Phenotypic and genotypic variability of patients with 5-α reductase type 2 deficiency

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Background and Objectives

The steroid 5-**α** reductase type 2 (SRD5A2) enzyme converts testosterone to dihydrotestosterone, which is required for virilisation of the male external genitalia.

5-α reductase type 2 deficiency is a rare inherited disorder affecting genetic males, resulting from mutations in the *SRD5A2* gene, causing 46,XY DSD (Disorder of Sex Development). Therefore a mutated SRD5A2 enzyme results in boys with undervirilised features at birth. If the disorder is not apparent at birth and the child is raised as a girl, the disorder can be picked up later in life during puberty.

We describe the clinical features, investigation results and management of the patients with SRD5A2 deficiency at a regional paediatric endocrine centre.

Method

Retrospective data was collected from the historic medical records of SRD5A2 deficiency patients seen at Birmingham Children's Hospital from 1993 to 2014.

11 patients were identified in total. Medical data was found for 9 of these patients.

Results

The median age of patients presenting before puberty (N=5) was 1 year 1 month.
The median age of patients presenting during puberty (N=4) was 14 years 1 month.

6 patients had a history of consanguinity between parents or a family history of 46,XY DSD. Out of these, 4 patients were found to be from the same family (3 siblings and a cousin).

Karyotype testing confirmed 46 XY in all patients.

Clinical features	Number (n=5)
Micropenis	5
Hypospadias	5
Undescended testes	4
Penoscrotal transposition	2
Ambiguous genitalia	1
Bifid scrotum	1

Figure 1. Summary of clinical features of 5 patients presenting at birth or before puberty

Clinical features	Number (n=3)
Hypospadias	2
Micropenis	2
Palpable testes	2
Voice change	1
Primary amenorrhea	1
No breast development	1
Gynaecomastia	1
Normal vagina	1

Figure 2. Summary of clinical features of patients presenting during puberty

Ultrasound features	Number (n=3)
No uterus	3
No ovaries	3
Testes within enlarged labia	2
Mass in the right inguinal region	1

Figure 3. Summary of abdominal ultrasound results

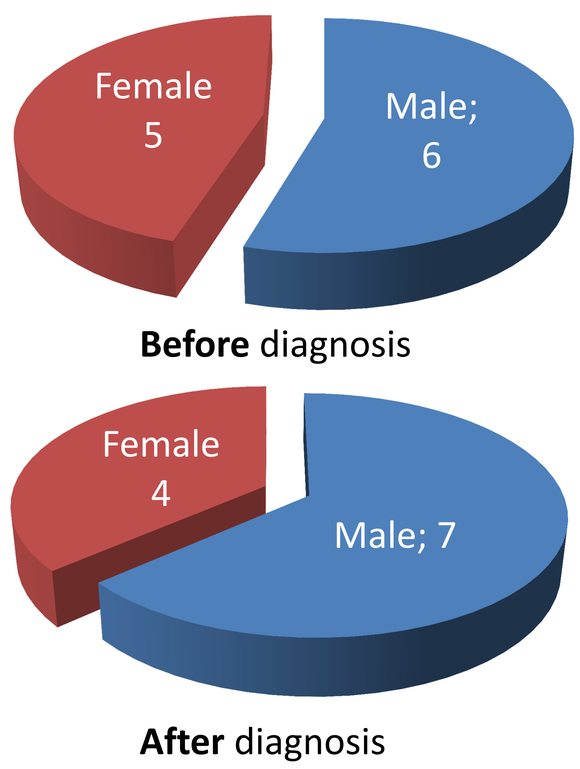

Figure 4. Pie chart showing distribution of chosen genders before and after diagnosis

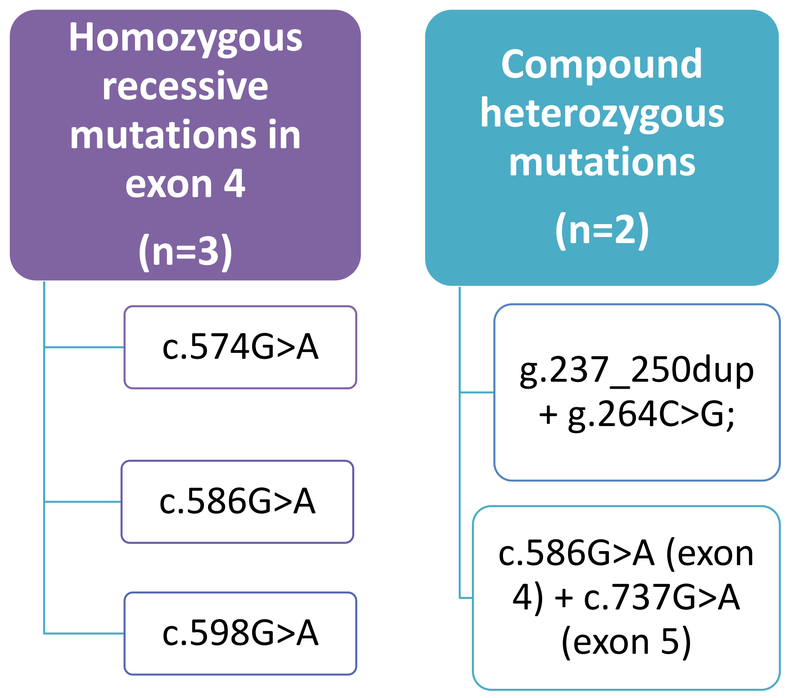

Figure 5. Genotype analysis of 5 patients showing the mutations responsible for abnormal SRD5A2 gene

Management	Number (n=7)
Psychology review	7
Dihydrotestosterone 2.5% gel	5
Hypospadias repair	4
Oestrogen replacement therapy	2
Orchidopexy	1

Figure 6. Summary of management chosen

Conclusion

SRD5A2 deficiency is a heterogeneous condition with regards to its clinical presentation at different ages. We have shown it can be caused by several different mutations in the *SRD5A2* gene; either through homozygous recessive or compound heterozygous mutations.

Our results revealed one of the female patients underwent a change in gender after diagnosis at puberty. They required extensive psychological and medical input during this life changing event. Better understanding of the phenotypic features we have described can facilitate timely diagnosis, management and relevant psychological counselling for future SRD5A2 patients and their families.