INTRODUCTION

- 46, XX Testicular Disorder of Sex Development is characterized by:
  - 46, XX karyotype
  - Normal to ambiguous male external genitalia.
  - 2 testicles.
  - Azoospermia.
  - Absence of Mullerian structures.
  - 80-90% of patients present after puberty with infertility, gynecomastia, and small testes.
  - 10-20% present at birth with genital ambiguity.

CLINICAL PRESENTATION

- 2 month old infant was referred to our Multidisciplinary Urogenital clinic with genital ambiguity.
- Birth history: full term, with no complications, birth weight of 3.4kg.
- Called a boy at birth, genital anomalies noted.
- Antenatal history: non-contributory.
- Family history: non-consanguineous parents, no history of CAH, infertility or genital ambiguity.
- 3 year old brother who is healthy.

PHYSICAL EXAMINATION

- No dysmorphic features or malformations.
- General exam was unremarkable.
- Genital Exam:
  - Well developed scrotum that was brist with rugae and pigmentation.
  - Bilateral testes were palpable in the scrotum, of a normal size and consistency.
  - Phallus size in the normal range, with penile curvature, penoscrotal transposition and penoscrotal hypospadias.

INVESTIGATIONS AT 2 MONTHS

<table>
<thead>
<tr>
<th>TESTS</th>
<th>RESULTS</th>
<th>REF. RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH</td>
<td>1.3 IU/L</td>
<td>(0.1-4.8)</td>
</tr>
<tr>
<td>FSH</td>
<td>2.0 IU/L</td>
<td>(0.15)</td>
</tr>
<tr>
<td>TESTOSTERONE</td>
<td>3.7 nmol/L</td>
<td>&lt; 16.0</td>
</tr>
<tr>
<td>ANDROSTENEDIONE</td>
<td>2.5 nmol/L</td>
<td>(0.2-1.6)</td>
</tr>
<tr>
<td>17-OHP</td>
<td>2.1 nmol/L</td>
<td>(0.0-0.9)</td>
</tr>
<tr>
<td>DHEA-S</td>
<td>1.8 μmol/L</td>
<td>&lt; 4.0</td>
</tr>
</tbody>
</table>

GENETIC TESTING

- US scrotum: Both gonads were 1 x 0.9 x 0.6 cm in size, consistent with testes, no abnormalities seen.

DISCUSSION

- SRY (sex determining region Y) is a transcription factor that regulates testes development.
- SOX (SRY-box) are a family of genes that encode proteins homologous to SRY.
- SOX genes are involved in a wide range of developmental processes including neurogenesis and sexual determination.
- SOX3: located in a highly conserved region on the X chromosomes.
- SOX9: activates testis differentiation pathway.
- SOX3 upregulates SOX9 and initiates Sertoli cell differentiation.
- Transgenic mice overexpressing SOX3 led to frequent XX testicular DSD.
- A cohort of 3/16 patients with SRY(+), 46, XX testicular DSD, rearrangements of SOX3 locus were identified.
- This case strongly emphasize the major role of SOX3 gene in testes determination.

IN CONCLUSION

- 46, XX Testicular Disorder of Sex Development are rare, and can range from normal male external genitalia to ambiguous.
- Following those patients in a multidisciplinary clinic is crucial, to address each aspect of their care.
- The clinical variation in 46XX males can’t be completely explained by the presence and absence of SRY gene.
- Other genetic mutations have been identified in 46XX Testicular DSD (RSP01, SOX9,10, SPFH1, DMRT1, BPEB2, and DAX1).

CLINICAL COURSE

- Underwent 1st stage hypospadias repair at 1 year of age.
- 2nd stage scheduled at 18 months of age.
- Clinically doing well.
- Microarrays for both parents were negative.

CONTACT DETAILS

- FOR FURTHER QUESTIONS OR COMMNETS, FEEL FREE TO CONTACT ME:
  - fahed.aljaser@gmail.com