exon 2 c.182G>A p.Gly61Glu	Known	17	Continues in female gender
4	female	15.8	Primary amenorhea inguinal mass	female	0.1	Exon 2 c.182G>A p.Gly61Glu	Known	27	Continues in female gender
5	female	17.3	Primary amonerrhea and virilization	female, cliteromegaly	0.12	Exon 9 c.639_640 insA p.E214Rfs*4	Novel	20.4	Continues in female gender
6	female	15.8	Primary amonerrhea	female	-	Exon 9 c.639_640 insA p.E214Rfs*4	Novel	18.2	Continues in female gender
7	male	5	Penoscrotal hypospadias, bilateral inguinal mass	male	8.35	[Exon 1]; [Exon 10] c.[139A>G];[704T>C]	[Known];[Known]	11	Continues in male gender
8	female	3.3	Bilateral inguinal mass	female, mild cliteromegaly	0.08	Intron 3 c.277+4A>T	Known	17.2	Continues in female gender
9	female	3.7	Bilateral inguinal mass	female	0.06	Exon 3 c.277G>A (p.Glu93Lys)	Known	8	Continues in female gender
10	female	0.5	Bilateral inguinal mass	Female, cliteromegaly	0.1	Intron 8 c.607-1G>A	Known	14	Continues in female gender

Conclusions:

- 17ß-HSD3 deficiency presents with a wide spectrum of clinical findings
- Testosterone/androstenedione ratio may be misleading
- Molecular diagnosis is necessary for diagnosis and guides families for genetic counseling.